SKYEPHARMA PLC
Form 20-F
June 27, 2003

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As filed with the Securities and Exchange Commission on June 27, 2003

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F

(Mark One)

o REGISTRATION STATEMENT PURSUANT TO SECTION 12(b)
OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934
OR

ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2002
OR

o TRANSITION REPORT PURSUANT TO SECTION 13
OR 15(d) OF THE SECURITIES AND EXCHANGE ACT OF 1934
For the transition period from N/A to N/A

Commission file number: 0-29860

SKYEPHARMA PLC

(Exact name of Registrant as specified in its charter)

England and Wales
(Jurisdiction of incorporation or organization)

105 Piccadilly, London W1J 7NJ, England
(Address of principal executive offices)

Securities registered or to be registered pursuant to Section 12(b) of the Act: None

Securities registered or to be registered pursuant to Section 12(g) of the Act:

Ordinary shares of 10p each ("ordinary shares") represented by American Depositary Shares ("ADSs")
quoted on the NASDAQ National Market System, each ADS representing ten ordinary shares.

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act: None.

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by this annual report:

ordinary shares, nominal value 10p each 613,458,067

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 of 1934 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:

Yes __X__ No _____

Indicate by check mark which financial statement item the registrant has elected to follow:

Item 17 _____ Item 18 __X__

TABLE OF CONTENTS

PRESENTATION OF INFORMATION

In this Annual Report on Form 20-F ("Form 20-F"), the term "ordinary shares" refers to the ordinary shares, nominal value 10 pence each, of SkyePharma PLC ("SkyePharma" or the "Company", and together with its consolidated subsidiaries, the "Group") and the term "ADSs" refers to American Depositary Shares each representing the right to receive 10 ordinary shares and evidenced by American Depositary Receipts ("ADRs").

The Company publishes its consolidated financial statements expressed in pounds sterling. In this annual report, references to "pounds sterling", "£", "pence" or "p" are to the lawful currency of the United Kingdom; references to "U.S. dollars" or "$" are to the lawful currency of the United States; references to "Euro" or "€" are to the lawful currency of the members of the European Union that have adopted the single European currency; references to "$ Canadian" or "Cdn$" are to the lawful currency of Canada, references to "Swiss francs", "Chf" or "Sfr" are to the lawful currency of Switzerland and references to "Swedish Krona", "SKr" are to the lawful currency of Sweden. Solely for the convenience of the reader, this annual report contains translations of certain pound sterling amounts into U.S. dollar amounts at specified rates. Unless otherwise stated, the translations of pounds sterling into U.S. dollars have been made at the noon buying rate in New York City for cable transfers in pounds sterling, as certified for customs purposes by the Federal Reserve Bank of New York (the "Noon Buying Rate"). No representation is made that pounds sterling have been, could have been or could be converted into U.S. dollars at the rates indicated or at any other rate.

The Company prepares its consolidated financial statements in accordance with generally accepted accounting principles in the United Kingdom ("U.K. GAAP"), which differ in certain significant respects from generally accepted accounting principles in the United States ("U.S. GAAP"). For a description of the principal differences between U.K. GAAP and U.S. GAAP as they relate to SkyePharma and a reconciliation to U.S. GAAP of the Company's U.K. GAAP retained profit/(loss) for the years ended December 31, 2002, 2001 and 2000 and shareholders' funds at December 31, 2002, see Note 30 of the Notes to the Consolidated Financial Statements included in Item 18 of this Form 20-F.

STATISTICAL DATA

Except where otherwise indicated, figures included in this Form 20-F relating to pharmaceutical market sales are based on syndicated industry sources, including IMS Health, Inc. ("IMS") or from the Company's collaborative partners. IMS is a market research firm internationally recognized by the pharmaceutical industry.

FORWARD-LOOKING STATEMENTS

This Form 20-F contains certain forward-looking statements as defined in Section 21E of the Securities Exchange Act of 1934 with respect to the financial condition, results of operations and business of the Company and certain of the plans and objectives of the board of directors of the Company with respect thereto. Such statements may generally, but not always, be identified by the use of words such as "anticipates",

"should", "expects", "estimates", "believes" or similar expressions. Such statements in this Form 20-F include, but are not limited to, statements under the following headings: (1) "Item 4: Information on the Company"; (2) "Item 5: Operating and Financial Review and Prospects"; (3) "Item 8: Financial Information"; and (4) "Item 11: Quantitative and Qualitative Disclosures About Market Risk". Specific risks faced by the Company are described under "Risk Factors" on pages 8 to 19. By their nature, forward-looking statements involve risk and uncertainty, and the factors described in the context of such forward-looking statements in this Form 20-F could cause actual results and developments to differ materially from those expressed in or implied by such forward-looking statements.

EXCHANGE RATE INFORMATION

The table below sets forth, for the periods and dates indicated, certain information concerning the Noon Buying Rates for pounds sterling expressed in U.S. dollars per pound. The period average data set forth below is the average of the Noon Buying Rates on the last day of each full month during the period.

Fluctuations in the exchange rate between the pound sterling and the U.S. dollar will affect, among other things, the U.S. dollar equivalent of the pound sterling price of the ordinary shares on the London Stock Exchange ("LSE"), which is likely to affect the market prices of the ADSs in the United States.

	High	Low	Period Average	Period End
1998	1.7222	1.6114	1.6602	1.6628
1999	1.6765	1.5515	1.6146	1.6150
2000	1.6538	1.3997	1.5156	1.4955
2001	1.5045	1.3730	1.4382	1.4543
2002	1.6095	1.4074	1.5025	1.6095
2003 (through June 24, 2003)	1.6840	1.5500	1.6089	1.6607

	High	Low
December 2002	1.6095	1.5555
January 2003	1.6482	1.5975
February 2003	1.6480	1.5727
March 2003	1.6129	1.5624
April 2003	1.6000	1.5500
May 2003	1.6484	1.5930
June 2003 (through June 24, 2003)	1.6840	1.6278

For a discussion of the impact of exchange rate fluctuations on the Company's operating results, see "Item 5: Operating and Financial Review and Prospects Operating Results".

PART I

Item 1: Identity of Directors, Senior Management and Advisers

Not applicable

Item 2: Offer Statistics and Expected Timetable

Not applicable

Item 3: Key Information

Selected Financial Data

The selected financial data set forth below for the Company, for the years ended December 31, 2002, 2001, 2000, 1999 and 1998 have been derived from, and should be read in conjunction with the Company's Consolidated Financial Statements set forth beginning on page F-1. The Consolidated Financial Statements of the Company for the years ended December 31, 2001, 2000, 1999 and 1998 have been audited by PricewaterhouseCoopers, independent Chartered Accountants. The Consolidated Financial Statements of the Company for the year ended December 31, 2002 have been audited by PricewaterhouseCoopers LLP, independent Chartered Accountants.

The selected financial data has been prepared on the basis of U.K. GAAP, which differs in certain significant respects from U.S. GAAP. A description of these differences and a reconciliation to U.S. GAAP of the Company's U.K. GAAP retained profit/(loss) for the years ended December 31, 2002, 2001 and 2000 and shareholders' funds at December 31, 2002 and 2001 are set out in Note 30 to the Consolidated Financial Statements.

For exchange rate information, see "Exchange Rate Information" on page 4 of this Form 20-F. Solely for the convenience of the reader, the pound sterling amounts as of and for the year ended December 31, 2002 have been translated into U.S. dollars at the noon buying rate on December 31, 2002 of $1.6095 per £1.00.

For a discussion of the impact of exchange rate fluctuations on the Company's operating results, see "Item 5: Operating and Financial Review and Prospects.

The following table sets forth selected consolidated financial information as of and for the five years ended December 31, 2002.

SkyePharma PLC

	Year ended December 31,					
Consolidated Income Statement Data	**1998**	**1999**	**2000**	**2001**	**2002**	**2002**
	(in thousands, except per share data)					
U.K. GAAP[1]						
Turnover[2][3]	£10,925	£17,739	£24,292	£46,126	£69,573	$111,978
Cost of sales[4]	(10,630)	(14,854)	(15,598)	(18,820)	(24,830)	(39,964)
Gross profit	295	2,885	8,694	27,306	44,743	72,014
Selling, marketing & distribution expenses[5]	(4,230)	(3,161)	(3,844)	(4,804)	(4,769)	(7,676)
Administration expenses[6]	(6,781)	(12,584)	(12,630)	(16,025)	(20,192)	(32,499)
Research and development expenses[7]	(5,712)	(6,728)	(13,104)	(17,918)	(29,285)	(47,134)
Other operating income			2,900	6,342	14,219	22,885
Group operating (loss)/ profit	(16,428)	(19,588)	(17,984)	(5,099)	4,716	7,590
Share of operating (loss)/profit in Joint Venture	14	(48)				
Associated undertaking				(578)		
Total operating (loss)/profit	(16,414)	(19,636)	(17,984)	(5,677)	4,716	7,590
Reversal of provision for loss on disposal of fixed asset investment		381				
	(16,414)	(19,225)	(17,984)	(5,677)	4,716	7,590

	Year ended December 31,					
(Loss)/profit on ordinary activities before interest and taxation						
Interest receivable	1,396	1,364	1,806	1,251	1,081	1,740
Interest payable	(6,993)	(1,391)	(3,508)	(4,951)	(4,464)	(7,185)
Taxation	(85)	(132)	(4)	(75)	(224)	(361)
Net (loss)/profit[3][8]	£(22,096)	£(19,414)	£(19,690)	£(9,452)	£1,109	$1,784
Basic weighted average number of shares[9]	384,871	467,214	508,228	526,250	577,018	577,018
Diluted weighted average number of shares[9]	384,871	467,214	508,228	526,250	597,095	597,095
Basic and diluted (loss)/profit per ordinary share[9]	(5.7)p	(4.2)p	(3.9)p	(1.8)p	0.2p	$0.003
U.S. GAAP[1]						
Turnover	£10,925	£17,739	£24,103	£44,192	£42,586	$68,542
Group operating loss	£(16,107)	£(28,440)	£(26,953)	£(27,517)	£(36,205)	$(58,272)
Net loss under U.S. GAAP	£(21,789)	£(28,218)	£(29,201)	£(43,868)	£(45,261)	$(72,848)
Basic and diluted net loss per share[9]	(5.7)p	(6.0)p	(5.7)p	(8.3)p	(7.8)p	$(0.13)
Principal Reconciling Differences to U.S. GAAP						
Purchase accounting and goodwill	307	(8,804)	(5,146)	(24,672)	(328)	(528)
Sale of royalty interest			(2,900)	(7,564)	(19,405)	(31,232)
Revenue recognition			(189)	(1,934)	(26,987)	(43,435)
Other reconciling items			(1,276)	(246)	350	563

For information on the impact of acquisitions during the years ended December 31, 2002 and December 31, 2001, see Note 27 of the Notes to the Consolidated Financial Statements.

(1) All results, under U.K. GAAP and U.S. GAAP, represent continuing operations.

(2) Turnover in 1999 includes £3,520,000 from acquisitions in respect of the operations of SkyePharma Inc. SkyePharma Inc. was previously called DepoTech Corporation, and was renamed SkyePharma Inc. as of April 27, 1999.

