-----BEGIN PRIVACY-ENHANCED MESSAGE----- Proc-Type: 2001,MIC-CLEAR Originator-Name: webmaster@www.sec.gov Originator-Key-Asymmetric: MFgwCgYEVQgBAQICAf8DSgAwRwJAW2sNKK9AVtBzYZmr6aGjlWyK3XmZv3dTINen TWSM7vrzLADbmYQaionwg5sDW3P6oaM5D3tdezXMm7z1T+B+twIDAQAB MIC-Info: RSA-MD5,RSA, PNdjxXF593OS0LLTM+xxa7P56LiwUKdclwsx9Se6or9uzkxg4NuZxjBlla469DpY 8Mg920M469Sxm0Rdz5/pEA== 0000921895-00-000221.txt : 20000411 0000921895-00-000221.hdr.sgml : 20000411 ACCESSION NUMBER: 0000921895-00-000221 CONFORMED SUBMISSION TYPE: 10-K PUBLIC DOCUMENT COUNT: 4 CONFORMED PERIOD OF REPORT: 19991231 FILED AS OF DATE: 20000329 FILER: COMPANY DATA: COMPANY CONFORMED NAME: SHEFFIELD PHARMACEUTICALS INC CENTRAL INDEX KEY: 0000894158 STANDARD INDUSTRIAL CLASSIFICATION: PHARMACEUTICAL PREPARATIONS [2834] IRS NUMBER: 133808303 STATE OF INCORPORATION: DE FISCAL YEAR END: 1231 FILING VALUES: FORM TYPE: 10-K SEC ACT: SEC FILE NUMBER: 001-12584 FILM NUMBER: 583057 BUSINESS ADDRESS: STREET 1: 425 WOODSMILL RD CITY: ST LOUIS STATE: MO ZIP: 63017 BUSINESS PHONE: 3145799899 MAIL ADDRESS: STREET 1: 425 WOODSMILL RD CITY: ST LOUIS STATE: MO ZIP: 63017 FORMER COMPANY: FORMER CONFORMED NAME: SHEFFIELD MEDICAL TECHNOLOGIES INC DATE OF NAME CHANGE: 19940606
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FORM 10-K

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, 1999
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. / /

The aggregate market value at March 20, 2000 of the voting stock of the registrant held by non-affiliates (based upon the closing price of $6.00 per share of such stock on the American Stock Exchange on such date) was approximately $136,000,000. Solely for the purposes of this calculation, shares held by directors and 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 individuals 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 20, 2000, there were outstanding 27,872,802 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, 1999 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 5, 2000 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

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, lower risk pharmaceutical products that utilize the Company's unique proprietary pulmonary delivery technologies. The Company is in the development stage and, as such, has been principally engaged in the development of its pulmonary delivery systems. The Company and its development partners currently has nine products in various stages of development.

In 1997, the Company acquired the Metered Solution Inhaler ("MSI"), a portable nebulizer-based pulmonary delivery system, through a worldwide exclusive license and supply arrangement with Siemens AG ("Siemens"). During the second half of 1998, the Company acquired the rights to an additional pulmonary delivery technology, the Aerosol Drug Delivery System ("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 Corporation, plc, 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 Group SpA ("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%). 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 by the Company. Zambon has committed to fund the development costs for respiratory compounds delivered by the MSI as well as making certain milestone payments and royalties on net sales resulting from these MSI products to the Company. Initial products for respiratory disease therapy include albuterol, ipratropium, cromolyn and inhaled steroids.

As part of a strategic alliance with Elan, a world leader in pharmaceutical delivery technology, the Company is developing therapies for systemic (non-respiratory) 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(TM) 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"), 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, subject to further agreement with Zambon.

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. In 1998, industry sources estimate there were approximately 35.5 million asthma patients and 49.5 million COPD patients in the world. 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. There is also 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 -- eliminating the side effects usually associated with systemic administration.

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 60 mph -- 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, only 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) interchangeable drug cartridges containing multiple doses of drug in solution 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 interchangeable 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

Through development alliances with strategic partners, Zambon and Elan, 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: The Company initiated a Phase I/II pediatric clinical trial in September 1999 comparing the safety and efficacy of albuterol to the market-leading metered dose inhaler. Sheffield initiated a Phase II clinical trial in December 1999 which will compare the MSI to a conventional albuterol metered dose inhaler. Findings from Phase I/II studies demonstrated that the MSI, when compared to a commercially available metered dose inhaler, delivered comparable amounts of albuterol to the whole lung, significantly reduced oropharyngeal deposition, and achieved equivalent single-dose therapeutic efficacy and tolerability.

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: The Company 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 metered dose inhaler and placebo in patients with COPD. An Investigational New Drug Application ("IND") is being prepared for filing with the Food and Drug Administration ("FDA").

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 metered dose inhaler and nebulizer solution.

Status: An IND is being prepared for filing with the FDA.

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.

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 are expected to 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 developing 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 in discussions with a number of companies for the outlicensing and development 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 deliver less than 20% of the drug to the lungs of the patient. The remaining 80% 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 causes relaxation of the smooth muscles of the gastrointestinal tract that decreases activity of the stomach.

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 and in-vitro trials indicate that up to 50% of drug emitted by the ADDS reaches the lungs with oral deposition reduced to less than 10%. Because of this increase in efficiency, ADDS should require less drug per actuation than existing devices to achieve the same therapeutic effect. This will 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 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 unique features of ADDS are:

Aerosol Flow-Control Chamber. 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) optimize timing of dose discharge with inspiratory breath for maximum drug deposition in lungs.

Synchronizing Trigger Mechanism. 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 dramatic increase in the amount of drug delivered to the lungs. Only small amounts of drug deposit in the mouth and throat. A triggering and timing mechanism that is synchronized with the patient's inspiratory breath control the discharge of the metering valve. ADDS can accommodate different 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 discarded as candidates for aerosol delivery.

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

Improved Drug Delivery Efficiency. The majority of the drug emitted by the ADDS is delivered to the lungs while less than 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 eliminates 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 in the ADDS is ergotamine. 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. 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 in discussions with a number of companies for the

outlicensing and development 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 vastly 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.

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 new joint venture to develop three inhaled steroid products to treat certain respiratory diseases that will utilize Elan's Nanocrystal(TM) dispersion technology and Sheffield's pulmonary delivery systems. Because of the difficulties in formulating steroids for delivery through a solution-based inhalation system, no steroid products are currently available in the United States for delivery through a nebulizer. Elan's Nanocrystal(TM) technology will allow for such a formulation. The estimated worldwide market for inhaled steroids is $2 billion annually and growing at 20% per year. The three products being developed 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, subject to further agreement with Zambon. 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. The Company intends to initiate in-vitro validation testing of UPDAS to confirm Elan's preliminary results and to develop data to support patent filings. A plan for additional development of UPDAS will be prepared based upon the results of this confirmational testing.

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 ("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. The Company intends to complete the in-vitro testing necessary to substantiate the unique absorption properties of the Enhancing Technology that have been identified by Elan. After this work is completed and analyzed, the Company plans to determine the appropriate patent strategy to take and to begin development of the Enhancing Technology for use in the Company's 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 may be 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.

Anti-Proliferative Technologies

The Company holds rights to certain compounds and their uses for the treatment of conditions characterized by unregulated cell proliferation or cell growth and sickle cell anemia. The Company's intellectual property portfolio consists of clotrimazole ("CLT"), its metabolites and a number of proprietary new chemical entities co-owned by the Company termed the Trifens(TM). Such compounds have demonstrated promise in therapeutic applications for treating a number of conditions characterized by unregulated cell proliferation, such as cancer (including multiple drug resistance cases) and certain proliferative dermatological conditions, as well as sickle cell anemia and secretory diarrhea.

The Company entered into a license arrangement with Lorus Therapeutics, Inc. (formerly Imutec Pharma Inc.) in November 1997. 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. The initial IND for the lead compounds is planned to be filed in early 2000.

The Company is actively seeking to partner or license the use of clotrimazole and the Trifens in the fields of sickle cell anemia and gastrointestinal disorders.

RBC-CD4 Electroinsertion Technology

The Company is the worldwide licensee of certain technology (the "RBC-CD4 Electroinsertion Technology") relating to the electroinsertion of full-length CD4 protein into red blood cells for use as a potential therapeutic in the treatment of HIV that leads to AIDS. The Company has signed an option agreement with a private investment group that had a prior interest in the RBC-CD4 Electroinsertion Technology to sell the Company's rights to this HIV/AIDS technology. As consideration for the option, the third party will fund an additional study related to the RBC-CD4 Electroinsertion Technology. If this option is exercised, the Company will retain a one-third interest in all future commercial and sublicensing results.

Liposome-CD4 Technology

The Company is the worldwide licensee of certain technology (the "Liposome-CD4 Technology") relating to the incorporation of CD4 antigens into liposome bilayers and their use as a potential therapeutic agent in the treatment of HIV/AIDS. The Company entered into a sublicense agreement in July 1996 with SEQUUS Pharmaceuticals, Inc. for the continued development and commercialization of the Liposome-CD4 Technology.

HIV/AIDS Vaccine

The Company holds an exclusive worldwide license to a potential HIV/AIDS vaccine and diagnostic test under development at the French Institute of Health and Medical Research. The Company is seeking a partner for this technology.

UGIF Technology - Prostate Cancer

The Company holds an exclusive worldwide license to a growth regulatory factor, termed Urogenital Sinus Derived Growth Inhibitory Factor ("UGIF"), which could serve as a potential prostate cancer therapy. Identification of UGIF as a growth inhibitory factor for certain prostate cells was based upon laboratory studies conducted at Baylor Medical College. The Company is seeking a partner for this technology.

Government Regulation

The Company's research and development activities and, ultimately, the 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 Environmental Protection Agency 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 AG 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, one U.S. patent application is pending, two U.S. provisional applications and five foreign patent applications are pending. They provide protection through 2017 for the MSI device, the dosator cartridges and their combinations.

Aerosol Drug Delivery System Patents

As of the December 31, 1999, two U.S. patents have issued, one notice of allowance has been received, and two U.S. and four foreign applications are pending. The issued and allowed 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 market place 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(TM) 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 20, 2000, the Company employed 15 persons, five of whom are executive officers.

Certain Risk Factors that May Affect Future Results, Financial Condition and Market Price of Securities

Significant Liquidity Restraints; Need for Additional Financing; Uncertainty of Obtaining Additional Funding

The Company's cash available for funding its operations as of December 31, 1999 was $3.9 million. As of such date, the Company had trade payables of $0.8 million and current research obligations of $0.4 million. In addition, committed and/or anticipated funding of research and development after December 31, 1999 is estimated at approximately $4.1 million, of which $4.0 million has been committed to be funded by Elan through the issuance of the Company's Series E Cumulative Convertible Preferred Stock. The Company needs to raise substantial additional capital to fund its operations. The Company intends to seek such additional funding through collaborative or partnering arrangements, the extension of existing arrangements, or through public or private equity or debt financings. There can be no assurance that additional financing will be available on acceptable terms or at all. If additional funds are raised by issuing equity securities, further dilution to shareholders may result. If adequate funds are not available, the Company may be required to delay, reduce the scope of, or eliminate one or more of its research or development programs or obtain funds through arrangements with collaborative partners or others that may require the Company to relinquish rights to certain of its technologies, product candidates or products that the Company would otherwise seek to develop or commercialize. If adequate funds are not available from operations or additional sources of funding, the Company's business will suffer a material adverse effect.

The Company's operations to date have consumed substantial amounts of cash. The negative cash flow from operations is expected to continue in the foreseeable future. The development of the Company's 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. The Company's future capital requirements will depend on many factors, including continued progress in out-licensing the early stage technologies and developing the Company's pulmonary delivery technologies, the ability of the Company 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. The inability of the Company to raise additional funds at the pace dictated by these and other factors, either from operations or additional sources of funding, will result in a material adverse effect on the Company's business.

No Commercialization of Products to Date

The Company has not yet begun to generate revenues from the sale of products. The Company's products will require significant additional development, clinical testing and investment prior to commercialization. The Company does not expect regulatory approval for commercial sales of any of its products in the immediate future. There can be no assurance that such products

will be successfully developed, proven to be safe and efficacious in clinical trials, able to meet applicable regulatory standards, able to obtain required regulatory approvals, or produced in commercial quantities at reasonable costs or be successfully commercialized and marketed.

Royalty Payment Obligations

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

Potential Loss of Rights Upon Default

Under the terms of existing agreements, the Company is obligated to make certain payments to its licensors. In the event that the Company defaults on the payment of an installment under the terms of an existing licensing agreement, its rights thereunder could be forfeited. As a consequence, the Company could lose all rights under a license agreement to the related licensed technology, notwithstanding the total investment made through the date of the default. There can be no assurance that unforeseen obligations or contingencies will not deplete the Company's financial resources and, accordingly, sufficient resources may not be available to fulfill the Company's commitments.

Rapid Technological Change; Competition

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. There can be no assurance that the Company will have a competitive advantage in its fields of technology or in any of the other fields in which the Company may concentrate its efforts.

The Company's success will depend upon its ability to develop and maintain a competitive position in the research, development and commercialization of products and technologies in its 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. There can be no assurance that developments by others will not render the Company's products or technologies obsolete or not commercially viable or that the Company will be able to keep pace with technological developments.

Government Regulation

The Company's 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 the expenditure of substantial resources by the Company. Delays in obtaining FDA approval would adversely affect the marketing of products to which the Company has rights and the Company's 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 the Company's 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. 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. To date, the Company has not received final regulatory approval from the FDA or any other comparable foreign regulatory authority in respect of any product or technology.

Risks Incident to Patent Applications and Rights

The Company's success will depend in part on its ability to obtain patent protection for its 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. There can be no assurance that the Company will develop or receive sublicenses or other rights related to proprietary technology that are patentable, that any patents pending will issue, or that any issued patents will provide the Company with any competitive advantages or will not be challenged by third parties. Furthermore, there can be no assurance that others will not independently duplicate or develop similar products or technologies to those developed by or licensed to the Company. If the Company is required to defend against charges of patent infringement or to protect its own proprietary rights against third parties, substantial costs will be incurred and the Company could lose rights to certain products and technologies.

Reliance on Third Parties; No Marketing or Manufacturing Capabilities

The Company does not currently have its own sales force or an agreement with another pharmaceutical company to market the Company's products that are in development. When appropriate, the Company may build or otherwise acquire the necessary marketing capabilities to promote its products. There can be no assurance that the Company will have the resources available to build or otherwise acquire its own marketing capabilities, or that agreements with other pharmaceutical companies can be reached to market the Company's products on terms acceptable to the Company.

In addition, the Company does not intend to manufacture its own products. While the Company has already entered into two manufacturing and supply agreements related to the MSI system and one related to the ADDS, there can be no assurance that these manufacturing and supply agreements will be adequate or that the Company will be able to enter into future manufacturing and supply agreements on terms acceptable to the Company.

Dependence Upon Obtaining Healthcare Reimbursement

The Company's ability to commercialize human therapeutic and diagnostic products may indirectly 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. There can be no assurance that reimbursement price levels will be sufficient to provide a return to the Company on its investment in new products and technologies.

Adequacy of Product Liability Insurance

The use of the Company's proposed products and processes during testing, and after approval, may entail inherent risks of adverse effects that could expose the Company to product liability claims and associated adverse publicity. Although the Company currently maintains general liability insurance, there can be no assurance that the coverage limits of the Company's insurance policies will be adequate. The Company currently maintains clinical trial product liability insurance of $2.0 million per event for certain clinical trials and intends to obtain insurance for future clinical trials of products under development. There can be no assurance, however, that the Company will be able 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 the Company in excess of the Company's insurance coverage would have a material adverse effect upon the Company and its financial condition. The Company intends to require its licensees to obtain adequate product liability insurance. However, there can be no assurance that licensees will be able to maintain or obtain adequate product liability insurance on acceptable terms or that such insurance will provide adequate coverage against all potential claims.

Potentially Limited Trading Market; Possible Volatility of Stock Price.

The Common Stock is listed for trading on American Stock Exchange (the "AMEX") under the symbol "SHM". The Company does not presently satisfy the listing guidelines of the AMEX, including the AMEX 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. The Company has sustained net losses for its four most recent fiscal years and, at December 31, 1999, had stockholders' equity of $0.7 million. The failure to meet the AMEX listing guidelines may result in the Common Stock no longer being eligible for listing on the AMEX and trading, if any, of the Common Stock would thereafter be conducted in the over-the-counter market. If the Company's Common Stock were to be delisted from the AMEX, it may be more difficult for investors to dispose of, or to obtain accurate quotations as to the market value of the Common Stock.

In the event of the delisting of the Company's Common Stock from the AMEX, the regulations of the Securities and Exchange Commission ("Commission") promulgated under the Securities Exchange Act of 1934, as amended ("Exchange Act"), require additional disclosure relating to the market for penny stocks. Commission 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 the Company's securities become subject to the regulations applicable to penny stocks (i.e., by AMEX delisting), the market liquidity for the Company's securities could be severely affected. In such an event, the regulations on penny stocks could limit the ability of broker-dealers to sell the Company's securities and thus the ability of purchasers of the Company's securities to sell their securities in the secondary market. In the absence of an active trading market, holders of the Common Stock may experience substantial difficulty in selling their securities.

Volatility of Market Price of Securities

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

Authorization of Preferred Stock

The Company's 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 control of the Company and preventing shareholders from receiving a premium for their shares in connection with a change of control. The

Company 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. The Company also issued shares of its Series C Cumulative Convertible Preferred Stock (Series C Preferred Stock") in connection with the consummation of an agreement with Elan in June 1998. In October 1999, in conjunction with a licensing agreement with Elan, the Company issued shares of its Series D Cumulative Convertible Exchangeable Preferred Stock ("Series D Preferred Stock") and Series F Cumulative Convertible Preferred Stock ("Series F Preferred Stock"). In addition, the Company also has a commitment from Elan to purchase shares of its Series E Cumulative Convertible Non-Exchangeable Preferred Stock (Series E Preferred Stock") at the Company's 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, as holder of the outstanding Series C, D and E Preferred Stock, the Company has no present intention to issue any additional shares of its preferred stock; however, there can be no assurance that the Company will not issue additional shares of its preferred stock in the future.

Outstanding Options, Warrants and Convertible Securities; Dilution

As of December 31, 1999, the Company had reserved approximately 7,783,000 shares of its Common Stock for issuance upon exercise of outstanding options and warrants convertible into shares of its Common Stock, including shares of Common Stock issuable upon the exercise of options and warrants held by officers and directors of the Company. In addition, as of December 31, 1999, the Company had $2,000,000 principal amount of a Convertible Promissory Note, 12,780 shares of its Series C Preferred Stock, 12,015 shares of Series D Preferred Stock, and 5,000 shares of Series F Preferred Stock outstanding. Each of the convertible securities provide for conversion into shares of Common Stock of the Company at a discount to the market price at December 31, 1999. The Series C, D and F Preferred Stock are convertible into 9,063,830 shares, 2,472,222 shares, and 1,470,588 shares, respectively, of Common Stock. The Convertible Promissory Note is convertible into 1,142,857 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 shares of the Company's Common Stock and could materially impair the Company's ability to raise capital through the future sale of its 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.

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
1998:		
Fourth Quarter.....	$ 2.500	$ .938
Third Quarter.....	2.500	1.063
Second Quarter.....	2.313	.625
First Quarter.....	1.438	.625

The closing sale price for the Company's Common Stock on the AMEX on March 20, 2000 was $6.00 per share. At March 20, 2000, there were approximately 434 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 1999, the Company issued stock dividends totaling 866 shares of Series C Preferred Stock and cash dividends for fractional shares of $2,277. No dividends were paid or declared during 1999 on the Company's Series D and E Preferred Stock.

The following unregistered securities were issued by the Company during the quarter ended December 31, 1999:

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
~~October 1999~~	~~Common stock warrants~~	~~150,000~~	~~$6.00~~	~~Licensor/Investor pursuant to financing arrangement~~
~~December 1999~~	~~Common stock options~~	~~14,400~~	~~$3.6875~~	~~Employees pursuant to Employee Stock Option Plan~~

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, 1999, 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, 1999, 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 1999 and 1998 is summarized below:

	Three Months Ended			
	Mar 31	Jun 30	Sep 30	Dec 31
	---	---	---	---
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)
1998:				
Total revenues	$ --	$ 350,000	$ --	$ --
Operating loss	(2,221,531)	(13,219,472)	(1,999,198)	(929,170)
Net loss	(2,263,048)	(13,303,121)	(2,142,410)	(851,882)
Basic and diluted net loss per share	(.17)	(.67)	(.08)	(.03)

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, 1999, 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 5, 2000, 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 5, 2000, 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 5, 2000, 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 5, 2000,

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:
Report of Independent Auditors
Consolidated Balance Sheets as of December 31, 1999 and 1998
Consolidated Statements of Operations for the years ended December 31, 1999, 1998 and 1997 and for the period October 17, 1986 (inception) to December, 31 1999
Consolidated Statements of Stockholders' Equity (net capital deficiency) for the period from October 17, 1986 (inception) to December 31, 1999
Consolidated Statements of Cash Flows for the years ended December 31, 1999, 1998 and 1997 and for the period from October 17, 1986 (inception) to December 31, 1999
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)
4.2	Certificate of Designation defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series A Cumulative Convertible Redeemable Preferred Stock	(7)
4.3	Certificate of Designations defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series B Cumulative Convertible Redeemable Preferred Stock	(11)

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)
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.	(16)

NO.	REFERENCE	
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.	(16)
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.	(16)
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	(15)
10.6.6	Employment Agreement dated as of November 17, 1997 between the Company and Judy Roeske-Bullock	(14)
10.7	Agreement of Sublease dated as of November 17, 1995 between the Company and Brumbaugh Graves Donohue & Raymond relating to 30 Rockefeller Plaza, Suite 4515, New York, New York	(2)
10.8	1993 Stock Option Plan, as amended	(15)
10.9	1993 Restricted Stock Plan, as amended	(2)
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 Exchange Act of 1934, as amended). (9)

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 (13)

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).