(3) RTP Pharma Inc. ("RTP") was acquired on December 27, 2001. During the period December 27, 2001 to December 31, 2001 RTP made no contribution to turnover and contributed a loss of £39,000 to the Company's net loss. In the period from July 19, 2001 to December 27, 2001, SkyePharma owned 40.2% of RTP and the results of its operations were included in "Results from associated undertakings". On December 27, 2001 SkyePharma achieved control of RTP. RTP was renamed SkyePharma Canada Inc. on April 24, 2002. In 2002, SkyePharma Canada Inc. contributed revenue of £3.9 million, but negatively impacted the full year results by £1.9 million (2001: £0.6 million) primarily due to the amortisation of goodwill.

(4) Cost of sales in 1999 includes £2,669,000 from acquisitions in respect of the operations of SkyePharma Inc.

(5) Selling, marketing and distribution expenses in 1999 include £1,870,000 from acquisitions in respect of the operations of SkyePharma Inc.

(6) Administration expenses in 1999 include £4,559,000 from acquisitions in respect of the operations of SkyePharma Inc.

(7) Research and development expenses in 1999 includes £3,273,000 from acquisitions in respect of the operations of SkyePharma Inc.

(8) In May 2002, SkyePharma acquired the entire drug delivery business of Bioglan AB of Sweden which negatively impacted the full year results for the Company by £1.6 million being primarily the operating loss of the Swedish unit.

(9)

The Company has calculated net (loss)/profit per share data using the weighted average number of shares issued and outstanding for each period as set out in the table above. Basic and diluted (loss)/profit per ordinary share are set out in the table above. In the years ended December 31, 1998 to 2001, there is no difference between basic and diluted (loss)/profit per share since all potential ordinary shares including convertible bonds, warrants and options are anti-dilutive. In 2002 there is a difference between basic and diluted (loss)/profit per share due to the existence of dilutive potential ordinary shares at December 31, 2002. Since the number of dilutive potential ordinary shares at December 31, 2002 is small, basic and diluted (loss)/profit per share are the same when expressed to one decimal place.

SkyePharma PLC

	As of December 31,					
Consolidated Balance Sheet Data	**1998**	**1999**	**2000**	**2001**	**2002**	**2002**
	(in thousands, except number of shares)					
U.K. GAAP						
Fixed assets	£30,337	£83,591	£112,374	£157,391	£165,421	$266,245
Cash and short term bank deposits	30,925	13,674	42,878	26,892	28,061	45,164
Total assets	68,855	106,734	163,825	200,583	231,906	373,253
Net Assets[(1)]	6,235	72,057	68,952	95,145	124,270	200,013
Share Capital	42,710	49,409	54,132	58,402	62,546	100,668
Number of shares	427,098,454	494,086,980	517,322,768	560,023,339	613,458,067	613,458,067
U.S. GAAP						
Total assets	169,788	197,557	290,317	306,121	330,907	532,593
Net Assets[(1)]	146,668	157,362	145,929	142,570	138,530	222,964

(1) Net Assets is equivalent to shareholders' funds.

For a reconciliation of the Company's U.K. GAAP shareholders' funds to U.S. GAAP, see Note 30 of the Notes to the Consolidated Financial Statements.

RISK FACTORS

The Company is exposed to certain risks that arise from the activity of developing and manufacturing drug products.

Extensive government regulation may cause increased costs and delays in developing and marketing products

The Company is subject to extensive government regulation. The U.S. Food and Drug Administration ("FDA"), European and other national regulatory authorities require rigorous pre-clinical testing, clinical trials and other approval procedures for human drugs. Numerous regulations also govern the manufacturing, safety, labeling, storage, record keeping, reporting and marketing of human drugs. These requirements vary widely from country to country and the time required to complete pre-clinical testing and clinical trials and to obtain regulatory approvals to sell drugs is uncertain. The process of obtaining these approvals and complying with applicable government regulations is time consuming and expensive. If the FDA or other national regulatory authorities require additional clinical trials, the Company could face increased costs and significant development delays before the Company will be able to sell its products commercially. In addition, changes in regulatory policy or additional regulations adopted during product development could also result in delays or rejections.

Most of the products that the Company develops will require a new drug application filing with the FDA before they can be marketed in the United States. Based on current practice, the Company expects that it will take less than two years from the date of filing for the FDA to approve a new drug application for a product formulation, although the Company cannot predict the exact time required with any certainty.

A number of products using the Company's technologies have not yet been approved by regulators. These product candidates are at various stages of development, ranging from pre-clinical to Phase III clinical trials. The Company cannot be certain that it will obtain further regulatory approvals of any of such products. Potential products will require expensive and lengthy testing and regulatory clearances before they can be sold commercially. Products may not prove safe and effective in clinical trials, meet applicable regulatory standards, or be capable of being made at acceptable cost or successfully commercialized. In addition, pre-clinical or clinical testing may not accurately predict safety or

effectiveness in broader human use. Unexpected delays in the regulatory approval process may also occur. Even if the FDA and other regulatory authorities approve potential products for marketing, the products still may not achieve broad market acceptance.

Competition and technological change may render the Company's products or technologies uncompetitive or obsolete

The drug development industry is highly competitive and rapidly evolving, with significant developments expected to continue at a rapid pace. The Company's success will depend on maintaining a competitive position and developing efficient and cost-effective products and technologies. The Company's products will compete with other drugs and methods for delivering drugs. The Company cannot be certain that any of its products will have advantages that will be significant enough to cause medical professionals to use them. New drugs or further development in alternative drug delivery methods may provide greater benefits or may offer comparable performance at lower cost than the Company's methods. The Company cannot be certain that developments by other companies will not render its products or technologies uncompetitive or obsolete.

Many of the Company's competitors have longer operating histories and greater financial, marketing and other resources. Such competitors may prove to be more successful in developing competing technologies, obtaining regulatory approvals and marketing their products than the

Company because of greater financial resources, stronger sales and marketing teams or other factors.

The Company will face a variety of competitors with respect to the products it is developing under its collaborative arrangements with leading pharmaceutical companies. Specifically,

- products developed and produced by such collaborative arrangements may compete with products produced internally by one or more of the Company's other collaborative partners;
- proprietary and generic products developed and produced by such collaborative arrangements may face competition from generic substitutes produced by other companies; and
- generic products developed and produced by the Company may compete against branded products produced by one or more of the Company's collaborative partners.

Due to the Company's reliance on the important financial and technological contributions made by the Company's pharmaceutical company partners, any of these outcomes could adversely affect the Company's business.

The Company's business may give rise to product liability claims not covered by insurance or indemnification

The design, development and manufacture of the Company's products involve an inherent risk of product liability claims.

The Company has obtained product liability insurance in respect of the improved outcome or new pharmaceutical products the Company is developing in conjunction with the Company's collaborative partners although the Company generally relies on indemnity provisions in its agreements with such partners to protect the Company against the possibility of product liability claims. This product liability insurance also covers liabilities associated with the commercial sale of products marketed by third parties using the Company's technology.

The Company has obtained clinical trial product liability insurance for current human clinical trials and bio-equivalence studies involving its products under development and the Company intends to obtain insurance for future clinical trials and bio-equivalence studies of additional products under development. The Company cannot be certain, however, that it will be able to obtain or maintain insurance for any of its future human clinical trials or bio-equivalence studies.

The Company believes that its product liability insurance, together with the indemnity provisions in its collaborative agreements, is adequate for current operations. However, the coverage limits of the Company's insurance or the indemnity provisions in the Company's collaborative agreements may not be adequate to cover all potential claims. Product liability insurance, especially in respect of the Company's U.S. operations, is expensive and may be difficult to maintain. In addition, product liability insurance may not be available to the Company in the future on commercially reasonable terms, if at all. A successful claim against the Company in excess of the Company's insurance coverage

or outside the scope of the indemnity given by its collaborative partners could adversely affect the results of operations.

The Company's revenues may be reduced and costs increased as a result of third-party payor cost containment measures

The Company's ability to achieve profitability in its businesses depends in part on the extent to which appropriate levels of reimbursement for products and related treatments are obtained from government authorities, private health insurers and other organizations, such as health maintenance organizations. These third-party payors are increasingly challenging the pricing of pharmaceutical products. The trend toward managed healthcare in the United States and the growth of organizations such as health maintenance organizations in the United States could significantly influence the purchase of pharmaceutical products, resulting in lower prices and reduced demand

for the Company's products under development. Such cost containment measures could affect the Company's ability to sell products under development and may adversely affect the Company.

Healthcare reform proposals may adversely affect the Company's business

The efforts of governments to contain or reduce the cost of health care will continue to affect the business and financial condition of drug companies. A series of health care reform proposals announced in recent years have created uncertainty that could adversely affect the Company's ability to raise funds and to identify and reach agreements with potential partners. If such proposals are eventually adopted, business could be adversely affected. Furthermore, the Company's ability to commercialize potential products may be adversely affected to the extent that such proposals have an adverse effect on the business, financial condition and profitability of other companies that are current or prospective collaborators for some of such products.

The Company's results of operations tend to fluctuate

The Company's operating revenues principally derive from contract development. Contract development revenues, except for revenue derived from contract manufacturing, are tied to a number of unpredictable factors, such as scientific developments, the timing of regulatory approvals, the market introduction of new products and other factors. As a result, the Company's results of operations tend to fluctuate materially on a monthly, semi-annually and yearly basis and, therefore, make period-to-period and period-on-period comparisons inappropriate at this stage in the Company's development. The Company believes that its revenues will continue to fluctuate in the near to medium term as a result of the factors described above.

The Company may not sustain profitability

In 2002, SkyePharma reported a full year net profit for the first time. As of December 31, 2002, the Company had accumulated consolidated equity shareholders' funds of £113.0 million. While the Company's internal forecasts indicate that the Company may also achieve profitability in 2003, this is dependent upon the level of milestone payments and license fees received, the timing of contract development revenues and the amount of discretionary investment the Company chooses to make in furthering its own product portfolio and other factors, including those described below, and therefore the Company cannot assure you that it will be able to sustain profitability. In addition, because the Company typically achieves most of its revenues in the second half of the year, even if the Company were to achieve a net profit in 2003, it may report a net loss in the first half of the year. See "Item 5: Operating and Financial Review and Prospects".

The Company's future profitability will additionally depend, among other things, on whether it will, alone or together with its partners, be able to:

- develop products utilizing its technologies, either independently or in collaboration with other pharmaceutical companies;
- receive necessary regulatory and marketing approvals;
- establish and enhance its manufacturing;

achieve market acceptance for such products;

receive royalties on products that have been approved, marketed or submitted for marketing approval with regulatory authorities in line with the Company's current forecasts; and

maintain sufficient funds to finance its activities.

The Company is dependent on Geomatrix , DepoFoam and inhalation technologies as to which further successful development is uncertain

The Company's ability to increase revenues and achieve profitability is largely dependent on its Geomatrix, DepoFoam and inhalation technologies. Approximately 16% of the Company's revenues for the year ended December 31, 2002 was derived from royalties, product sales, contract development and milestone payments relating to its Geomatrix technologies, approximately 46% relating to its DepoFoam technologies and approximately 4% relating to its inhalation technologies. In order to increase revenues from Geomatrix, DepoFoam and inhalation technologies, the Company must continue to obtain new development contracts with third parties or develop, license and manufacture new formulations of commercially available drugs. The Company cannot assure you that it will be able to obtain such contracts or successfully develop new formulations internally.

The Company has successfully developed drug products incorporating four Geomatrix technologies which are currently on the market. However, the Company cannot assure you that it will be able to develop successfully future products incorporating these delivery systems. The development and formulation of oral controlled-release products is difficult and time-consuming. Each drug compound is different, and there can be no assurance that a drug delivery system that works with one product will work with another.

The Company is currently formulating products utilizing other Geomatrix technologies. However, the Company cannot assure you that these efforts will be successful. One of these technologies, the Multiple Pulse System, has only been subject to limited in vivo (human) clinical testing. Consequently, the Company cannot assure that drugs utilizing the Multiple Pulse System will be successfully formulated and approved.

The Company has successfully developed one drug product incorporating DepoFoam technologies which was approved by the FDA in April 1999 and a second product, DepoMorphine , is due to be filed with the FDA in mid 2003. However, the Company cannot assure you that it will be able to develop successfully future products utilizing the DepoFoam technologies. The development and formulation of injectable controlled-release products is difficult and time-consuming. Each drug compound is different and there can be no assurance that a drug delivery system that works with one product will work with another.

The Company is developing two advanced inhalation technologies to deliver medicines via a patient's lungs without relying on chloro-fluoro-carbon ("CFC")-based propellants. The Company has successfully developed one drug product incorporating its inhalation technologies, the Foradil® Certihaler , which has completed Phase III clinical trials and for which a new drug application ("NDA") has been submitted to the FDA and to health authorities in the European Union. However, there can be no assurance that this drug will be approved. The Company cannot assure you that it will be able to develop successfully future products utilizing the inhalation technologies. The development and formulation of inhalation products is difficult and time-consuming. Each drug compound is different, and there can be no assurance that a drug delivery system that works with one product will work with another.

Even after a product incorporating the Geomatrix, DepoFoam or inhalation technologies has been successfully formulated and approved, its commercial success is not assured. In order to gain medical and commercial acceptance, a product generally must demonstrate some performance improvements and other benefits over products incorporating the same or similar drug compounds. In some cases, these benefits may be difficult to establish.

The failure by the Company's collaborative partners to fulfill their obligations to the Company to provide funding, obtain regulatory approvals and conduct marketing activities could adversely affect the Company's business

The Company's ability to develop and market its present and future products depends in large part on its ability to maintain its existing, and enter into new, collaborations with third parties. If any

of the Company's partners becomes insolvent or terminates or otherwise fails to fulfill its obligations with the Company, the Company's business could be adversely affected. Among other things, the Company faces the following specific risks with respect to collaborative partners:

Funding. The Company has entered into a number of collaborative arrangements with leading pharmaceutical companies for the development and commercialization of products using its technologies. Some of the Company's collaborative partners are development stage companies whose business prospects are uncertain and who face similar risks as the Company. If the Company becomes unable to continue to obtain funding for its development activities through its collaborative arrangements or if its collaborative partners fail to make payments due under the development and commercialization agreements, the Company's business would be adversely affected.

Regulatory Approvals. In addition, the Company generally depends upon its collaborative partners to secure the necessary regulatory approvals for improved outcome and new pharmaceuticals utilizing its technologies. In these cases, the Company has no control over the timing and location of the regulatory filings. Its partners may follow a regulatory strategy that does not maximize the royalty income that the Company will receive from its technologies. In addition, the Company's partners may choose not to file for regulatory approval of a product successfully formulated with the technologies. Even if the Company's partners do file for regulatory approval, they may fail to devote the necessary resources and expertise to secure the approval.

Marketing. At present the Company is not involved in the consumer marketing of improved outcome or new products formulated with its technologies. The Company depends on its collaborative partners for such marketing. The majority of the Company's partners are not obligated to market products incorporating its technologies, even if such products are successfully developed and approved. Although the Company has no reason to believe that its partners will not market a successfully developed and approved product, the Company cannot assure you that this will be the case. The Company's future revenues largely depend on the success of such marketing efforts, which are beyond its control. For example, Paxil® CR was approved by the FDA in February 1999 but was not launched by GlaxoSmithKline until April 2002.

If the Company is unable to obtain additional funding on favorable terms, it will adversely affect the Company's research and development and ability to commercialize its products

The Company believes that its currently available funds will be sufficient for the needs of its operations through at least the next twelve months.

If the Company's currently available funds and internally generated cash flow are not sufficient to satisfy its financing needs, the Company would be required to seek additional funding through other arrangements with corporate collaborators, through bank borrowings or through public or private sale of its securities, including equity securities. Any such collaboration could result in limitations on the Company's ability to control the research, development and commercialization of resulting products, if any, as well as its profits therefrom. In addition, the terms of any future bank borrowings could place restrictions on the Company's ability to take certain actions, and any equity financing could result in dilution to the Company's shareholders. The Company does not currently have any committed sources of additional capital. There can be no assurance that additional funds will be available on a timely basis, on favorable terms or at all, or that such funds, if raised, would be sufficient to permit the Company to continue to conduct its operations. If adequate funds are not available, the Company may be required to curtail significantly, or discontinue, one or more of its research and development programs.

The Company's ability to meet its future capital requirements will depend on many factors. These include:

the Company's ability to maintain existing collaborative arrangements and to establish and maintain new collaborative arrangements with others;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

complying with regulatory requirements; competing technological and market developments;

changes in the Company's existing research relationships; and

the effectiveness of product commercialization activities and arrangements.

For more information on the Company's liquidity and capital resources, see "Item 4: Information on the Company Business Operations Collaborative Arrangements" and "Item 5: Operating and Financial Review and Prospects".

A failure to obtain and maintain patents and proprietary rights may adversely affect the Company's business

The Company's success, competitive position and amount of royalty income will depend in part on its ability to obtain and maintain patent and trade secret protection, particularly for its drug delivery technologies.

The Company believes that patent and other intellectual property protection of its drug delivery and formulation technologies is important to its business and that its future will depend in part on its ability to obtain patents, maintain confidential and trade secret information and to operate without infringing the intellectual property rights of others.

While the Company intends to prosecute patents aggressively, the process of obtaining patents is lengthy and expensive. There can be no assurance that patents will be granted in connection with any of the Company's currently pending or future applications or that they will be valid and of sufficient scope and strength to provide the Company with meaningful legal protection or any commercial advantage. In addition, intellectual property protection may be unavailable or limited in some of the countries in which the Company does business. The laws of some foreign countries do not afford the Company's inventions the same degree of legal protection as the laws of the United States. In addition, patent laws may change over time. The Company cannot predict the effect that any such changes would have on its business and its ability to protect commercially sensitive information. If the Company fails to obtain or maintain sufficient protection for its current and future products and technologies, its ability to successfully commercialize these products and technologies could be adversely affected.

The Company, from time to time, may receive notifications of alleged infringement of patents owned by third parties. The Company may not, in all cases, be able to successfully defend itself in court or resolve such allegations through licensing or settlement. Moreover, whether or not the Company is successful in enforcing its own patents or in defending itself against claims of alleged infringements of patents owned by third parties, doing so is time-consuming and costly and may result in the diversion of management resources.

The Company also relies on trade secrets and other unpatented proprietary information in its product development activities. To the extent that the company relies on trade secrets and unpatented know-how to maintain its competitive technological position, there can be no assurance that others may not independently develop the same or similar technologies. The Company seeks to protect trade secrets and proprietary knowledge, in some cases through clauses in confidentiality agreements with its employees, consultants, advisors and collaborators. Nevertheless, these agreements may not effectively prevent disclosure of the Company's confidential information and may not provide the Company with an adequate remedy in the event of unauthorized disclosure of such information. If the Company's employees, scientific consultants or collaborators develop

inventions or processes independently that may be applicable to the Company's products under development, disputes may arise about ownership of proprietary rights to those inventions and processes. Such inventions and processes will not necessarily become the Company's property, but may remain the property of those persons or their employers. Protracted and costly litigation could be necessary to enforce and determine the scope of the Company's proprietary rights. Failure to obtain or maintain patent and trade secret protection, for any reason, would adversely affect the Company's business.

The Company has entered into a number of collaborative arrangements with leading pharmaceutical companies for the development and commercialization of improved outcome and new products. In connection therewith, the Company shares certain of its proprietary knowledge with such collaborative partners. Although the Company's patents and other proprietary rights are designed to protect the Company from infringement by such collaborative partners, there can be no assurance that the Company's patents or other proprietary rights will prevent its collaborative partners from developing similar or functionally equivalent products. In addition, the Company's arrangements with its collaborative partners frequently contain representations, warranties and other assurances given by the Company regarding the scope of its own intellectual property and the non-infringement by the Company of intellectual property owned by third parties. If the Company were found to be

in breach of any of these provisions, its partners could sue the Company for damages, which could have a material adverse effect on the Company's business, results of operations and financial condition.

The Company engages in collaborations, sponsored research agreements and other arrangements with academic researchers and institutions some of which have received and may receive funding from government agencies. Although the Company seeks to retain ownership of all intellectual property rights pertaining to inventions which may result from such collaborations, there can be no assurance that the governments, the institutions or researchers or other third parties will not have rights to such inventions to the extent permitted under applicable law.

For more information on the Company's patents and proprietary rights, see "Patents and Proprietary Rights".

The Company may not be able to maintain its exclusive technology rights to DepoFoam from the Research Development Foundation

The Company's DepoFoam business depends in part on its ability to continue to use technology rights that the Research Development Foundation ("RDF") assigned to a subsidiary of the Company, on an exclusive basis. Under the RDF agreement, RDF has the right to terminate the agreement or to convert the exclusive nature of the rights granted under the agreement into a nonexclusive right if the subsidiary does not satisfy its contractual obligations, including making certain minimum annual payments, where the technology is used to enable formulation work. RDF may also terminate the agreement if the subsidiary becomes bankrupt, breaches the agreement or contests the patents included in this technology. The termination of the subsidiary's agreement with RDF or its conversion to a nonexclusive agreement would adversely affect the Company's DepoFoam business.

A failure to comply, or the costs of complying, with environmental, health and safety regulations could adversely affect the Company's business

The Company's business is also subject to regulation relating to the protection of the environment and health and safety, including those governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials. The Company believes that it is in compliance in all material respects with all such laws, rules, regulations and policies applicable to the Company. However, there can be no assurance that the Company will not be required to incur significant costs to comply with such environmental and health and safety laws and regulations in the future. The Company's research and development involves the controlled use

of hazardous materials. Although the Company believes that its safety procedures for handling and disposing of such materials comply with the standards prescribed by applicable regulations, the risk of contamination or injury from these materials cannot be completely eliminated. In the event of such contamination or injury, the Company could be held liable for any damages that result and any such liability could have a material adverse effect on the Company's business, financial condition or results of operations.

A failure to manage expansion effectively could adversely affect the Company's business

Management of the Company's growth, as well as the commencement of commercial manufacturing and marketing of the Company's product candidates, will require continued expansion and improvement of the Company's systems and internal controls and an increase in the Company's manufacturing, marketing and sales operations. In addition, the Company intends to continue to add new personnel. Any failure to manage growth effectively and integrate new personnel on a timely basis could adversely affect the Company's business.