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)

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)

NO. REFERENCE

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). (16)

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 (16)

	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).	
10.27	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).	(16)
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 Exchange Act of 1934, as amended).	(16)
10.29	Registration Rights Agreement dated as of October 18, 1999 by and between Elan and the Company.	(16)
13	Portions of the Company's Annual Report to Stockholders for the year ended December 31, 1999 relating to Items 6, 7 and 8.	(1)
21	Subsidiaries of Registrant	(1)
23.1	Consent of Ernst & Young LLP	(1)
27	Financial Data Schedule	(1)

- ----------

(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, 1997 filed with the Securities and Exchange Commission.
(15) 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.
(16) Incorporated by reference to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 2, 1999.

(b) Reports on Form 8-K

(1) Current Report on Form 8-K filed with Securities and Exchange Commission on October 22, 1999.

(2) Current Report on Form 8-K with the Securities and Exchange Commission on November 2, 1999.

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 27, 2000 /S/ Loren G. Peterson

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 - ---------- Thomas M. Fitzgerald	Chairman and Director	March 27, 2000
/S/ Loren G. Peterson - ---------- Loren G. Peterson	Director, President and Chief Executive Officer	March 27, 2000
/S/ John M. Bailey - ---------- John M. Bailey	Director	March 27, 2000
/S/ Digby W. Barrios - ---------- Digby W. Barrios	Director	March 27, 2000
/S/ Todd C. Davis - ---------- Todd C. Davis	Director	March 27, 2000
/S/ Scott A. Hoffmann - ---------- Scott A. Hoffmann	Vice President, Chief Financial Officer, Treasurer and Secretary (Chief Financial and Chief Accounting Officer)	March 27, 2000

Sheffield Pharmaceuticals, Inc. Exhibit 13
(a development stage enterprise)

SELECTED FINANCIAL INFORMATION
(In dollars, except per share information)

	Year Ended December 31				
	1999	1998	1997	1996	1995
CONSOLIDATED STATEMENT OF OPERATIONS DATA:					
Revenues:					
Contract research revenue	$ 399,378	$ --	$ --	$ --	$ --
Sublicense revenue	--	350,000	500,000	510,000	--
Total revenues	399,378	350,000	500,000	510,000	--
Operating costs and expenses:					
Acquired research and development in-process technology	15,000,000	13,325,000	1,650,000	--	--
Research and development	3,421,734	2,351,301	3,729,193	3,841,818	4,424,154
General and administrative	2,277,136	3,043,070	4,627,567	3,831,204	2,979,437
Total operating costs and expenses	20,698,870	18,719,371	10,006,760	7,673,022	7,403,591
Loss from operations	(20,299,492)	(18,369,371)	(9,506,760)	(7,163,022)	(7,403,591)
Interest income	91,941	60,273	56,914	163,664	80,610
Interest expense	(162,237)	(251,363)	(39,292)	(9,531)	(64,736)
Minority interest in loss of subsidiary	2,985,000	--	--	--	--
Net loss	$(17,384,788)	$(18,560,461)	$ (9,489,138)	$ (7,008,889)	$ (7,387,717)
Basic and diluted net loss per share	$ (.64)	$ (.85)	$ (.80)	$ (.65)	$ (.90)
Basic and diluted weighted average common shares outstanding	27,236,715	21,931,040	11,976,090	10,806,799	8,185,457
CONSOLIDATED BALANCE SHEET DATA:					
Working capital (net deficiency)	$ 3,344,174	$ 1,456,833	$ (837,564)	$ 1,433,773	$ 1,585,675
Total assets	5,048,655	2,862,521	689,937	2,773,884	2,221,050
Long-term debt & redeemable preferred stock	2,000,000	1,000,000	4,019,263	27,206	--
Accumulated deficit	(73,409,828)	(55,156,763)	(36,157,290)	(26,588,652)	(19,579,763)
Stockholders' equity (net capital deficiency)	671,073	655,205	(4,716,751)	1,695,837	1,792,363

No cash dividends have been paid on Common Stock for any of the periods presented.

Loss per share is based upon the weighted average number of common and certain common equivalent shares outstanding.

See consolidated financial statements and accompanying footnotes.

Sheffield Pharmaceuticals, Inc.
(a development stage enterprise)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion 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, including without limitation, risks set forth in Part I of the Company's Form 10-K for the year ended December 31, 1999.

The discussion and analysis below should be read in conjunction with the Financial Statements of the Company and the related Notes to Financial Statements included on pages 7 - 18 in this Annual Report.

Overview

Sheffield Pharmaceuticals, Inc. ("Sheffield" or the "Company") is a specialty pharmaceutical company focused on development and commercialization of later stage, lower risk pharmaceutical products that utilize the Company's unique proprietary pulmonary delivery technologies. Through its alliances with Elan Corporation, plc ("Elan"), Zambon Group SpA ("Zambon"), and Siemens AG ("Siemens"), Sheffield is currently developing nine respiratory and non-respiratory therapies to be delivered through its proprietary Metered Solution Inhaler ("MSI") and Aerosol Drug Delivery System ("ADDS") to address unmet market needs.

The consolidated financial statements include the accounts of Sheffield and its wholly owned subsidiaries, Systemic Pulmonary Delivery, Ltd. ("SPD"), Ion Pharmaceuticals, Inc., and CP Pharmaceuticals, Inc., and its 80.1% owned subsidiary Respiratory Steroid Delivery, Ltd. ("RSD").

The Company is in the development stage and to date has been principally engaged in research, development and licensing efforts. The Company has generated minimal operating revenue and will require additional capital which the Company intends to obtain through out-licensing as well as through equity and debt offerings to continue to operate its business. Even if the Company is able to successfully develop new products, there can be no assurance that the Company will generate sufficient revenues from the sale or licensing of such products to be profitable.

In October 1999, Elan International Services, Ltd. ("Elan

International"), an affiliate of Elan, and the Company formed a new joint venture, RSD, to develop certain respiratory steroid products. Under the terms of the agreement, the Company issued to Elan International 12,015 shares of Series D Cumulative Convertible Exchangeable Preferred Stock ("Series D Preferred Stock"), for $12.015 million. In turn, the Company made an equity investment of $12.015 million representing an initial 80.1% ownership in RSD. RSD paid $15.0 million to license certain pulmonary NanoCrystal(TM) technology from Elan Pharmaceutical Technologies, a division of Elan. Elan International has also committed to purchase, on a drawdown basis, up to an additional $4.0 million of the Company's Series E Cumulative Convertible Preferred Stock ("Series E Preferred Stock"). The Series E Preferred Stock will be utilized by the Company to fund its portion of RSD's operating and development costs. In addition to the above, the Company issued to Elan International 5,000 shares of Series F Convertible Non-Exchangeable Preferred Stock ("Series F Preferred Stock"), for $5.0 million. The proceeds of the Series F Preferred Stock will be utilized by Sheffield for its own operating purposes.

In June 1998, the Company and Elan International formed a joint venture, SPD, to develop certain systemic applications for use in the Company's pulmonary technologies. The Company issued 5.6 million shares of Common Stock and 11,500 shares of Series C Cumulative Convertible Preferred Stock ("Series C Preferred Stock") for $17.5 million. In turn, the Company made an equity investment of $17.5 million in SPD, representing a 100% ownership interest. Under the terms of the agreement, SPD acquired the Ultrasonic Pulmonary Drug Absorption System and the Absorption Enhancing Technology from Elan for $12.5 million. SPD is responsible for the development of these technologies. Elan agreed to make available to the Company an additional $2.0 million in funding in the form of a convertible note, at the option of the Company. In July 1998, SPD acquired from Aeroquip Corporation, the ADDS, a new generation metered dose inhaler for $825,000. SPD holds the rights to all systemic disease applications of the ADDS technology. Sheffield retained the rights to develop respiratory disease applications of the ADDS.

In June 1998, the Company entered into an agreement with Zambon for a sublicense to the Company's proprietary MSI drug delivery system. Zambon received an exclusive world-wide marketing and development sublicense for respiratory products to be delivered by the MSI including four drugs previously under development by Sheffield. Sheffield retained certain co-promotion rights in the U.S. for respiratory drugs as well as the worldwide marketing and development rights for all applications of the MSI delivery system outside the respiratory therapeutic area. As part of this transaction, Zambon agreed to fund all remaining development costs relating to these respiratory products, paid the Company an up-front fee of $2.15 million in the form of an equity investment of 2.6 million shares of Common Stock, and will pay the Company milestone payments upon marketing approval for each of the four products and royalties upon commercialization. In addition, Zambon has committed to provide Sheffield with an interest-free line of credit upon the achievement of certain technical milestones.

Results of Operations

Revenue

Contract research revenue was $399,378 for the year ended December 31, 1999. There were no contract research revenues in 1998 and 1997. The 1999 contract research revenues primarily represent revenue earned from a collaborative research agreement with Zambon relating to the development of respiratory applications of the MSI. Costs of contract research revenue approximate such revenue and are included in research and development expenses on the consolidated statement of operations. Future contract research revenues and expenses are anticipated to fluctuate depending, in part, upon the success of current clinical studies, and obtaining additional collaborative agreements.

Sublicense revenue of $350,000 for the year ended December 31, 1998 relates to a sublicense agreement entered into during 1997 with Lorus Therapeutics, Inc. (formerly Imutec Pharma Inc.) ("Lorus"). The agreement licensed 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 will provide funding and management of the development program. The Company received $500,000 in cash upon signing the agreement in 1997 and received 583,188 shares of Lorus stock with a value of $350,000 in 1998. At December 31, 1999 the Company's investment in Lorus had a market value of $519,387. There were no such sublicense revenues in 1999.

Acquisition of Research & Development In-Process Technology

Acquisition of research and development in-process technology for the years ended December 31, 1999, 1998 and 1997 was $15.0 million, $13.3 million, and $1.7 million, respectively. In 1999, the Company licensed certain pulmonary NanoCrystal(TM) technology from Elan for $15.0 million. This entire payment was expensed as the license agreement restricts the Company's use of the NanoCrystal(TM) technology to certain respiratory steroid products that are currently research and development projects. In 1998, the Company acquired the ADDS from Aeroquip Corporation for $825,000 and certain pulmonary delivery technologies from Elan for $12.5 million. The 1997 amount is attributable to the acquisition of Camelot Pharmacal, LLC, a specialty pharmaceutical company. The 1998 and 1997 acquisitions were expensed in the year acquired since the technologies had not demonstrated technological feasibility and had no alternative future uses.