Any failure by the Company to fulfill its obligations to its collaborative partners in respect of manufacturing and any failure by the Company to enter into new, or maintain its existing, manufacturing arrangements could adversely affect the Company's business

The Company has its own manufacturing sites in Lyon, France, Muttenz, Switzerland and San Diego, California. However, for the manufacture of certain of its existing products, and certain of those currently in development, including Foradil and Propofol, it will depend on manufacturing partners. If the Company loses one of its current manufacturing partners or fails to enter into agreements with new manufacturing partners, if it experiences delays in finding such partners or if it is unable to enter into commercially viable arrangements with them, its ability to manufacture its existing products and those in development and to meet its obligations in its existing collaborative arrangements, could be adversely affected.

If the Company's manufacturing facilities fail to meet required standards, it could result in delays in manufacturing and additional costs

Manufacturing operations take place at the Company's facilities in Lyon, France, Muttenz, Switzerland and San Diego, California. Limited manufacturing activities are conducted in Muttenz.

The Company acquired the Lyon facility in 1997, and it plans to use it for scale-up manufacturing as well as for manufacturing commercial quantities of its product candidates. The Company has completed its Geomatrix manufacturing suite in the Lyon facility and has expanded its operations to include production activities for dry powder inhaler products. The Company believes that it has substantially brought the facility into compliance with current good manufacturing practices (cGMP) and FDA standards. The FDA has inspected the Lyon facility in respect of three products, and in July 2001 the FDA approved the Lyon facility for the commercial manufacturing of one of these products, Dilacor XR1. There can be no assurance, however, that the Lyon facility will ultimately be found to be in compliance with cGMP or other regulatory requirements for the purposes for which the Company plans to use the facility. On May 14, 2002, the Company announced that it had signed a non-binding letter of intent with Kowa Company Ltd ("Kowa") to evaluate Kowa's acquisition of a 50% interest in the Lyon facility. Kowa and the Company are still evaluating this proposal.

DepoCyt® is the first approved injectable drug product using the Company's DepoFoam technology. The Company's DepoFoam manufacturing operations in San Diego, California have passed FDA and EMEA inspections but may need to pass pre-approval inspections by other regulatory agencies for countries in which there are further regulatory filings to market DepoCyt. In October 1999, SkyePharma Inc. discovered that two lots of DepoCyt did not meet specifications and recalled these lots. Investigations identified that unannounced changes in a supplier's manufacturing process for a raw material resulted in product that did not meet all specifications

throughout the shelf life. SkyePharma Inc. and Chiron Corporation, the Company's U.S. marketing partner prior to Enzon, voluntarily withdrew DepoCyt from the market. There were no adverse events attributed to the recalled batches and the product was made available to patients on a compassionate basis. In March 2001, the FDA gave clearance to return DepoCyt to the market.

Failure to comply could result in significant delays in the Company's planned manufacturing efforts. The Company also could incur significant additional expense in bringing the facility into compliance with cGMP or other regulatory requirements. The Company cannot assure you that it will be able to complete its plans successfully for additional scale-up manufacturing or for manufacturing commercial quantities of its product candidates.

A failure to scale up the Company's DepoFoam manufacturing operations successfully could adversely affect the Company's business

If the Company fails to scale-up its DepoFoam manufacturing operations successfully its business may be adversely affected. In particular, the Company may be unable to supply DepoCyt to its North American marketing partner, Enzon Pharmaceuticals, Inc. ("Enzon") or DepoMorphine to its North American marketing partner, Endo Pharmaceuticals Inc. ("Endo") for its launch in 2004. For all other DepoFoam products, the Company will need to scale-up its current manufacturing operations significantly. The Company will also need to comply with regulations in the United States and foreign countries relating to achieving the prescribed quality and required levels of production of its DepoFoam products and obtaining marketing approval.

The Company may not be able to obtain the materials necessary to manufacture its DepoFoam products

The Company currently relies on a limited number of suppliers for materials used to manufacture its DepoFoam products. Some of these materials are purchased only from one supplier. If the Company cannot obtain the materials it needs from its existing suppliers, the Company may not be able to access alternative sources of supply within a reasonable period of time or at commercially reasonable rates. In addition, regulatory requirements applicable to drugs tend to make the substitution of suppliers costly and time-consuming. The unavailability of adequate commercial quantities, the inability to develop alternative sources, a reduction or interruption in supply or a significant increase in the price of materials could adversely affect the Company's ability to manufacture and market its DepoFoam products.

The Company's manufacturing process may not be suitable for all of the DepoFoam products the Company desires to commercialize

To date, SkyePharma Inc. has relied on a particular proprietary method of manufacturing its potential DepoFoam products. The Company cannot be certain that this method will be applicable to all potential products it desires to commercialize. The problems that may arise include:

- the Company may not be able to meet manufacturing challenges that arise concerning particular drugs to be incorporated in DepoFoam;

the Company's manufacturing process may not result in viable yields of DepoFoam products; and

the physical and chemical stability of DepoFoam products may vary.

If the Company decides to pursue alternative manufacturing methods for some or all of its drugs, it cannot be certain that these methods will prove to be commercially practical or that it will have the right to use any alternative methods.

The Company may expend significant time and resources relating to existing and potential legal proceedings and the eventual outcome of such proceedings may differ materially from management's current estimates and beliefs

The Company is currently involved in various legal proceedings, including actions claiming alleged violations of antitrust laws and infringement of intellectual property rights. Although the Company cannot predict the outcome of these proceedings with certainty, the Company believes, based on information received, that these actions are without merit and is vigorously contesting these claims. Contesting these claims, however, may involve the expenditure of significant management time and resources of the Company. In addition, we cannot exclude the possibility that, contrary to management's current estimates and beliefs, the eventual outcome of such matters could have a material adverse effect on our financial position, results of operations or liquidity. You should read "Item 8: Financial Information Legal Proceedings" for further information on our pending litigation.

The Company may not be able to obtain the rights to the drugs it desires to deliver through DepoFoam

The Company's ability to develop and commercialize its DepoFoam technology will depend on whether it and its partners can access the drugs that are to be delivered through DepoFoam. At times, the Company intends to rely on its partners' ability to provide this access. The Company cannot be certain, however, that its partners will have appropriate drug candidates for its DepoFoam technology. In addition, the Company or its partners may be alleged or determined to be infringing on third parties' rights and may be prohibited from using the drug or be found liable for damages. Any restriction on access or liability for damages would adversely affect the Company's business.

The Company may incur substantial costs related to its use of hazardous materials

The Company's research and development on DepoFoam products involves the use of hazardous materials, chemicals and various radioactive compounds. The Company cannot completely eliminate the risk of accidental contamination or injury from these materials. If such an accident occurs, the Company could be held liable for any damages that result and any such liability could exceed its resources. The Company may incur substantial cost to comply with environmental regulations.

If the Company is unable to retain key personnel or attract new personnel, it could have an adverse effect on the Company's business

The Company relies upon a number of key executives and employees, including Ian Gowrie-Smith, its Executive Chairman and Michael Ashton, its Chief Executive Officer. In addition, the Company's future operating results depend in part upon its ability to attract and retain other qualified management, scientific, technical, marketing and support personnel. Competition for such personnel is intense, and there can be no assurance that the Company will be able to continue to attract and retain such personnel. The loss of the services of any of the Company's key executives or employees could materially adversely affect the Company.

Potential conflicts of interests may arise from related party transactions

The Company and certain of its principal shareholders or their affiliates and other related parties have engaged in several significant transactions among themselves in the past and may continue to do so from time to time in the future. Certain of these transactions provide for significant payments to certain principal shareholders, directors and executive officers upon achievement of specified milestones or profit hurdles. As a result of these arrangements, conflicts of interest may arise between and among the Company, certain principal shareholders, directors and executive officers because of their independent pecuniary interests.

The Company acquired Jago Holding AG and its subsidiaries ("Jago") in May 1996 from Dr. Jacques Gonella, who was, up until June 6, 2001, a Director of the Company, for a combination of cash and shares. In addition to the initial purchase price, the Company agreed to an earn-out arrangement with Dr. Gonella whereby Dr. Gonella was entitled to receive payments dependent on certain revenues related to Geomatrix technologies. On March 31, 2000, certain amendments were made to the 1996 Acquisition Agreement for Jago and a Settlement Agreement was signed establishing the full and final settlement of the deferred consideration payable to Dr. Gonella. For a description of the earn-out arrangement with Dr. Gonella, see "Item 7: Major Shareholders and Related Party Transactions Certain Arrangements in Respect of the Jago Acquisition".

The Company acquired Krypton Limited ("Krypton") in a share-for-share exchange in January 1996 from a series of trusts in which Ian Gowrie-Smith, who is the Executive Chairman of the Company, certain former directors and a former employee of the Company had interests. Pursuant to an earn-out arrangement, the Company agreed to pay additional consideration consisting of ordinary shares and warrants dependent upon certain milestones relating to achieving regulatory approvals for the sale of certain Krypton products and the sales and profitability of such products. See "Item 7: Major Shareholders and Related Party Transactions Certain Arrangements in Respect of the Krypton Acquisition".

At June 24, 2003, assuming the Company was to convert its convertible preferred shares of Astralis into common stock of Astralis, the Company would own 25.4% of Astralis LTD ("Astralis"). The Company is a party to several agreements concerning the development of Astralis' novel injectable vaccine therapy, for the treatment of all forms of psoriasis, a chronic skin disorder. See "Item 7: Major Shareholders and Related Party Transactions Other Arrangements".

Although the Company anticipates that all future related party transactions and agreements will be on terms no less favorable to the Company than it could obtain in comparable contracts with unaffiliated third parties, there can be no assurance that conflicts of interest will not arise between the Company and the principal shareholders or their affiliates in certain circumstances.

Principal shareholders may influence the outcome of shareholder approvals and hinder a change in control that might be in your interest

As of June 24, 2003, certain principal shareholders and the directors and officers of the Company as a group owned approximately 18.3% of the outstanding ordinary shares. As a result, certain directors, officers and such shareholders may be in a position to exert influence in the election of the Company's directors and officers and other corporate actions that require shareholder approval. The Board of Directors of the Company consists of nine people.

Exchange rate fluctuations may adversely affect the Company's results of operations and financial position

Approximately 70% of the Company's sales for the year ended December 31, 2002, were derived from customers located outside the United Kingdom. Since the revenue and expenses of the Company's foreign operations are generally denominated in U.S. dollars, Euros and Swiss francs, exchange rate fluctuations between such currencies and the pound sterling will subject the Company to foreign exchange risk with respect to the reported results of its foreign operations. The Company does not currently hedge against the effect of currency translation on its reported results, but does, where appropriate, seek to hedge its exchange rate risk on particular transactions. Fluctuations between local currencies and pounds sterling may materially adversely affect the Company's financial condition and results of operations. See "Item 5: Operating and Financial Review and Prospects".

The Company's ordinary shares trade on the London Stock Exchange in pounds sterling and the ADSs trade on The Nasdaq National Market in U.S. dollars. The value of the ADSs in U.S. dollars may fluctuate as a result of fluctuations in the U.S. dollar/ pound sterling exchange rate.

The market prices of the Company ordinary shares and ADSs may be adversely affected by market volatility

Companies like SkyePharma have, in recent years, experienced dramatic stock price volatility. The following factors may cause the market price of the Company's ordinary shares or ADSs to fluctuate significantly:

- announcements of technological innovations or new products by competitors and others;
- the status of submissions to the FDA or its international equivalent;

variations in results of operations, market condition, analysts' estimates and the stock market generally; and

stock market perceptions of the pharmaceutical, biotechnology and/ or drug delivery industries specifically.