Research and Development

Research and development expenses were $3.4 million for the year ended December 31, 1999 compared to $2.4 million and $3.7 million for the years ended December 31, 1998 and 1997, respectively. The increase of $1.0 million from 1998 to 1999 is due to modifications being made to the MSI to enhance its commercial appeal prior to the start of Phase III MSI-albuterol clinical trials, and with work associated with the development of a therapy for breakthrough pain delivered through the MSI, as well as a migraine therapy delivered through the ADDS. These increases were partially offset by the shifting of responsibility for development expenses of the respiratory applications of the MSI to the Company's partner, Zambon. The decrease of $1.3 million from 1997 to 1998 reflects both the Company's shifting of responsibility for development expenses of the respiratory applications of the MSI to Zambon and continued winding down of its early stage research projects. This decrease was partially offset by development costs associated with the ADDS technology acquired in July 1998.

General and Administrative Expenses

General and administrative expenses were $2.3 million for the year ended December 31, 1999 compared to $3.0 million and $4.6 million for the years ended December 31, 1998 and 1997, respectively. The decrease of $0.7 million from 1998 to 1999 was primarily attributable to indirect costs associated with completing both the 1998 Zambon and Elan agreements. In addition, the decrease between years resulted from 1998 costs associated with both the retention of the Company's former investor relations firm and settlement of a dispute with the innovator of one of the Company's early stage research projects. The decrease from 1997 to 1998 of $1.6 million was due to lower compensation expense reflecting fewer employees during 1998 and the extension of certain option and warrant agreements in 1997. The 1998 decrease also reflects lower consulting costs resulting from indirect expenses associated with two financings completed in 1997, and a loss realized on the sale of securities during 1997.

Interest

Interest income was $91,941 for the year ended December 31, 1999 as compared to $60,273 and $56,914 for the years ended December 31, 1998 and 1997, respectively. The $31,668 increase in interest income in 1999 from 1998 was primarily due to larger balances of cash available for investment.

Interest expense was $162,237 for the year ended December 31, 1999 as compared to $251,363 and $39,292 for the years ended December 31, 1998 and 1997, respectively. The decrease of $89,126 in 1999 as compared to 1998 primarily reflects the 1998 conversion of the Company's Series A Cumulative Convertible Preferred Stock and 6% Convertible Subordinated Debentures into Common Stock, partially offset by higher outstanding balances of a convertible promissory note with Elan. The increase of $212,071 in 1998 as compared to 1997 was primarily due to interest paid on the Company's Series B Cumulative Convertible Redeemable Preferred Stock ("Series B Preferred Stock") and a convertible promissory note issued to Elan, both of which were originally issued in 1998.

Minority Interest in Subsidiary

Minority interest in loss of subsidiary was $2.985 million for the year ended December 31, 1999. RSD, a consolidated and 80.1% owned subsidiary of the Company, incurred a loss of $15.0 million in 1999 resulting from the license of certain pulmonary NanoCrystal(TM) technology from Elan. The minority interest in loss of subsidiary represents Elan's portion, or 19.9%, of RSD's 1999 losses. Elan's investment in RSD, shown as minority interest in subsidiary on the consolidated balance sheets, was $0 at December 31, 1999.

Liquidity and Capital Resources

At December 31, 1999, the Company had $3.9 million in cash and cash equivalents compared to $2.5 million at December 31, 1998. The increase of $1.4 million reflects $16.7 million in net proceeds from the issuance of the Company's Series D and Series F Preferred Stock and proceeds from the issuance of a convertible promissory note to Elan of $1.0 million. These increases were

partially offset by $16.1 million of cash disbursements used primarily to fund operating activities, including a $15.0 million license fee paid to Elan as part of the 1999 inhaled steroid development agreement, partially offset by the receipt of a $1.0 million interest-free advance against future milestone payments from Zambon.

In October 1999, as part of a licensing agreement with Elan, the Company received gross proceeds of $17.0 million related to the issuance to Elan of 12,015 shares of Series D Preferred Stock and 5,000 shares of Series F Preferred Stock. In turn, the Company made an equity investment of $12.015 million in a joint venture, RSD, representing an initial 80.1% ownership. The remaining proceeds from the above-mentioned preferred stock issuance will be utilized for general operating purposes. As part of the agreement, Elan has also committed to purchase, on a drawdown basis, up to an additional $4.0 million of the Company's Series E Preferred Stock. The proceeds from the Series E Preferred Stock will be utilized by the Company to fund its portion of RSD's operating and development costs.

In May 1999, in conjunction with the completion of its Phase I/II MSI-albuterol trial, Zambon provided the Company with a $1.0 million interest-free advance against future milestone payments. Upon the attainment of certain future milestones, the Company will recognize this advance as revenue. If the Company does not achieve these future milestones, the advance must be repaid in quarterly installments of $250,000 commencing January 1, 2002. The proceeds from this advance are not restricted as to their use by the Company. Upon the achievement of certain other technical milestones, Zambon will provide an additional $1.0 million advance under the terms of the agreement.

On April 15, 1998, the Company issued 1,250 shares of its Series B Preferred Stock in a private placement for an aggregate purchase price of $1.25 million. The proceeds were used to make a payment to Siemens pursuant to the MSI license agreement. During 1998, the Company entered into a sublicense agreement with Zambon that provided the Company $2.15 million in gross proceeds from the sale of 2.6 million shares of Common Stock. The Company also entered into an agreement with Elan that provided the Company approximately $17.5 million of gross proceeds from the sale of 4.6 million shares of Common Stock and 11,500 shares of the Company's Series C Preferred Stock. The proceeds from the Elan transaction were used to purchase certain pulmonary device delivery technologies from Elan for $12.5 million, the ADDS for $825,000 from Aeroquip Corporation, and to redeem $1.25 million principal amount of Series B Preferred Stock. The remaining proceeds from the Elan transaction were used for research and development, working capital and general corporate purposes. Also, as part of the 1998 Elan agreement, Elan agreed to make available to the Company a convertible promissory note that provides the Company the right to borrow up to $2.0 million, subject to satisfying certain conditions. No more than $0.5 million may be drawn under the note in any calendar quarter and at least one-half of the proceeds must be used to fund SPD's development activities. As of December 31, 1999, $2.0 million was outstanding under this note.

Since its inception, the Company has financed its operations

primarily through the sale of securities and convertible debentures, from which it raised an aggregate of approximately $70.7 million through December 31, 1999, of which approximately $30.0 million has been spent to acquire certain in-process research and development technologies, and $24.7 million has been incurred to fund certain ongoing technology research projects. The Company expects to incur additional costs in the future, including costs relating to its ongoing research and development activities, and preclinical and clinical testing of its product candidates. The Company may also bear considerable costs in connection with filing, prosecuting, defending and/or enforcing its patent and other intellectual property claims. Therefore, the Company will need substantial additional capital before it will recognize significant cash flow from operations, which is contingent on the successful commercialization of the Company's technologies. There can be no assurance that any of the technologies to which the Company currently has or may acquire rights can or will be commercialized or that any revenues generated from such commercialization will be sufficient to fund existing and future research and development activities.

Because the Company does not expect to generate significant cash flows from operations for at least the next few years, the Company believes it will require additional funds to meet future costs. The Company will attempt to meet its capital requirements with existing cash balances and through additional public or private offerings of its securities, debt financing, and collaboration and licensing arrangements with other companies. There can be no assurance that the Company will be able to obtain such additional funds or enter into such collaborative and licensing arrangements on terms favorable to the Company, if at all. The Company's development programs may be curtailed if future financings are not completed.

While the Company does not believe that inflation has had a material impact on its results of operations, there can be no assurance that inflation in the future will not impact financial markets which, in turn, may adversely affect the Company's valuation of its securities and, consequently, its ability to raise additional capital, either through equity or debt instruments, or any off-balance sheet refinancing arrangements, such as collaboration and licensing agreements with other companies.

Year 2000 Compliance

The inability of computers, software and other equipment utilizing microprocessors to recognize and properly process data fields containing a two-digit year is commonly referred to as the Year 2000 compliance issue. Such systems that are not Year 2000 compliant may not have been able to properly interpret dates beyond the Year 1999, which may have led to business disruptions in the U.S. and internationally. The potential costs and uncertainties associated with the Year 2000 issue depended on a number of factors, including software, hardware and the nature of the industry in which a company operates. Additionally, companies had to coordinate with other entities with which they electronically interact, such as customers, creditors and borrowers.

During 1998, the Company conducted an assessment of its computer systems to identify systems that could be affected by the Year 2000 issue. All identified systems that could have potentially been affected by the turnover to the Year 2000 were tested. During the second quarter of 1999, all noncompliant internal software and hardware were replaced or upgraded to reach compliance. To date, the Company has experienced no adverse effect on its internal software and hardware by the Year 2000 turnover.

The Company relies on several universities and independent laboratories (collectively, "CROs") for conducting a significant portion of the research and development of its technologies and products. In addition, the Company relies on its strategic alliance partners to perform certain manufacturing, research and development activities related to its products in development. To date, the Company has experienced no adverse effect from computer failures of any of its CROs on which the Company relies. However, there can be no assurance that if these CROs and/or strategic alliance partners (or their significant vendors) were to experience future computer failures related to the Year 2000 turnover, these failures would not have a material adverse effect on the Company's business, including the possibility of material delays in the progress of clinical trials, product development and future receipt of product sales and related royalties.

Given the lack of legacy systems at the Company, the limited number of issues that have arisen to date, and the level of development activity, the Company has not developed a formal contingency plan for its worse case scenario. While the Company does not anticipate that its worst case scenario will occur, in the event that any of its major CROs or strategic alliance partners suffer material Year 2000 disruptions that negatively impact the Company, the Company will evaluate the materiality of the disruptions at that time. Following the completion of any necessary evaluation, the Company will determine whether to delay the related clinical trials or other research and development while corrective efforts are being implemented. Depending on the anticipated period of time it will take to complete such efforts, the Company may consider replacing the applicable CRO with another Year 2000 compliant provider.

The total cost to the Company of these Year 2000 compliance activities was approximately $20,000. The Company does not expect to incur any future significant costs related to these activities.