Issuances or sales of a substantial number of the Company's ordinary shares or ADSs could adversely affect their market price

Issuances or sales of a substantial number of ordinary shares or ADSs could adversely affect the market price of the ordinary shares and ADS. As of June 24, 2003, certain principal shareholders and the directors and officers of the Company, as a group, held 18.3% of the Company's outstanding ordinary shares. Subject to the satisfaction of certain conditions, Mr. Gowrie-Smith has agreed in principle to a divorce settlement including the transfer of beneficial holdings of 10,996,943 Ordinary Shares of the Company. Details of any changes in beneficial holdings will be announced at the appropriate time. Shares may be eligible for future sale subject to the conditions imposed by Rule 144 and Regulation S under the Securities Act.

The Company's shareholders may not receive a return on their shares other than through the sale of their shares

Under current U.K. law, the company's accumulated realized profits must exceed its accumulated realized losses (on a non-consolidated basis) before dividends can be paid. The Company has not paid dividends in the past ten years on its ordinary shares. The Company intends to retain earnings, if any, for use in its business and does not anticipate paying any cash dividends in the foreseeable future. Accordingly, other than through the sale of their shares, the Company's shareholders may not receive a return.

Item 4: Information on the Company

HISTORY AND DEVELOPMENT

Overview

SkyePharma PLC is a public limited company organized under the laws of England and Wales with its registered office at 105 Piccadilly, London W1J 7NJ, telephone number + 44 (0) 20 7491 1777. SkyePharma PLC was formerly named Black & Edgington plc and incorporated on March 10, 1910. It was engaged in the provision of temporary structures for major events. In January 1996, the Board of Directors changed the name of the Company to SkyePharma PLC and the nature of its activities to pharmaceuticals. Today the Company is a specialty pharmaceutical company, using its multiple drug delivery technologies: oral, injectable, inhalation, topical and enhanced solubility to create a product pipeline for out-licensing to marketing partners.

The Company, as currently operated, was formed substantially from the 1996 acquisition of Jago, the 1999 acquisition of DepoTech Corporation and the 2001 acquisition of RTP Pharma Inc. In addition, the Company has acquired certain technologies as set out below.

Corporate Acquisitions

Jago, a Swiss drug delivery company which commenced operations in 1983, was acquired by the Company in May 1996. The total consideration paid by the Company to acquire Jago was approximately £100.8 million in cash (plus a prepayment of $6.0 million (£3.9 million)) and approximately 30.7 million ordinary shares (valued at 75 pence per share). To finance the Jago acquisition and to provide additional working capital for the Company, the Company issued and sold approximately 187.8 million ordinary shares in a public offering in the United Kingdom in May 1996 at a price of 75 pence per share. In the fundraising associated with the transaction, Dr. Gonella, the vendor, purchased 84,789,463 ordinary shares of the Company at a purchase price of 75 pence per share. The Company agreed to pay additional consideration in respect of the Jago acquisition pursuant to an earn-out arrangement. See "Item 7: Major Shareholders and Related Party Transactions Certain Arrangements in Respect of the Jago Acquisition". On March 31, 2000 a settlement agreement was signed establishing the full and final settlement of the deferred consideration payable to the vendor of Jago, Dr. Gonella. The settlement was approved by shareholders at the Company's Annual General Meeting held on July 11, 2000 to be made entirely in shares and 6 million ordinary shares and 24 million Deferred Shares were issued. Following the US launch and first commercial sale of Paxil by GlaxoSmithKline in April 2002, 12 million Deferred Shares automatically converted into 12 million Ordinary Shares. Through the acquisition of Jago, SkyePharma acquired the Geomatrix range of oral

controlled release systems and a new generation of inhalation technologies.

In October 1998, the Company acquired 16% of the common stock of DepoTech Corporation of San Diego for a consideration of £2.9 million. On March 10, 1999, the Company completed the acquisition of the outstanding shares by issuing to the former DepoTech shareholders 28,311,070 SkyePharma ordinary shares in the form of ADSs, valued at £20.0 million, plus the right to receive additional shares if one or both of two conditions occur. On April 1, 1999, the first condition, the approval by the FDA of DepoCyt for sale to the public, occurred and the Company issued to the former DepoTech shareholders an additional 16,177,849 SkyePharma ordinary shares valued at £9.8 million, in the form of ADSs. On April 4, 2000 the Company announced that the final contingent payment on the acquisition of DepoTech had been triggered following the signing of a contract to utilize DepoFoam technology for a macromolecule which fulfilled the second condition. As a result 12,132,600 shares were issued, in the form of ADSs, on April 25, 2000 at a value of £13.3 million. In connection with the acquisition, the Company agreed that outstanding warrants to purchase DepoTech common stock on the effective date of the merger would become warrants to purchase the Company's ordinary shares. Following the issue of shares on April 25, 2000, the former DepoTech shareholders became entitled to a further 458,144 warrants with a value of £0.2 million. Taking into account these final payments, the total consideration paid on the

acquisition of DepoTech was £49.4 million. DepoTech had been developing the DepoFoam technology. The DepoFoam system is a proprietary, injectable technology that provides controlled drug delivery for an extended period of time, improving bioavailability profiles and clinical outcomes. On April 27, 1999, DepoTech was renamed SkyePharma Inc. SkyePharma Inc. is SkyePharma's center for the development and manufacture of injectable, sustained-release therapeutic products.

On July 19, 2001, the Company acquired an initial 40.2% interest in RTP Pharma Inc. of Montreal, Canada for $20 million (£14.2 million) in SkyePharma ordinary shares and acquired $5.0 million (£3.5 million) of preferred shares in RTP for cash. RTP specialized in improving the solubility of drugs using its Insoluble Drug Delivery ("IDD ") technology platform. During the 90 days following July 19, 2001, the Company acquired $10 million (£6.9 million) of preferred shares in RTP in return for the issue of additional SkyePharma ordinary shares. The remaining shareholders were given the right to require the Company to purchase the remaining 59.8% of the outstanding common shares prior to January 1, 2004, in the event that certain key milestones were achieved, which, amongst other factors, included profitability, partnerships and licensing agreements. The Company also had the right, under certain circumstances, principally the achievement of profitability, to purchase the remaining common shares prior to January 1, 2004, in return for the issue of SkyePharma ordinary shares. On December 27, 2001, agreement was reached to acquire the majority of the outstanding voting shares in RTP. In the interim period, RTP had achieved certain of the key milestones, given which, the Directors of the Company were of the view that it was in the Company's best interests to negotiate with RTP's remaining shareholders to acquire their holdings. On March 13, 2002, the Company announced the completion of the acquisition of the outstanding voting shares in RTP in return for the issue of SkyePharma ordinary shares to the value of $20.6 million (£14.2 million). The total consideration of $56.5 million (£39.4 million) including acquisition costs for 100% of RTP comprised 49,959,367 ordinary shares and $5.8million (£4.1 million) cash. The issued shares were subject to selling restrictions, which, other than in limited circumstances, ranged from a minimum of 12 months to 24 months. On April 24, 2002, RTP was renamed SkyePharma Canada Inc. ("SkyePharma Canada"). On March 12, 2003, the selling restrictions on 17,255,926 shares, issued to Elan as a former shareholder of RTP, were lifted. In April 2003, Elan sold its entire shareholding in SkyePharma. In consideration for the loss of the former RTP shareholders' certain option rights, which were agreed on July 19, 2001, when the Group acquired an initial 40.2% interest in RTP, deferred consideration has been agreed. If the SkyePharma share price is below 82 pence on June 30, 2003, then the Company is required to issue 200,000 additional shares, or pay an amount in cash, for each penny difference between the actual share price and 82 pence. At December 31, 2002, in the opinion of the Directors, the outcome could not be estimated with any degree of certainty. Therefore, this deferred consideration was not recognized at December 31, 2002. The share price, as calculated under the terms of the agreement, on June 24, 2003, the latest practicable date prior to the filing of this report, was 63 pence. At this price, to settle its obligation, the Company would have to issue up to 3.8 million new shares or pay an amount in cash. The Company has recently substantially reduced the staff of SkyePharma Canada by outsourcing its activities to other SkyePharma sites.

Krypton, a Gibraltar-based company which holds development rights to certain generic drugs, was acquired by the Company in January 1996. The total consideration paid by the Company to acquire Krypton was £12.0 million satisfied by the issue of 30 million ordinary shares and warrants to subscribe for an additional 3 million ordinary shares at an effective exercise price of 40 pence per share. The Company has agreed to pay additional consideration in respect of the Krypton acquisition if certain milestones and profit hurdles are met. See "Item 7: Major Shareholders and Related Party Transactions Certain Arrangements in Respect of the Krypton Acquisition". To date, no payments have been made under the Krypton earn-out arrangements.

In January 1997, the Company acquired a pharmaceutical manufacturing and production facility near Lyon, France. See "Item 4: Information about the Company Business Operations Manufacturing".

Technology Acquisitions

On July 30, 1999, the Company acquired intellectual property, license agreements, know-how and trademarks related to nano-particulate drug delivery technology for the delivery of poorly soluble drugs from Medac GmbH ("Medac") a private German pharmaceutical company. As consideration for the acquisition, the Company made an initial cash payment of $2.5 million and issued 3,067,286 ordinary shares with a market value of $2.5 million to Medac on the date of signing the agreement. The agreement provided for additional consideration in the form of cash and SkyePharma PLC ordinary shares for a total value of $5.0 million. On April 17, 2000, a further $3.0 million in cash was paid to Medac due to compliance by the vendor with certain terms specified in the agreement. On July 21, 2000, the Company issued a further 1,461,455 shares with a market value of $2.0 million to Medac as deferred consideration due upon the satisfactory transfer of the nano-particulate technology and know-how to SkyePharma. In addition, future royalties will be paid to Medac on net sales of marketed products using nano-particulate technology.

In October 1999, the Company acquired the tangible assets and intellectual property of Hyal Pharmaceutical Corporation in Canada ("Hyal") from the court appointed receiver and administrator of Hyal, for a total consideration of Cdn$14.0 million (£5.7 million) plus acquisition expenses of £0.2 million. The consideration was satisfied by the set-off of Cdn$11.6 million of SkyePharma secured and unsecured debt owed by Hyal including the interest due and Cdn$2.4 million in cash. In addition, and because Hyal was in receivership at this time, SkyePharma indemnified the receiver to the extent that Cdn$11.6 million exceeded the amount that SkyePharma may ultimately be entitled to receive as a creditor of Hyal. This indemnity was secured by an irrevocable letter of credit open for up to one year in the amount of Cdn$1.0 million. During 2000, the letter of credit was called to recover the shortfall in the receivership process. As a result, in April 2001, SkyePharma received 8.0 million shares representing seven Hyal shares for every dollar shortfall in the process. In addition the Company acquired the 0.7 million shares issued to Meditech Research Limited ("Meditech"), another creditor of Hyal, for Cdn$0.1 million in May 2001. As a result the total Company shareholding in Hyal (now renamed Cade Struktur) is 0.9 million shares following a 10 for 1 share consolidation. As at June 2003, this represents approximately 16.8% of Cade Struktur. The shares have been recorded at zero cost. Hyal was a drug delivery company that developed products using its topical drug delivery technologies, based on hyaluronan ("HA"), a natural polymer, which are primarily designed to maintain efficacy and localize delivery of drugs to the skin for the treatment of a variety of skin disorders. Following the sale of all related intellectual property and the reorganization of the company, Cade Struktur is now involved solely in the pursuit of financing and development of infrastructure related projects in the former East Germany.