SHEFFIELD PHARMACEUTICALS, INC. AND SUBSIDIARIES
(a development stage enterprise)
Consolidated Balance Sheets

Assets	December 31, 1999	1998
Current assets:		
Cash and cash equivalents (Note 1)	$ 3,874,437	$ 2,456,290
Marketable equity security (Notes 1 and 8)	519,387	127,774
Prepaid expenses and other current assets	145,237	39,035

Total current assets	4,539,061	2,623,099
Property and equipment (Note 1):		
Laboratory equipment	407,624	317,032
Office equipment	178,797	175,062
Leasehold improvements	15,000	1,323
Total at cost	601,421	493,417
Less accumulated depreciation and amortization	(311,752)	(253,995)
Property and equipment, net	289,669	239,422
Patent costs (Note 1)	204,283	--
Other assets	15,642	--
Total assets	$ 5,048,655	$ 2,862,521
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 773,206	$ 615,138
Sponsored research payable	421,681	449,805
Note payable - related party (Note 9)	--	101,323
Total current liabilities	1,194,887	1,166,266
Convertible promissory note (Note 7)	2,000,000	1,000,000
Unearned revenue (Note 3)	1,000,000	--
Other long-term liabilities	182,695	41,050
Commitments and contingencies	--	--
Total liabilities	4,377,582	2,207,316
Minority interest in subsidiary (Note 1)	--	--
Stockholders' equity (Notes 5 & 6):		
Preferred stock, $.01 par value, authorized 3,000,0000 shares:		
Series C cumulative convertible preferred stock, authorized 23,000 shares; 12,780 and 11,914 shares issued and outstanding at December 31, 1999 and 1998, respectively	128	119
Series D cumulative convertible exchangeable preferred stock, authorized 21,000 shares; 12,015 and no shares issued and outstanding at December 31, 1999 and 1998, respectively	120	--
Series F convertible non-exchangeable preferred stock, 5,000 shares authorized; 5,000 and no shares issued and outstanding at December 31, 1999 and 1998, respectively	50	--
Common stock, $.01 par value, authorized 60,000,000 and 50,000,000 shares at December 31, 1999 and 1998, respectively; issued and outstanding, 27,308,846 and 27,058,419 shares at December 31, 1999 and 1998, respectively	273,088	270,584
Notes receivable in connection with sale of stock	--	(10,000)
Additional paid-in capital	73,638,128	55,773,491
Other comprehensive income (loss)	160,287	(899,336)

Other comprehensive income (loss)	169,387	(222,226)
Deficit accumulated during development stage	(73,409,828)	(55,156,763)
Total stockholders' equity	671,073	655,205
Total liabilities and stockholders' equity	$ 5,048,655	$ 2,862,521

See notes to consolidated financial statements.

SHEFFIELD PHARMACEUTICALS, INC. AND SUBSIDIARIES
(a development stage enterprise)
Consolidated Statements of Operations
For the Years Ended December 31, 1999, 1998 and 1997 and for the Period
from October 17, 1986 (inception) to December 31, 1999

	Years ended December 31,			October 17, 1986 (inception) to December 31,
	1999	1998	1997	1999
Revenues:				
Contract research revenue (Note 1)	$ 399,378	$ --	$ --	$ 399,378
Sublicense revenue (Note 8)	--	350,000	500,000	1,360,000
Total revenues	399,378	350,000	500,000	1,759,378
Expenses:				
Acquisition of research and development in-process technology (Notes 2 & 8)	15,000,000	13,325,000	1,650,000	29,975,000
Research and development	3,421,734	2,351,301	3,729,193	25,025,424
General and administrative	2,277,136	3,043,070	4,627,567	21,842,465
Total expenses	20,698,870	18,719,371	10,006,760	76,842,889
Loss from operations	(20,299,492)	(18,369,371)	(9,506,760)	(75,083,511)
Interest income	91,941	60,273	56,914	606,041
Interest expense	(162,237)	(251,363)	(39,292)	(573,355)
Minority interest in loss of subsidiary (Note 1)	2,985,000	--	--	2,985,000
Loss before extraordinary item	(17,384,788)	(18,560,461)	(9,489,138)	(72,065,825)
Extraordinary item	--	--	--	42,787
Net loss	$(17,384,788)	$(18,560,461)	$ (9,489,138)	$(72,023,038)
Accretion of mandatorily redeemable preferred stock	--	(23,900)	(79,500)	(103,400)
Net loss - attributable to common shares	$(17,384,788)	$(18,584,361)	$ (9,568,638)	$(72,126,438)
Basic and diluted weighted average common shares outstanding (Note 1)	27,236,715	21,931,040	11,976,090	7,917,966
Basic and diluted net loss per share of common stock (Note 1):				
Loss before extraordinary item	$ (.64)	$ (.85)	$ (.80)	$ (9.10)
Extraordinary item	--	--	--	.01
Net loss per share	$ (.64)	$ (.85)	$ (.80)	$ (9.09)

See notes to consolidated financial statements.

SHEFFIELD PHARMACEUTICALS, INC. AND SUBSIDIARIES
(a development stage enterprise)
Consolidated Statements of Stockholders' Equity (Net Capital Deficiency)
For the Period from October 17, 1986 (Inception) to December 31, 1999

	Preferred stock	Common Stock	Notes receivable in connection with sale of stock	Additional paid-in capital	Other comprehen -sive income (loss)
Balance at October 17, 1986	$ --	$ --	$ --	$ --	$ --
Common stock issued	--	11,334,252	--	17,024,469	--
Reincorporation in Delaware at $.01 par value	--	(11,220,369)	--	11,220,369	--
Common stock subscribed	--	--	(110,000)	--	--
Common stock options issued	--	--	--	75,000	--
Comprehensive income (loss):					
Unrealized loss on marketable securities	--	--	--	--	(39,232)
Net loss	--	--	--	--	--
Comprehensive income (loss)	--	--	--	--	--
Balance at December 31, 1996	--	113,883	(110,000)	28,319,838	(39,232)
Issuance of common stock in connection with acquisition of Camelot Pharmacal, LLC	--	6,000	--	1,644,000	--
Common stock issued	--	6,612	37,400	1,041,750	--
Common stock options and warrants issued	--	--	--	165,868	--
Common stock options extended	--	--	--	215,188	--
Accretion of issuance costs for Series A preferred stock	--	--	--	--	--
Comprehensive income (loss):					
Unrealized gain on marketable securities	--	--	--	--	39,232
Net loss	--	--	--	--	--
Comprehensive income (loss)	--	--	--	--	--
Balance at December 31, 1997	--	126,495	(72,600)	31,386,644	--
Common stock issued	--	144,089	62,600	12,472,966	--
Series C preferred stock issued	115	--	--	11,499,885	--
Series C preferred stock dividends	4	--	--	413,996	--
Accretion of issuance costs for Series A preferred stock	--	--	--	--	--
Comprehensive income (loss):					
Unrealized loss on marketable securities	--	--	--	--	(222,226)
Net loss	--	--	--	--	--
Comprehensive income (loss)	--	--	--	--	--
Balance at December 31, 1998	119	270,584	(10,000)	55,773,491	(222,226)
Common stock issued	--	2,504	10,000	89,059	--
Series C preferred stock dividends	9	--	--	865,991	--
Series D preferred stock issued	120	--	--	12,014,880	--

Series F preferred stock issued	50	--	--	4,691,255	--
Common stock warrants issued	--	--	--	203,452	--
Comprehensive income (loss):					
Unrealized gain on marketable securities	--	--	--	--	391,613
Net loss	--	--	--	--	--
Comprehensive income (loss)	--	--	--	--	--
Balance at December 31, 1999	$ 298	$ 273,088	$ --	$73,638,128	$ 169,387

	Deficit accumulated during development stage	Total stockholders' equity (net capital deficiency)
Balance at October 17, 1986	$ --	$ --
Common stock issued	--	28,358,721
Reincorporation in Delaware at $.01 par value	--	--
Common stock subscribed	--	(110,000)
Common stock options issued	--	75,000
Comprehensive income (loss):		
Unrealized loss on marketable securities	--	--
Net loss	(26,588,652)	--
Comprehensive income (loss)	--	(26,627,884)
Balance at December 31, 1996	(26,588,652)	1,695,837
Issuance of common stock in connection with acquisition of Camelot Pharmacal, LLC	--	1,650,000
Common stock issued	--	1,085,762
Common stock options and warrants issued	--	165,868
Common stock options extended	--	215,188
Accretion of issuance costs for Series A preferred stock	(79,500)	(79,500)
Comprehensive income (loss):		
Unrealized gain on marketable securities	--	--
Net loss	(9,489,138)	--
Comprehensive income (loss)	--	(9,449,906)
Balance at December 31, 1997	(36,157,290)	(4,716,751)
Common stock issued	--	12,679,655
Series C preferred stock issued	--	11,500,000
Series C preferred stock dividends	(415,112)	(1,112)
Accretion of issuance costs for Series A preferred stock	(23,900)	(23,900)
Comprehensive income (loss):		
Unrealized loss on marketable securities	--	--
Net loss	(18,560,461)	--
Comprehensive income (loss)	--	(18,782,687)
Balance at December 31, 1998	(55,156,763)	655,205

Common stock issued	--	101,563
Series C preferred stock dividends	(868,277)	(2,277)
Series D preferred stock issued	--	12,015,000
Series F preferred stock issued	--	4,691,305
Common stock warrants issued	--	203,452
Comprehensive income (loss):		
Unrealized gain on marketable securities	--	--
Net loss	(17,384,788)	--
Comprehensive income (loss)	--	(16,993,175)
Balance at December 31, 1999	$(73,409,828)	$ 671,073

See notes to consolidated financial statements.