In December 2000, SkyePharma licensed rights to three further topical drug delivery technologies, Crystalip, DermaStick and the ES-Gel system, from Bioglan AB, a subsidiary of Bioglan Pharma PLC ("Bioglan"). Under the terms of the agreement SkyePharma paid $9.0 million in cash and obtained certain exclusive development and commercial rights in relation to new products from the Crystalip and DermaStick technologies and also the right to develop with Bioglan two new products using the ES-Gel system.

In May 2002, SkyePharma acquired the entire drug delivery business of Bioglan AB, of Sweden for £3.6 million in cash including acquisition costs and the assumption of £0.4 million of net liabilities. The acquired rights included Bioglan's Biosphere® injectable technology and those rights to DermaStick, Crystalip and ES-Gel topical drug delivery technologies that had remained with Bioglan after the January 2001 development and commercialization licensing agreement with Bioglan.

On January 14, 2003, SkyePharma announced a strategic investment in Micap PLC ("Micap"), a private company providing patented micro-encapsulation technology to the food, cosmetic, agrochemical and pharmaceutical industries. Micro-encapsulation technology is a process by which tiny droplets or particles of liquid or solid material are surrounded or coated with a continuous film of polymeric material. These micro-capsules have a number of benefits such as converting liquids to solids, separating reactive compounds, providing environmental protection and improved ease of

handling. The Company subscribed for 2,500,000 Ordinary Shares at a price of 80 pence as part of a fundraising of 3,125,000 Ordinary Shares approved by Micap's shareholders at an Extraordinary General Meeting on January 13, 2003. The remaining 625,000 Ordinary Shares were subscribed for by the Sigma Technology Venture Fund, an existing shareholder. SkyePharma has also obtained an option for the use of the technology for drug delivery. During 2003, SkyePharma will investigate the pharmaceutical applications of Micap's micro-encapsulation technology, particularly in the areas of oral and topical drug delivery. SkyePharma can exercise its option to complete a technology access and license agreement, the terms of which are agreed, at the end of this period. In addition SkyePharma will be paid for the services it performs during the investigation period.

On June 28, 2003, Micap will hold an extraordinary general meeting to seek shareholders' approval of a proposal for conducting an initial public offering of its shares in connection with a listing on the Alternative Investment Market of the London Stock Exchange PLC. The Company and Sigma Technology Venture Fund, another existing shareholder, have irrevocably undertaken to vote in favor of this proposal.

BUSINESS OPERATIONS

Overview

The Company is a specialty pharmaceutical company, using its multiple drug delivery technologies to create a product pipeline for out-licensing to marketing partners. The Company develops novel therapeutic drugs based on its five technology platforms for delivering drugs to the human body; oral, injectable, inhalation, topical and enhanced solubilization.

The following table shows the Company's turnover, operating profit and net profit for the three years ended December 31, 2002.

	Year Ended December 31, 2000	Year Ended December 31, 2001	Year ended December 31, 2002
		(in £ thousands)	
Turnover	24,292	46,126	69,573
Operating (loss)/profit	(17,984)	(5,099)	4,716
Retained (loss)/profit	(19,690)	(9,452)	1,109

Oral

A significant part of the Company's business is developing applications of its Geomatrix technologies. Geomatrix is a range of technologies by which drugs taken orally in tablet form are formulated so as to control the amount, timing and location of the release of the drug in the body. There are currently eight Geomatrix technologies designed to meet a wide range of therapeutic objectives. The technologies are flexible and can be modified to apply to a variety of pharmaceutical products.

The Company collaborates with large pharmaceutical companies to develop Geomatrix formulations of their proprietary products. The company focuses its research and development efforts on the reformulation of existing drugs using its technologies rather than the discovery of new chemical compounds. In reformulating an existing drug, the Company seeks to enhance the therapeutic and commercial value of the product by creating an improved outcome formulation that may mitigate certain side effects, reduce dosing or help protect against competition from generic drug products. There are six drugs currently being marketed that use the Company's Geomatrix technologies: one in Europe, Canada and other territories in Africa, Asia and Latin America (Xatral 10mg OD®), one in the United States (Paxil®CR), two in Germany (Cordicant-Uno® and Diclofenac-ratiopharm-uno®), one in Switzerland (Madopar DR®) and one in Belgium (Coruno®). In June 2003, the FDA approved Xatral OD for marketing in the United States as UroXatral . The Company is also collaborating with several other pharmaceutical companies to commercialize its

Geomatrix technologies, including King Pharmaceuticals Inc., Merck KGaA and GlaxoSmithKline PLC. There are currently three drug candidates using Geomatrix technologies in human studies.

For further information see "Drug Delivery Platforms Oral" below.

Injectable

The Company's primary injectable technology is DepoFoam. The Company has combined many drugs with DepoFoam and performed studies on these combinations showing that they often achieve sustained controlled release of the drugs. These features allow the Company to develop new formulations of drug products aimed at treating different diseases and symptoms or allow for more convenient administration by reducing the number or frequency of injections. The potential products include drugs which have already been shown to be useful or potentially useful in humans as well as new drugs in development at other pharmaceutical companies which may potentially benefit from DepoFoam. The Company does not conduct research and development to discover new drugs.

The Company's first approved drug product using its DepoFoam technology is DepoCyt. DepoCyt combines DepoFoam with cytarabine, a drug used for the treatment of cancers which have spread to the fluid surrounding the brain and spinal cord. DepoCyt is currently marketed by Enzon in North America. The Company's second potential injectable drug product is DepoMorphine, a sustained- release encapsulated morphine sulphate, for acute pain management following surgery. DepoMorphine has been licensed to Endo for the North American market. In addition to DepoCyt and DepoMorphine, the Company is currently working on DepoBupivacaine, a DepoFoam formulation of the local anaesthetic bupivacaine, for the treatment of regional pain and a DepoFoam formulation of Interferon alpha-2b with GeneMedix. The Company is also evaluating, in conjunction with undisclosed corporate partners, DepoFoam formulations of several additional compounds, including macromolecules.

The Company's second sustained-release injectable technology is the Biosphere drug delivery system. In 2003, the Company announced that the Biosphere technology had been successfully used in pre-clinical studies to deliver a protein drug human growth hormone over an extended period of time. In addition to the human growth hormone, the Company is also evaluating, in conjunction with Chugai Pharmaceutical Co. Ltd ("Chugai") and other undisclosed corporate partners, Biosphere formulations of other proteins and peptides.

For further information see "Drug Delivery Platforms Injectable" below.

Inhalation

The Company is developing advanced technologies to deliver medicines via a patient's lungs without relying on CFC-based propellants, which are considered environmentally harmful. The Company is working with two types of such inhalation systems. The first is a metered dose inhaler ("MDI") that relies on non-CFC propellants to deliver the required therapy. The other is a dry powder inhaler ("DPI"), marketed as "SkyeHaler," that requires no propellant but instead is breath-activated to deliver drugs in a fine powder suspension. In its MDI development work, the Company focuses on the formulation of drugs for use in MDIs manufactured by others. In its dry powder inhaler development work, the Company focuses both on the development of the device and dry powder formulation.

The Company currently has the aerosol formulations of formoterol, budesonide and salbutamol in various stages of development for use with non-CFC MDIs. The Company has developed a DPI device with the compound formoterol with Novartis, the Foradil Certihaler, which has completed Phase III clinical trials and for which an NDA was submitted to the FDA and to health authorities in the EU. In December 2002, the Company has entered into three collaborative arrangements to commercialize its inhalation drug delivery technology and is developing two further products internally.

For further information see "Drug Delivery Platforms Inhalation" below.

Topical

The Company's topical drug delivery technologies are primarily designed to maintain efficacy and localize delivery of drugs to the skin for the treatment of a variety of skin disorders. The Company's portfolio of topical drug delivery technologies consist of HA-based technologies, Crystalip, DemaStick and the ES-Gel system.

The first approved drug product using the Company's HA-based technology is Solaraze , a topical gel used to treat actinic keratosis, a pre-cancerous skin condition caused by over-exposure to the sun. Solaraze is licensed to Quintiles Transnational Corp. ("Quintiles") in the United States and to Shire Pharmaceuticals plc ("Shire") in Europe and Australia. It is currently marketed in the United States and various countries in Europe. In addition to Solaraze, the Company has been developing Hyclinda, a topical gel to treat acne. The Company is developing various other early stage products under its Crystalip, DermaStick and ES-Gel systems.

For further information see "Drug Delivery Platforms Topical" below.

Solubilization

Solubility of drugs is an essential factor for all drug delivery systems, independent of the route of administration. Poor solubility leads to a range of problems including poor bioavailability, increased toxicity, variability of absorption when taken with food and poor efficacy. The Company believes that a large number of existing marketed drugs and newly synthesized compounds have solubility problems.

The Company's solubilization technologies consist of two complementary technologies, the nano-particulate and the IDD technologies. Nano-particulate technology aims to improve a drug's solubility by reducing the size of the particules. It has been demonstrated in laboratory testing that the saturation solubility of many drugs can be improved by reducing particle size below one micron in diameter.

The Company is using its solubilization technology platform to enhance the uptake and safety of water-insoluble drugs across a broad range of therapeutic classes including anesthetics, anti-cancer agents and immune suppressants. It is intended that the solubilization technologies will be used to complement and enhance the Company's other drug delivery systems.

The Company currently has a number of proprietary IDD based products in various stages of clinical development including propofol, fenofibrate, and busulfan. In 2002 the Company granted an exclusive license to Endo to the U.S. and Canadian marketing and distribution rights for Propofol IDD-D . The Company has disclosed alliances with Baxter Healthcare Corporation ("Baxter"), Schering Plough Corporation, and other undisclosed partners on drugs formulated using IDD technology.

For further information see "Drug Delivery Platforms Solubilization" below.

Strategy

The Company has a dual strategy: to become the world's leading specialty pharmaceutical company powered through excellence in drug delivery, and to utilize this expertise and its multiple delivery technologies to create a product pipeline for out-licensing to marketing partners. In addition the Company will continually strive to maintain its leadership position in drug delivery. The Company's strategy for achieving these objectives consists of the following elements:

Selectively Fund a Number of Key Projects to a Later Stage of Development. The Company's strategy in recent years has been to take certain products to a late stage of development, prior to licensing the products to marketing partners. This has allowed the Company to increase its share of the potential revenue streams from these products. An example of this is DepoMorphine, a product the Company developed through from early stage development to Phase III clinical trials prior to entering into an out-licensing arrangement with Endo for the North American marketing rights in December 2002.

Develop Existing and New Collaborative Agreements. In order to increase the market exposure of its products and to capitalize on its collaborative partners' market position and distribution capabilities, the Company intends to continue to develop its projects with its existing collaborative partners and to seek new partners. The Company's existing collaborative arrangements typically provide for a customer-funded development project and contemplate a licensing arrangement (which may be entered into at the same time as the development project or at a later date) under which, if a project is commercialized by the collaborative partner, the Company receives license fees and royalty payments from product sales. In recent years the Company has focused on undertaking additional value added services, such as assuming responsibility for development and regulatory activities, and retaining manufacturing rights that has allowed it to increase its share of the potential revenue stream from these collaborations.

Commercialization of the Company's Core Technologies. The Company currently has a portfolio of eight Geomatrix systems, of which four have been commercialized. The Company is focusing on developing and commercializing the remaining four systems, either in conjunction with its collaborative partners or through its own internal development activities. Similarly, of the Company's two injectable depot technologies, DepoFoam and Biosphere, only DepoFoam has to-date been commercialised. The Company will be seeking to develop and commercialise Biosphere and its other drug delivery technologies.

Realize Research and Development Synergies between the Company's Technologies. The Company believes that additional shareholder value can be created by the realization of research and development synergies between the Company's technologies. For example, the DepoFoam and Biosphere technologies' ability to encapsulate a wide spectrum of water-soluble drugs, involving small molecules, proteins and peptides, could expand the scope of the Company's inhalation technologies, particularly in the field of proteins and peptides. Additionally, the Company's solubilization technologies will be used to complement and enhance the Company's other drug delivery systems.

Broadening the Company's Drug Delivery Technology Base. The Company's pharmaceutical customers are increasingly requesting a broader range of delivery solutions. The Company is currently well placed with its oral, injectable, inhalation, topical and enhanced solubilization technologies. The Company intends to seek to acquire additional add-on technologies which are complementary to its existing technologies. Management intends to focus on technologies it believes are capable of commercial realization in the near term and will also seek to acquire or license new drug delivery platforms and enabling technologies.

Seek to Retain Manufacturing Rights on Future Collaborations. The Company believes that retaining manufacturing rights to its products should enable it to capture greater revenue and generate production economies of scale that may not be available to pharmaceutical companies seeking to apply the Company's technologies to only one or a few products. The Company employs personnel who specialize in manufacturing, to commercial quantities, products utilizing the Company's technologies.

Drug Delivery Platforms

This section provides a more detailed description of the Company's various drug delivery platforms and their application to particular drugs and drug candidates.

Oral

The Geomatrix Oral Technologies

The original Geomatrix technology was developed by a team of researchers at the University of Pavia in Italy in the early 1980s. Subsequently, the Company acquired the technology and pursued the development of the Geomatrix platform of oral controlled-release systems. The effort has

produced a platform of proprietary Geomatrix controlled-release systems that can be applied to a broad range of drugs on a commercial scale.

The Geomatrix systems control the amount, timing and location of the release of drug compounds in the human body. Geomatrix technologies can improve the efficacy of orally administered drugs and enhance compliance by patients with prescribed medical treatments by permitting the drug to be taken less frequently, by reducing side effects and by causing the drug to be released at more specific locations within the body. This is achieved through the construction of a tablet with two basic components: a core containing the active drug or drugs in an hydrophillicmethylcellulose, or "HPMC", matrix formulation and one or two additional barrier layers. The HPMC matrices govern the release profile of a drug dependent on the viscosity of the HPMC used whilst the barrier layers control the surface area diffusion of the drug or drugs out of the core. The "release profile" refers to the rates at which a drug tablet releases the active drug component over the period of time after the drug is taken. In addition, the tablet may be coated if, for example, this would ease any gastric irritation that otherwise would be caused by the drug compound, or for other functional purposes.

The combination of different chemical components in the core and barrier layers, each with different rates of swelling, gelling and erosion, allows the production of tablets with a wide range of predictable and reproducible drug release profiles. The rate of drug release is a function of the viscosity of the HPMC and the exposed surface area from which the drug diffuses. When the tablet is first swallowed, the drug concentration is high but the surface area is small; as time goes by and the core swells, the surface area expands to compensate for the decrease in drug concentration.

The Company believes that the Geomatrix systems enjoy a competitive advantage in the drug delivery industry because of the ease with which Geomatrix tablets can be manufactured. Unlike certain competing drug delivery systems that require off-site, customized production equipment and methods, Geomatrix tablets can be manufactured by readily available equipment that can be incorporated into widely used pharmaceutical production processes. In this way, Geomatrix may afford the pharmaceutical partner direct control over its production strategy while other drug delivery systems may entail incremental risks or costs related to their off-site, customized production requirements.

In addition to ease of manufacturing, the Company believes that the key features of the Geomatrix technologies are as follows:

Custom Design. Drugs can be formulated to deliver the release profile required by the client pharmaceutical company and drugs can be combined with other active substances to improve their effectiveness.

Versatility. Geomatrix can be applied to a wide range of small molecule drugs, including some with poor water solubility, and can target the site of release.

Controlled Rate of Diffusion. Geomatrix controls the rate of drug diffusion throughout the release process, ensuring 100% release of the active drug.

Reproducibility. Use of conventional high speed tableting processes allows a high degree of product consistency and uniformity.

Complete Disintegration. Geomatrix tablets disintegrate completely in the patient's digestive system and leave no solid residue.

Release Profiles. The flexibility of the Geomatrix technologies has enabled the Company to create a number of release profiles suitable for a broad variety of pharmaceuticals.

The following sets forth a brief description of the Geomatrix systems.

Zero Order Release. The Zero Order Release system provides a constant rate of drug release over a defined period of time. It is used primarily for drugs with short half-lives so that constant blood levels of the active drug compounds can be maintained with fewer doses. The Company has three approved Zero Order Release formulations currently on the market:

Cordicant-Uno in Germany, Coruno in Belgium and Xatral OD in several European countries. Paxil CR, currently marketed in the United States, has been developed using a combination of the Zero Order and Positioned Release technologies.

Binary Release. The Binary Release system is used to provide the controlled-release of two different drugs in a single formulation. The drugs may be released at different rates and times, if desired. This system is designed for drugs that work best in combination. The Company has one Binary Release formulation that was approved and launched in the third quarter of 1997: Madopar DR in Switzerland.

Quick Slow Release. The Quick Slow Release system provides a quick burst of drug release followed by a constant rate of release over a defined period of time. It is used primarily in drugs, such as arthritis medications, in which it is desirable to have an initial burst of release to achieve maximum relief in a short amount of time followed by a constant rate of release for sustained therapy. The Company has one approved Quick Slow Release formulation currently on the market: Diclofenac-ratiopharm-uno in Germany.

Slow Quick Release. The Slow Quick Release system provides an initial constant rate of release followed by a quick burst of drug release at a predetermined time. This release profile is designed for medications to treat diseases, such as angina, that would benefit from increased therapy when the patient is sleeping because of the high incidence of nocturnal attacks.

Positioned Release. The Positioned Release system is designed to deliver the tablet to a predetermined position in the digestive system before it begins to release the active drug compounds. This system is best suited to drugs for which it is desirable to begin release at a certain point in the gastrointestinal tract, for example in the case of drug compounds that are best absorbed by the human body at particular points in the upper gastrointestinal tract. Paxil CR, currently marketed in the United States, has been developed using a combination of the Zero Order and Positioned Release technologies.

Accelerated Release. The Accelerated Release system provides a constantly accelerating rate of drug release. This system is well suited for drugs such as H2-receptor antagonists that are preferentially absorbed in the upper part of the gastrointestinal tract.

Delayed Release. The Delayed Release system provides a predetermined time lag before it begins releasing drug molecules. This system is designed for drugs such as certain cardiovascular medications for which the desired dosing time may be several hours after the patient takes the drug.

Multiple Pulse. The Multiple Pulse system provides an initial quick burst of drug release followed by a predetermined period of no release followed by a second burst of drug release. This system is designed for treating diseases that require suppression or activation of a specific receptor twice a day where the receptor needs to be reset between drug interaction, such as appetite suppression and Attention Deficit Disorder. To date, the Multiple Pulse system has only been subject to limited in vivo (human) clinical testing.

Products formulated with the Zero Order, Binary Release, Quick Slow and Positioned Release systems are currently on the market. There can be no assurance, however, that the Company will be able to develop successfully future products incorporating such delivery systems. At present, there are no products on the market that have been formulated with the Company's Slow Quick, Accelerated Release, Delayed Release or Multiple Pulse systems. The Company is actively developing formulations utilizing some of these and other drug delivery systems, but there can be no assurance that these efforts will be successful.

Approved Geomatrix Products

To date, seven Geomatrix formulations of pharmaceutical products have received regulatory approval. Of these products, one is being marketed in Europe, Canada and other territories in

Africa, Asia and Latin America (Xatral 10mg OD), one in the United States (Paxil CR), two in Germany (Cordicant-Uno and Diclofenac-ratiopharm-uno), one in Switzerland (Madopar DR) and one in Belgium (Coruno). On June 16, 2003, the Company announced that the FDA had approved Sanofi-Synthelabo's NDA for Xatral OD, to be marketed in the United States as UroXatral. The U.S. launch of the drug is expected to occur in the second half of 2003.

The following table sets forth certain information regarding the approved Geomatrix products:

Product	Indication	Regulatory Approvals and Year of First Approval	Geomatrix System	Collaborative Partner
Paxil CR	Depression	United States (1999)	Positioned Release/Zero Order	GlaxoSmithKline
Xatral 10mg OD	Genito-Urinary	Europe (2000)	Zero Order	Sanofi-Synthelabo
Madopar DR	Parkinson's Disease	Switzerland (1996)	Binary	Hoffmann-La Roche
Coruno	Angina	Belgium (2002)	Zero Order	Therabel
Cordicant-Uno	Hypertension	Germany (1994)	Zero Order	Mundipharma
Diclofenac-ratiopharm-uno	Arthritis	Germany (1995)	Quick Slow	Ratiopharm
Dilacor® XR	Hypertension and Chronic Stable Angina	U.S. (1992)	Zero Order	Watson

Paxil CR is a modified release version of Paxil/Seroxat (paroxetine HCL) using a combination of the Positioned Release and Zero Order Geomatrix systems. Paxil is an FDA-approved drug that is currently marketed primarily in the United States and Europe and is an immediate release formulation prescribed for central nervous system disorders. According to information published by GlaxoSmithKline on its website, Paxil is its second largest product with worldwide sales in 2002 of £1.9 billion and £1.4 billion in the United States. Paxil CR was filed with the

FDA by SmithKline Beecham (now part of GlaxoSmithKline) in December 1997 and approved by the FDA in February 1999 for the 12.5 and 25mg dosage forms. In early 2001, GlaxoSmithKline, the Company's collaborative partner in the development of Paxil CR, announced that it had received an approvable letter from the FDA for a second CR indication, panic disorder. On April 19, 2002, Paxil CR was launched in the United States for the treatment of central nervous system and panic disorders.

Paxil CR has since been filed for a third indication, social anxiety and for continual usage for a fourth indication, pre-menstrual dysphoric disorder, a severe form of pre-menstrual syndrome. Paxil CR is currently in late stage clinical trials for intermittent usage for pre-menstrual dysphoric disorder. In June 2003, GlaxoSmithKline published the results of two studies on the use of Paxil CR in the treatment of social anxiety disorder and pre-menstrual dysphoric disorder and a third for another potential application, menopausal hot flushes.

Xatral 10mg OD is a once daily Zero Order Geomatrix formulation of alfuzosin used for the treatment of the functional symptoms of benign prostatic hyperplasia, a common condition in men over the age of 50, that was developed in conjunction with Sanofi-Synthelabo. Xatral is available in more than 80 countries world-wide as a two or three times a day formulation. In January 2000, Sanofi-Synthelabo announced that it had received the first batch of European marketing approvals for Xatral 10mg OD ("Xatral OD"). The product is now launched throughout Europe and also in Canada and other territories in Africa, Asia and Latin America.