SHEFFIELD PHARMACEUTICALS, INC. AND SUBSIDIARIES
(a development stage enterprise)
Consolidated Statements of Cash Flows
For the Years Ended December 31, 1999, 1998 and 1997 and
for the Period from October 17, 1986 (Inception) to December 31, 1999

	Years ended December 31,			October 17, 1986 (inception) to December 31,
	1999	1998	1997	1999
Cash flows from operating activities:				
Net loss	$(17,384,788)	$(18,560,461)	$(9,489,138)	$(72,023,038)
Adjustments to reconcile net loss to net cash used by development stage activities:				
Issuance of common stock, stock options/warrants for services	203,452	359,913	381,056	2,485,425
Depreciation and amortization	86,341	68,794	84,584	479,560
Non-cash acquisition of research and development in-process technology	--	--	1,650,000	1,650,000
(Increase) decrease in prepaid expenses & other current assets	(106,202)	8,343	(3,403)	(204,278)
(Increase) decrease in other assets	(219,925)	25,738	14,278	(160,884)
Increase (decrease) in accounts payable and accrued liabilities	154,418	(279,264)	440,817	185,866
(Decrease) increase in sponsored research payable	(28,124)	(20,963)	(109,389)	998,751
Increase in unearned revenue	1,000,000	--	--	1,000,000
Other	151,396	(285,826)	353,790	562,990
Net cash used by development stage activities	(16,143,432)	(18,683,726)	(6,677,405)	(65,025,608)
Cash flows from investing activities:				
Acquisition of laboratory and office equipment, and leasehold improvements	(136,588)	(131,772)	(53,543)	(585,712)
Other	10,000	132,200	160,798	117,998

Other	10,000	152,200	160,798	117,998
Net cash (used) provided by investing activities	(126,588)	428	107,255	(467,714)
Cash flows from financing activities:				
Payments on debt and capital leases	(709,701)	(54,020)	(50,925)	(836,174)
Net proceeds from issuance of:				
Debt	1,600,000	1,150,000	1,750,000	5,050,000
Common stock	--	8,150,000	--	21,418,035
Preferred stock	16,706,305	12,750,000	3,284,812	32,741,117
Proceeds from exercise of warrants/stock options	91,563	--	--	11,493,721
Other	--	(1,250,000)	--	(500,024)
Net cash provided by financing activities	17,688,167	20,745,980	4,983,887	69,366,675
Net increase (decrease) in cash and cash equivalents	1,418,147	2,062,682	(1,586,263)	3,873,353
Cash and cash equivalents at beginning of period	2,456,290	393,608	1,979,871	1,084
Cash and cash equivalents at end of period	$ 3,874,437	$ 2,456,290	$ 393,608	$ 3,874,437
Noncash investing and financing activities:				
Common stock, stock options and warrants issued for services	$ 203,452	$ 359,913	$ 381,056	$ 2,485,425
Common stock redeemed in payment of notes receivable	--	10,400	--	10,400
Acquisition of research and development in-process technology	--	--	1,650,000	1,655,216
Common stock issued for intellectual property rights	--	--	--	866,250
Common stock issued to retire debt	--	--	--	600,000
Common stock issued to redeem convertible securities	--	4,019,263	1,334,105	5,353,368
Securities acquired under sublicense agreement	--	350,000	--	850,000
Equipment acquired under capital lease	--	49,231	--	121,684
Notes payable converted to common stock	--	--	--	749,976
Stock dividends	868,277	596,195	182,352	1,646,824
Supplemental disclosure of cash information: Interest paid	$ 8,919	$ 186,519	$ 10,417	$ 276,320

See notes to consolidated financial statements.

SHEFFIELD PHARMACEUTICALS, INC. AND SUBSIDIARIES
(a development stage enterprise)

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation - 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 stockholders approved the proposal to reincorporate the Company in Delaware, which was effected on June 13, 1995. The Company is focused on the development and commercialization of later stage, lower risk pharmaceutical products that utilize the Company's unique proprietary pulmonary

delivery technologies.

The Company is in the development stage and to date has been principally engaged in research, development and licensing efforts. The Company has generated minimal operating revenue, sustained significant net operating losses, and requires additional capital that the Company intends to obtain through out-licensing as well as through equity and debt offerings to continue to operate its business. Even if the Company is able to successfully develop new products, there can be no assurance that the Company will generate sufficient revenues from the sale or licensing of such products to be profitable.

Principles of Consolidation - The consolidated financial statements include the accounts of Sheffield and its wholly owned subsidiaries, Systemic Pulmonary Delivery, Ltd. ("SPD"), Ion Pharmaceuticals, Inc., and CP Pharmaceuticals, Inc., and its 80.1% owned subsidiary, Respiratory Steroid Delivery, Ltd. ("RSD"). All significant intercompany transactions have been eliminated. Investments in affiliated companies that are 50% owned or less, and where the Company does not exercise control, are accounted for using the equity method.

Use of Estimates - The preparation of the financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Cash Equivalents - The Company considers all highly liquid instruments with original maturities of three months or less to be cash equivalents. Cash and cash equivalents include demand deposits held in banks, interest bearing money market funds, and corporate commercial paper with A1 or P1 short-term ratings.

Marketable Securities - Marketable securities consist of investments that can be readily purchased or sold using established markets. The Company's securities, which are classified as available-for-sale, are carried at market with unrealized gains and losses reported as a separate component of other comprehensive income within stockholders' equity.

Property and Equipment - Property and equipment are stated at cost. Depreciation is computed using the straight-line method over three or five year periods for leasehold improvements and office equipment, and five years for laboratory equipment. Assets under capital leases, consisting of office equipment, are amortized over the lesser of the useful life or the applicable lease terms.

Patent Costs - Costs associated with obtaining patents, principally legal costs and filing fees, are capitalized and being amortized on a straight-line basis over the remaining lives of the respective patents. The Company periodically evaluates the carrying amount of these assets based on current licensing and future commercialization efforts, and if warranted, impairment would be recognized.

Contract Research Revenue - Contract revenue from collaborative research agreements is recorded when earned and as the related costs are incurred. Payments received which are related to future performance are deferred and recognized as revenue in the period in which they are earned.

Research and Development Costs - Research and development costs ("R & D costs") are expensed as incurred, except for fixed assets to which the Company has

title, which are capitalized and depreciated over their estimated useful lives.

Income Taxes - The Company utilizes the liability method to account for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Fair Value of Financial Instruments - The carrying amounts of cash and cash equivalents, accounts payable, sponsored research payable and notes payable approximates fair value.

Basic Net Loss per Share of Common Stock - Basic net loss per share is calculated in accordance with Statement of Financial Accounting Standards ("SFAS") No. 128, Earnings Per Share. Basic net loss per share is based upon the weighted average common stock outstanding during each year. Potentially dilutive securities such as stock options, warrants, convertible debt and preferred stock, have not been included in any years presented as their effect is antidilutive.

Stock-Based Compensation - SFAS No. 123, Accounting for Stock-Based Compensation, defines a fair value method of accounting for stock options and similar equity instruments. As permitted by SFAS 123, the Company continues to account for such transactions under Accounting Principal Board Opinion No. 25, Accounting for Stock Issued to Employees ("APB 25"), and has disclosed in a note to the financial statements pro forma net loss and earnings per share as if the Company had applied the fair value method of accounting for its stock-based awards. Under APB 25, no expense is generally recognized at the time of option grant because the exercise price of the Company's employee stock option equals or exceeds the fair market value of the underlying common stock on the date of grant.

Comprehensive Income (Loss) - Effective January 1, 1998, the Company adopted SFAS No. 130, Reporting Comprehensive Income, which establishes standards for the reporting and display of comprehensive income and its components in a full set of general purpose financial statements and applies to all enterprises. Other comprehensive income or loss shown in the consolidated statements of stockholders' equity at December 31, 1999, 1998 and 1997 is solely comprised of unrealized gains or losses on marketable securities. The unrealized gain on marketable securities during 1997 includes reclassification adjustments of $324,915 for losses realized in income from the sale of the securities.

Segment Information - Effective January 1, 1998, the Company adopted SFAS No. 131, Disclosures about Segments of an Enterprise and Related Information, which establishes standards for the way that public business enterprises report information about operating segments in annual financial statements and requires that those enterprises report selected information about operating segments in interim financial reports. It also establishes standards for related disclosures about products and services, geographic areas and major customers. The Company operates in one reportable segment as defined by SFAS No. 131.

2. ACQUISITION

In April 1997, the Company, through its wholly owned subsidiary, CP Pharmaceuticals, Inc., completed its acquisition of Camelot Pharmacal, LLC ("Camelot"), a Missouri limited liability company, focusing on the development of specialty pharmaceuticals. The purchase price consisted of 600,000 shares of the Company's Common Stock (valued at $2.75 per share) and the assumption of certain liabilities in excess of tangible assets acquired of $8,262 (see Note 5). The transaction was treated as a purchase for accounting purposes, and accordingly, the assets and liabilities assumed have been recorded at their estimated fair market values at the date of acquisition. Since technological feasibility of the in-process research and development costs have not yet been established and the technology had no alternative future use at the acquisition date, the in-process research and development costs of $1,650,000 were immediately written-off and included in the results of operations as a non-recurring charge for the year ended December 31, 1997. Camelot had no revenue and minimal operating losses for the period ended April 24, 1997 and therefore pro forma disclosure has not been included.

3. UNEARNED REVENUE

In May 1999, in conjunction with the completion of the Phase I/II Metered Solution Inhaler ("MSI") albuterol trial, Zambon Group SpA ("Zambon") provided the Company with a $1.0 million interest-free advance against future milestone payments. Upon the attainment of certain future milestones, the Company will recognize this advance as revenue. If the Company does not achieve these future milestones, the advance must be repaid in quarterly installments of $250,000 commencing on January 1, 2002. The proceeds from this advance are not restricted as to their use by the Company (see Note 8).

4. LEASES

The Company leases its office space and certain equipment under noncancelable operating and capital leases that expire at various dates through 2003. At December 31, 1999, assets held under capital leases consisting of office equipment were $31,090, net of accumulated amortization of $18,141. Future minimum lease payments under capital and operating leases at December 31, 1999 are as follows:

	Capital Leases	Operating Leases
2000	$ 9,375	$ 182,411
2001	9,375	135,313
2002	9,375	80,412
2003	774	1,024
Total minimum lease payments	28,899	$ 399,160
Less amount representing interest	(5,692)	
Present value of net minimum lease payments	23,207	
Less current maturities of capital lease obligations	(6,435)	
Capital lease obligations	$ 16,772	

Rent expense relating to operating leases for the years ended December 31, 1999, 1998 and 1997 was $174,332, $143,126, and $190,584, respectively.

5. STOCKHOLDERS' EQUITY

Preferred Stock

In February 1997, 35,700 shares of Series A Cumulative Convertible Preferred Stock ("Series A Preferred Stock") were issued pursuant to a private placement. Holders of Series A Preferred Stock had the right, exercisable commencing May 29, 1997 and ending February 28, 1999, to convert shares of Series A Preferred Stock into shares of Common Stock. The number of shares of Common Stock issuable upon conversion of Series A Preferred Stock was determined by reference to the lesser of (i) $3.31875 and (ii) 85% of the "current market price" per share of Common Stock, where "current market price" means, with certain exceptions, the average of the closing bid prices of Common Stock for the 10 consecutive trading days ending the last trading day before the applicable conversion date. Each share of Series A Preferred Stock earned a cumulative dividend payable in shares of Common Stock at a rate per share equal to 7.0% of the original $100 purchase price per share of the Series A Preferred Stock payable at the time of conversion. As of December 31, 1997, 25,000 shares of Series A Preferred Stock were outstanding. Between August 26, 1997 and December 31, 1997, 10,700 shares of Series A Preferred Stock, plus related accrued dividends, were converted into 44,769 shares of Common Stock. In 1998, the remaining balance of the Company's outstanding Series A Preferred Stock, plus related dividends payable, were converted to Common Stock, resulting in the issuance of 4,075,797 shares of Common Stock.

In April 1998, the Company issued 1,250 shares of its Series B Cumulative Convertible Redeemable Preferred Stock ("Series B Preferred Stock") in a private placement for an aggregate purchase price of $1,250,000. In addition, the holder of Series B Preferred Stock was issued warrants to acquire 300,000 shares of Common Stock at any time up until and including April 15, 2001 for a price of $1.00 per share. Each share of Series B Preferred Stock earned a cumulative dividend payable at a rate per share equal to 6.0% per annum. On July 31, 1998, the Company redeemed all of the Series B Preferred Stock and accrued dividends for cash.

In June 1998, the Company issued 4,571,428 shares of Common Stock and 11,500 shares of Series C Cumulative Convertible Preferred Stock ("Series C Preferred Stock"), convertible into shares of Common Stock of the Company or of its wholly owned subsidiary, SPD, for $17.5 million pursuant to a definitive agreement with an affiliate of Elan Corporation, plc ("Elan"), Elan International Services, Ltd. ("Elan International"). The Series C Preferred Stock earns cumulative dividends payable in shares of Series C Preferred Stock at an annual rate of 7.0% on the stated value of each outstanding share of Series C Preferred Stock on the dividend date. Elan International also received a warrant to purchase 990,000 shares of Common Stock of the Company exercisable from December 31, 1998 through January 30, 2005 at an exercise price of $2.00 per share. Under the terms of the agreement, the Company, through SPD, acquired certain pulmonary delivery technologies for the sum of $12.5 million in cash (see Note 8). All of the outstanding Common Stock of SPD is pledged to Elan during the term of the agreement. Subject to certain conditions and the making of certain payments to the Company, Elan International has the option to acquire all or a portion of the outstanding stock of SPD. The net book value of SPD is $0.2 million as of December 31, 1999. The Company issued stock dividends totaling 866 and 414 shares of Series C Preferred Stock and cash dividends for fractional shares of $2,278 and $1,112 for the years ended December 31, 1999 and 1998, respectively.

In October 1999, pursuant to a definitive agreement, the Company and Elan International formed a new joint venture to develop certain respiratory steroid products. Under the terms of the agreement, the Company issued to Elan International 12,015 shares of Series D Cumulative Convertible Exchangeable Preferred Stock ("Series D Preferred Stock"), convertible into shares of Common Stock of the Company at $4.86 per Common Share or exchangeable for an additional 30.1% ownership interest in the new joint venture, for $12.015 million. The Series D Preferred Stock earns cumulative dividends payable in shares of Series D Preferred Stock at an annual rate of 7.0% on the stated value of each outstanding share of Series D Preferred Stock on the dividend date. Elan International has also committed to purchase, on a drawdown basis, up to an additional $4.0 million of the Company's Series E Cumulative Convertible Preferred Stock ("Series E Preferred Stock"), convertible into shares of Common Stock of the Company at $3.89 per Common Share. The Series E Preferred Stock will be utilized by the Company to fund its portion of the joint venture's operating and development costs. The Series E Preferred Stock earns cumulative dividends payable in shares of Series E Preferred Stock at an annual rate of 9.0% on the stated value of each outstanding share of Series E Preferred Stock on the dividend date. In addition to the above, the Company issued to Elan

International 5,000 shares of Series F Convertible Non-Exchangeable Preferred Stock ("Series F Preferred Stock"), convertible into shares of Common Stock of the Company at $3.40 per Common Share, for $5.0 million. The proceeds of the Series F Preferred Stock will be utilized by Sheffield for its own operating purposes. The holders of the Series F Preferred Stock may be entitled to receive dividends on a pari passu basis with the holders of Common Stock. As part of the transaction, Elan International also received a warrant to purchase 150,000 shares of Common Stock of the Company at an exercise price of $6.00 per share (see Note 8).

Common Stock

In April 1997, Camelot merged with and into CP Pharmaceuticals, Inc., a newly formed wholly owned subsidiary of the Company. The principals of Camelot at the time of the merger were Loren G. Peterson, Carl F. Siekmann and David A. Byron. Pursuant to the related agreement and plan of merger, Messrs. Peterson, Siekmann and Byron each received 200,000 shares of Common Stock. Following the consummation of the merger, each of Messrs. Peterson, Siekmann and Byron entered into employment agreements with Sheffield and received stock options providing each individual the right to purchase up to 400,000 shares of Common Stock (see Note 2).

During 1998, the Company entered into an agreement with Zambon for a sublicense to the Company's proprietary MSI drug delivery system (see Note 8). Pursuant to an option agreement dated April 15, 1998, the Company issued 800,000 shares of Common Stock for $650,000 in cash. On June 15, 1998, the Company entered into the definitive agreement, resulting in the issuance of an additional 1,846,153 shares of Common Stock for $1.5 million.

In June 1999, the stockholders of Sheffield approved an amendment to the Company's Certificate of Incorporation to increase the number of shares of Common Stock that the Company is authorized to issue from 50 million shares to 60 million shares.

Convertible Subordinated Debentures

In September 1997, the Company consummated a private placement of $1.75 million principal amount of its 6.0% Convertible Subordinated Debentures ("Debentures") due September 22, 2000. In addition, the Company granted the holder of the Debenture warrants to purchase 140,000 shares of the Company's Common Stock at $2.80 per share. A value of $115,500 was assigned to these warrants. The Debentures are convertible at the option of the holder from December 22, 1997 until maturity, subject to certain limitations, into a number of shares of Common Stock equal to (i) the principal amount of the Debenture being so converted divided by (ii) 75% of the market price of the Common Stock as of the date of conversion. For purposes of any conversion of Debentures, "market price" generally means the average of the closing prices of the Common Stock for the five trading day period proceeding the applicable conversion date. The Debentures also earn interest at a rate of 6.0% per annum that is payable by the Company, at the option of the holder and subject to certain conditions, in shares of its Common Stock at a conversion rate generally equal to the average of the closing prices of the Common Stock for the ten trading days preceding the applicable interest payment date. During 1998, the Debentures were converted to Common Stock resulting in the issuance of 2,925,941 shares of Common Stock.

6. STOCK OPTIONS AND WARRANTS

Stock Option Plan - The 1993 Stock Option Plan (the "Option Plan") was adopted by the Board of Directors in August 1992 and approved by the stockholders at the annual meeting in December 1993. An amendment to the Option Plan increasing the number of shares of Common Stock available for issuance thereunder from 3 million shares to 4 million shares received stockholder approval on July 15, 1998. The Option Plan permits the grant to employees and officers of the Company of both incentive stock options and non-statutory stock options. The Option Plan is administered by the Board of Directors or a committee of the Board, which determines the persons to whom options will be granted and the terms thereof, including the exercise price, the number of shares subject to each option, and the exercisability of each option. The exercise price of all options for Common Stock granted under the Option Plan must be at least equal to the fair market value on the date of grant in the case of incentive stock options, and 85% of the fair market value on the date of grant in the case of non-statutory stock options. Options generally expire five to ten years from the date of grant and vest either over time or upon the Company's Common Stock attaining a set market price for a certain number of trading days. As of December 31, 1999, options available for grant under the Option Plan are 1,528,600.

Restricted Stock Plan - The 1993 Restricted Stock Plan (the "Restricted Plan") was adopted by the Board of Directors in August 1992 and approved by the stockholders at the annual meeting in December 1993. The Restricted Plan authorized the grant of a maximum of 150,000 shares of Common Stock to key employees, consultants, researchers and members of the Company's Scientific Advisory Board. The Restricted Plan is administered by the Board of Directors or a committee of the Board, which determines the person to whom shares will be granted and the terms of such share grants. As of December 31, 1999, no shares have been granted under the Restricted Plan.

Directors Stock Option Plan - The 1996 Directors Stock Option Plan (the "Directors Plan") was adopted by the Board of Directors and approved by the stockholders on June 20, 1996. Under the Directors Plan, the maximum aggregate number of shares which may be optioned and sold is 500,000 shares of Common Stock. The Directors Plan initially granted each eligible director 15,000 stock options. To the extent that shares remain available, any new directors shall receive the grant of an option to purchase 25,000 shares. To the extent that shares remain available under the Directors Plan, on January 1 of each year commencing January 1, 1997, each eligible director shall be granted an option to purchase 15,000 shares. The exercise price of all options granted under the Directors Plan shall be the fair market value at the date of the grant. Options generally expire five years from the date of grant. As of December 31, 1999, there are 260,000 options available for grant under the Directors Plan.

SFAS No. 123 requires pro forma information regarding net income and earnings per share as if the Company has accounted for its stock options granted subsequent to December 31, 1994, under the fair value method of SFAS No. 123. The fair value of these stock options is estimated at the date of grant using a Black-Scholes option pricing model with the following weighted average assumptions for 1999, 1998, and 1997, risk-free interest rate ranging from 4.39% to 6.23%; expected volatility ranging from 0.526 and 0.694; expected option life of one to ten years from vesting and an expected dividend yield of 0.0%.

For purposes of pro forma disclosures, the estimated fair value of the stock options is amortized to expense over the options' vesting period. The Company's pro forma information is as follows:

	1999	1998	1997
Pro forma net loss.....	$17,807,124	$18,983,921	$9,500,810
Pro forma basic net loss per share of common stock.....	$.65	$.87	$.79

Transactions involving stock options and warrants are summarized as follows:

	Year Ended December 31,					
	1999		1998		1997	
	Common Stock Options/Warrants	Weighted Average Exercise Price	Common Stock Options/Warrants	Weighted Average Exercise Price	Common Stock Options/Warrants	Weighted Average Exercise Price
Outstanding, January 1	7,910,836	$ 2.55	4,781,290	$ 3.65	3,033,755	$ 4.49
Granted	555,040	2.97	3,162,910	1.81	3,683,039	3.92
Expired	315,422	3.92	283,504	4.48	327,500	3.18
Exercised	367,500	1.07	--	--	--	--
Canceled	--	--	180,500	5.64	1,608,004	4.11
Revalued(1)	--	--	430,640	--	--	--
Outstanding, December 31	7,782,954	$ 2.59	7,910,836	$ 2.55	4,781,290	$ 3.65
Exercisable at end of year	6,358,554	$ 2.51	5,028,336	$ 2.71	2,900,290	$ 3.88

(1) Certain warrants issued by the Company during 1995 contain antidilutive provisions. These warrants total 615,325, and have exercise prices ranging from $4.00 to $5.00 per share. Pursuant to the antidilutive provisions of the warrants, the common shares to be purchased under the warrants were increased to 1,045,965 and the related exercise prices were adjusted to a range of $2.44 to $2.81 per share.

During the period January 1, 1997 through December 31, 1999, the exercise prices and weighted average fair value of options and warrants granted by the Company were as follows:

Year	Number of Options/ Warrants	Weighted Average Exercise Price	Fair Value

1997	3,683,039	$1.50 - 6.00 .	$ 4.05
1998	3,162,910	$1.00 - 3.69 .	$ 0.99
1999	555,040	$0.82 - 6.00 .	$ 1.34

At December 31, 1999, outstanding warrants to purchase the Company's Common Stock are summarized as follows:

Exercise Prices	Range of Outstanding Warrants at December 31, 1999	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price
$0.73 - $2.00	1,737,410	3.98	$1.69
$2.25 - $3.00	1,520,605	.86	$2.58
$3.25 - $6.50	621,539	3.24	$4.16
	3,879,554	2.64	$2.43

At December 31, 1999, outstanding options to purchase the Company's Common Stock are summarized as follows:

Exercise Prices	Range of Outstanding Options at December 31, 1999	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price
$1.24 - $2.75	2,867,000	5.63	$2.34
$3.00 - $4.00	686,400	3.68	$3.51
$4.06 - $6.25	350,000	1.81	$4.59
	3,903,400	4.94	$2.75

7. CONVERTIBLE PROMISSORY NOTE

As part of the 1998 agreement with Elan, Elan agreed to make available to the Company a Convertible Promissory Note ("Note") that provides the Company the right to borrow up to $2.0 million, subject to satisfying certain conditions. No more than $500,000 may be drawn under the Note in any calendar quarter and at least one-half of the proceeds must be used to fund SPD's development activities. The principal outstanding under the Note bears interest at the prime rate plus 1% and, if not previously converted, matures on June 30, 2005. Prior to repayment, Elan has the right to convert all principal and accrued interest into shares of the Company's Common Stock at a conversion price of $1.75 per share. As of December 31, 1999, the outstanding principal balance of the Note was $2.0 million.

8. RESEARCH AND DEVELOPMENT AGREEMENTS

Pulmonary Delivery Technologies

In March 1997, the Company entered into exclusive supply and license agreements for the worldwide rights to the MSI system with Siemens AG ("Siemens"). The agreements call for Siemens to be the exclusive supplier of the MSI drug delivery system. The Company paid licensing fees of $1.1 million in both April 1997 and 1998, to Siemens pursuant to these agreements.

On June 15, 1998, the Company entered into an agreement with Zambon for a sublicense to the Company's MSI system. Under this transaction, Zambon received an exclusive world-wide marketing and development sublicense for respiratory products to be delivered by the MSI system including four drugs that had been under development by the Company. The Company maintained certain co-promotion rights in the U.S. for respiratory drugs as well as the worldwide marketing and development rights for all applications of the MSI delivery system outside the respiratory products. The Company was paid an up-front fee in the form of an equity investment and will receive milestone payments upon marketing approval for each of the four products and royalties upon commercialization (see Note 3).

On June 30, 1998, the Company issued certain equity securities pursuant to an agreement with Elan (see Note 5). Under the terms of the agreement, the Company, through its wholly owned subsidiary, SPD, acquired certain pulmonary delivery technologies from Elan for $12.5 million in cash. On July 15, 1998, SPD acquired from Aeroquip-Vickers, Inc. a new generation metered dose inhaler system called the Aerosol Drug Delivery System ("ADDS") for $825,000. The payments for these technologies were expensed during 1998 as acquired R&D in-process technology since the technologies acquired had not demonstrated technological feasibility and had no alternative future uses. SPD holds the rights to all systemic disease applications of the ADDS technology while Sheffield retains the rights to develop the respiratory disease applications of ADDS. The Company is responsible for the development of these technologies. Pursuant to its agreement with Elan, at December 31, 1999, the Company was committed to fund $98,000 of additional costs related to SPD's systemic development program.

On October 18, 1999, the Company issued certain equity securities pursuant to an agreement with Elan (see Note 5). Under the terms of the agreement, the Company, through its majority owned subsidiary, RSD, licensed certain pulmonary NanoCrystal(TM) technology from Elan for $15.0 million in cash. This payment was expensed as acquired R&D in-process technology as the license agreement restricts the Company's use of the NanoCrystal technology to certain respiratory steroid products that are currently research and development. The subsidiary is responsible for the development of certain respiratory steroid products. Pursuant to its agreement with Elan, at December 31, 1999, the Company was committed to fund $4.0 million to the subsidiary for the development of these products.

Early Stage Technologies

The Company also is party to a number of license and research

agreements, primarily with universities, hospitals, and research facilities, relating to early stage medical research projects that focus on the development of new compounds for the treatment of cancer, acquired immune deficiency syndrome and other diseases. As part of the Company's focus on later stage opportunities, the Company is seeking to out-license these projects. There can be no assurance that the Company will receive license fees or other payments related to these technologies. The Company believes these early stage technology license and research agreements will have no material impact on the financial position of the Company. For the year ended December 31, 1999, the Company funded approximately $2,000 related to these projects.

On November 20, 1997, the Company entered into a sublicense agreement with Lorus Therapeutics, Inc. (formerly Imutec Pharma Inc.) ("Lorus"). The agreement licenses rights to a series of clotrimazole-related compounds for the treatment of cancer, Kaposi's sarcoma and actinic keratosis to a newly formed company, NuChem Pharmaceuticals, Inc. ("NuChem"). In exchange, Lorus agreed to manage and fund the remaining development program. The Company received $500,000 in cash upon signing the agreement, which was recognized as revenue during the year ended December 31, 1997, and received 583,188 shares of Lorus stock valued at $350,000 which was recognized as revenue during the year ended December 31, 1998. In addition, the Company is entitled to receive additional payments upon the completion of certain milestones in the development of these compounds and retains a 20 percent ownership interest in NuChem.

9. RELATED PARTY TRANSACTIONS

During 1998, three executive officers provided funds for use by the Company comprised of short-term notes having a 7.0% annual interest rate, unpaid salaries and unreimbursed expenses. The largest amount outstanding to the executive officers during 1998 was $241,740. All amounts under the short-term notes were repaid in 1998.

During 1998, certain stockholders provided funds for use by the Company comprised of short-term notes totaling $150,000, bearing interest at the rate of 7.0% per annum. On September 8, 1998, the Company repaid principal of $50,000 plus accrued interest. The remaining balance of the short-term notes and accrued interest was repaid on May 12, 1999.

10. INCOME TAXES

At December 31, 1999, the Company had available net operating loss carryforwards for regular federal income tax purposes of approximately $39.4 million, of which $27.5 million will expire between 2007 and 2012, and $11.9 million will expire between 2018 and 2019, if not utilized. Utilization of the Company's net operating loss carryforwards may be subject to an annual limitation as a result of the "changes in ownership" provisions of the Internal Revenue Code Section 382. Future changes in ownership may limit net operating loss carryforwards generated in the year of change.

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant

components of the Company's net deferred tax asset at December 31, 1999 and 1998, which are considered noncurrent, are as follows:

Deferred Tax Assets	1999	1998
Net operating loss carryforwards	$ 14,957,000	$ 12,600,000
Costs capitalized for tax purposes	22,027,000	14,391,000
Deferred tax asset valuation allowance	(36,984,000)	(26,991,000)
Net deferred tax asset	$ --	$ --

The Company has recorded a valuation allowance for the entire deferred tax asset due to the uncertainty of its realization. The net change in the total valuation allowance for the year ended December 31, 1999 was an increase of $9,993,000. As a result of differences between book and tax requirements for writing off intangible assets acquired, such as in-process R & D technology, the Company has capitalized the in-process R & D technology for tax purposes. The deferred tax asset will be amortized into taxable income over a useful life of 15 years.

Report of Independent Auditors

The Board of Directors and Stockholders
Sheffield Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Sheffield Pharmaceuticals, Inc. and subsidiaries (a development stage enterprise) as of December 31, 1999 and 1998, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 1999 and for the period October 17, 1986 (inception) through December 31, 1999. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Sheffield

Pharmaceuticals, Inc. and subsidiaries at December 31, 1999 and 1998, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 1999 and the period from October 17, 1986 (inception) through December 31, 1999, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP
St. Louis, Missouri
March 1, 2000

EX-21
2
SUBSIDIARIES LIST

Exhibit 21

SUBSIDIARIES OF SHEFFIELD PHARMACEUTICALS, INC.

Name	Jurisdiction of Incorporation
1. Ion Pharmaceuticals, Inc. (100% owned subsidiary)	Delaware
2. CP Pharmaceuticals, Inc. (100% owned subsidiary)	Delaware
3. Systemic Pulmonary Delivery, Ltd. (100% owned subsidiary)	Bermuda
4. Respiratory Steroid Delivery, Ltd. (80.1% owned subsidiary)	Bermuda

EX-23.1
3
CONSENT

Consent of Independent Auditors

We consent to the incorporation by reference in the Registration Statements (Form S-3 No. 33-95732, Form S-3 No. 333-27753 and Form S-3 No. 333-38327) of Sheffield Pharmaceuticals, Inc. and in the related Prospectuses, in the Registration Statement (Form S-8 No. 33-95262) pertaining to the 1993 Stock Option Plan of Sheffield Pharmaceuticals, Inc., the 1993 Restricted Stock Plan of Sheffield Pharmaceuticals, Inc. and options granted to directors, officers, employees, consultants and advisors of the Company pursuant to other employee benefit plans of Sheffield Pharmaceuticals, Inc. and in the Registration Statement (Form S-8 No. 333-14867) pertaining to the 1993 Stock Option Plan of Sheffield Pharmaceuticals, Inc., the 1996 Directors Stock Option Plan of

Sheffield Pharmaceuticals, Inc., the 1996 Directors Stock Option Plan of Sheffield Pharmaceuticals, Inc. and options granted to directors, officers, employees, consultants and advisors of the Company pursuant to other employee benefit plans of Sheffield Pharmaceuticals, Inc. of our report dated March 1, 2000, with respect to the consolidated financial statements of Sheffield Pharmaceuticals, Inc. and subsidiaries incorporated by reference in its Annual Report (Form 10-K) for the year ended December 31, 1999.

/s/ Ernst & Young LLP
St. Louis, Missouri
March 23, 2000

EX-27
4
FINANCIAL DATA SCHEDULE

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~~This schedule contains summary financial information extracted from the condensed financial statements for the year ended December 31, 1999 and is qualified in its entirety by reference to such statements.~~

~~12-MOS~~	
~~DEC-31-1999~~	
~~DEC-31-1999~~	
~~3,874,437~~	
~~519,387~~	
~~0~~	
~~0~~	
~~0~~	
~~4,539,061~~	
~~601,421~~	
~~311,752~~	
~~5,048,655~~	
~~1,194,887~~	
~~0~~	
~~0~~	
~~298~~	
~~273,088~~	
~~397,687~~	
~~5,048,655~~	
~~0~~	
~~399,378~~	
~~0~~	
~~0~~	
~~20,698,870~~	
~~0~~	
~~162,237~~	
~~(17,384,788)~~	

~~0~~
~~(17,384,788)~~
~~0~~
~~0~~
~~0~~
~~(17,384,788)~~
~~(.64)~~
~~(.64)~~

~~-----END PRIVACY-ENHANCED MESSAGE-----~~