In December 2000, Sanofi-Synthelabo submitted an NDA with the FDA for Xatral OD. In October 2001, Sanofi-Synthelabo announced that an 'Approvable Letter' had been received from the FDA for Xatral, registered in the United States as UroXatral. Additional data requested by the FDA was filed by Sanofi-Synthelabo in December 2002. On May 29, 2003, Sanofi-Synthelabo announced that the Cardiovascular and Renal Drugs Advisory Committee of the FDA had voted unanimously (with one member abstaining) that the Company's clinical investigations showed that alfuzosin is not associated with a clinically-relevant prolongation of the QT interval. The QT interval is one of the parameters measured in an Electrocardiogram, which reflects the time for the heart to

recharge. On June 16, 2003, the Company announced that the FDA had approved Sanofi-Synthelabo's NDA for Xatral OD, to be marketed in the United States as UroXatral. The U.S. launch of the drug is expected to occur in the second half of 2003. Sanofi-Synthelabo is currently developing Xatral OD for a second indication, acute urinary retention, which is anticipated to be filed in 2003.

Madopar DR is a once per day Binary Geomatrix formulation of levodopa and benzerazide, a combination therapy indicated for the treatment of Parkinson's Disease which is approved for sale in Switzerland. Madopar DR was developed in conjunction with Hoffmann-La Roche AG (part of "Roche"). The Binary Geomatrix formulation of levodopa and benzerazide optimizes patient therapy and convenience by providing for the release of an enzyme inhibitor along with the drug compound without the co-administration of two pills. The Company is manufacturing this product for the Swiss market on behalf of Roche at its facility in Muttenz, Switzerland.

Coruno is a once per day Zero Order Geomatrix formulation of molsidimine, currently marketed in Europe and used to treat angina pectoris, a common symptom of coronary heart disease. Coruno was developed in conjunction with the Therabel Group and was approved by the Belgian regulatory authorities in 2002 for marketing in Belgium. Coruno was launched by Therabel in April 2003. The Geomatrix controlled release technology in Coruno enhances patient compliance and convenience by reducing the dosing requirement to once per day.

Cordicant-Uno is a once per day Zero Order Geomatrix formulation of nifedipine, a calcium channel-blocking agent indicated for hypertension, which is approved for sale in Germany. Cordicant-Uno was developed in conjunction with and is marketed by Mundipharma, a private German pharmaceutical company. The Geomatrix controlled release technology in Cordicant-Uno enhances patient compliance and convenience by reducing the dosing requirement to once per day.

Diclofenac-ratiopharm-uno is a once per day Quick Slow Geomatrix formulation of diclofenac, a nonsteroidal anti-inflammatory drug indicated for the acute and chronic treatment of rheumatoid and osteo-arthritis. Diclofenac-ratiopharm-uno, which is approved for sale in Germany, was developed in conjunction with and is marketed by Ratiopharm, a private German pharmaceutical company. The Geomatrix controlled-release technology in Diclofenac-ratiopharm-uno optimizes patient therapy by providing an initial burst of the drug for quick relief followed by a controlled-release for sustained therapy. It also optimizes patient compliance and convenience by reducing the dosing requirement to once per day.

Dilacor XR is a once per day Zero Order Geomatrix formulation of diltiazem hydrochloride, a calcium channel-blocking agent indicated for hypertension and for the management of chronic stable angina. Dilacor XR was developed in conjunction with Rhône Poulenc Rorer (now part of Aventis Pharma). In June 1997, Rhône Poulenc Rorer granted Watson Pharmaceuticals an exclusive worldwide license to market Dilacor XR. In addition to being approved in the United States, Dilacor XR is also approved for sale in Australia, New Zealand, Korea, the Philippines and Germany. Marketing exclusivity for this product in the United States expired in June 1995. The Company no longer receives royalties from this

product.

Geomatrix Products in Development

There are currently four products in the development process that utilize the Geomatrix technologies. In addition, the Company has a number of projects in earlier stages of development. The following table sets forth certain information regarding some of the products in the Company's development pipeline. For a description of the development process, including definitions for development status stages, see "Research and Development Development Process for Brand-Name Pharmaceuticals".

Product	Modified Release	Therapeutic Category	Development Status	Geomatrix System	Collaborative Partner
Ropinirole	Yes	Central Nervous System	Phase III	Undisclosed	GlaxoSmithKline
Undisclosed #1	Yes	Undisclosed	Phase II completed	Delayed Release	Merck KGaA
Ramipril	Yes	Cardiovascular	Feasibility	Undisclosed	King
Undisclosed #2	Yes	Undisclosed	Feasibility	Undisclosed	Undisclosed

Ropinirole is an FDA-approved drug that is currently marketed as Requip®, primarily in the United States and Europe by GlaxoSmithKline. As it is currently marketed, Requip is an immediate release formulation administered three times daily and is prescribed for Parkinson's disease, a chronic progressive disease in which the degeneration of nerve cells in the brain eventually impairs the ability to control body movements. The Company is currently developing a once-daily version using its Geomatrix technology. The Geomatrix formulation is expected to provide a simplified regime for patients on Requip therapy that will improve patient convenience. The once-daily version commenced Phase III clinical trials in June 2003.

Undisclosed # 1 is a new formulation of a drug being developed for Merck KGaA utilizing the Geomatrix delayed release technology to deliver the dose at a precise time interval after administration. The new formulation being developed by the Company is in the scale-up/ bio-batch stage of development.

Ramipril is an FDA-approved drug that is currently marketed in the United States and Puerto Rico as Altace® by King Pharmaceuticals, Inc. for the treatment of hypertension and post heart attack congestive heart failure. The Company is developing a modified-release formulation which should provide the product with extended duration of action and improved bioavailability. The new formulation being developed by the Company is in the feasibility stage.

Undisclosed # 2 is a new formulation of a drug being developed for an undisclosed partner utilizing the Geomatrix technology to control the release of the drug from the tablet and at the same time increase the drug's bioavailability. The new formulation being developed by the Company is in the feasibility stage.

Other Oral Products in Development

NK-104 is a new lipid-lowering agent that has been developed by Kowa and has received marketing authorization in Japan. Phase II trials have been completed in Europe and have commenced in the United States. NK-104 has been developed from a class of compounds called statins that have been shown to significantly reduce mortality in patients with high cholesterol and heart disease. The Company is responsible for formulation development and scale-up for certain formulations of NK-104 which the Company anticipates will lead to the commercial manufacture of the compound.

Injectable

DepoFoam Injectable Technologies

DepoFoam consists of tiny, lipid-based particles composed of hundreds to thousands of discrete water-filled chambers, containing the encapsulated drug, with each chamber separated from adjacent chambers by a lipid membrane. The particles are suspended in saline and the water-filled chambers containing the active. DepoFoam formulations can be delivered into the body by a number of routes, including under the skin, within muscle tissue, into brain and spinal fluid, within joints and within the abdominal cavity. Because the components of DepoFoam are similar to lipids normally present in the body, the material is biodegradable and biocompatible. Typically, a DepoFoam particle consists of less than 10% lipid, with the remaining 90% consisting of drug in solution. The resulting DepoFoam formulation is stored under refrigeration in ready-to-use form.

SkyePharma Inc. has tested DepoFoam formulations that release drugs over a period of days to weeks with the period of release defined by characteristics of DepoFoam and the drug. SkyePharma Inc. believes drugs may be released from DepoFoam particles as the drugs diffuse through the walls, by gradual erosion of the particles, and by processes involving the rearrangement of membranes. The nature of drug release may also be determined by the characteristics of each drug molecule. SkyePharma Inc. has demonstrated that DepoFoam can be used to encapsulate a wide spectrum of drugs, including small molecules, proteins, peptides, antisense oligonucleotides and DNA, aimed at treating different diseases and symptoms.

Advantages of DepoFoam

The Company believes DepoFoam addresses many of the limitations associated with traditional methods of delivering drugs. Most drugs are administered orally, by injection in intermittent and frequent doses or by continuous infusion. These latter methods of administration are not ideal for several reasons, including difficulty in achieving appropriate drug levels over time, problems with side effects, high costs due to frequent or continuous administration and poor patient compliance. Furthermore, innovations in biotechnology have led to an increase in the number of large-molecule protein and peptide drugs under development. These drugs, because of their large molecular size and susceptibility to degradation in the gastrointestinal tract or in the blood, must usually be administered by multiple injections often in a hospital or other clinical setting.

The Company believes that DepoFoam's key advantage over traditional methods of drug delivery, including injections and oral administration, is that the sustained-release characteristics of DepoFoam allow drugs to be administered less frequently and more conveniently. To attain the desired effect, conventional drug delivery often results in a dosage that delivers an initially high level of the drug followed by a sharp decline over a relatively short period of time, whereas DepoFoam formulations can provide a more consistent drug level over an extended period. As a result, DepoFoam products can potentially improve safety and effectiveness. For example, DepoCyt clinical trials have shown that DepoCyt has a therapeutic life of up to two weeks after a single intrathecal injection compared to less than one day with unencapsulated cytarabine.

The Company believes that key features of DepoFoam, including lower initial drug levels and delivery of appropriate drug levels over an extended period of time, make it superior not only to traditional methods of delivering drugs, but also to other sustained-release delivery formulations. The Company believes DepoFoam may:

Enhance safety and efficacy. DepoFoam drug delivery may improve the ratio of therapeutic effect to side effects by decreasing the initial concentrations of drug associated with side effects, while maintaining levels of drug at therapeutic, sub-toxic concentrations for an extended period of time.

Improve convenience and lower overall treatment costs. DepoFoam formulations of drugs may offer cost savings by reducing the need for continuous infusion, the frequency of administration and the number of visits a patient must make to the doctor.

Expand types of drugs which can be delivered over an extended period of time. DepoFoam may be able to deliver proteins, peptides and nucleic acids more effectively.

Expand indications of currently marketed drugs. The appropriate release of drugs from a DepoFoam formulation may allow such drugs to be marketed for indications where they are currently not thought to be useful because of the limitations of current delivery methods.

Improve products through reformulation. DepoFoam may offer the potential to produce new formulations of generic products that may be differentiated from the nonsustained-release versions by virtue of reduced dosing requirements, improved effectiveness, additional applications or decreased side effects.

Approved DepoFoam Injectable Products

DepoCyt is the first product, utilizing the Company's DepoFoam Injectable technology, to have received regulatory approval and to be marketed. DepoCyt combines the Company's DepoFoam with cytarabine, a drug used to treat neoplastic meningitis from lymphomas and solid tumors. It is currently marketed in North America by Enzon for the treatment of lymphomatous meningitis and is licensed for distribution to Nippon-Shinyaku in Japan.

Background

Cancer from solid tumors, leukemia (a form of cancer involving white blood cells) or lymphomas (a form of cancer involving tissues of the lymphatic system) can spread to the soft tissue membrane of the brain and spinal cord. This type of cancer is called neoplastic meningitis. Because of the blood-brain barrier, drugs in the bloodstream do not penetrate well into the fluid which surrounds the brain and spinal cord. Thus, when cancer cells spread to this membrane, the most effective therapy is to inject anti-cancer drugs directly into the fluid which surrounds the brain and spinal cord. Cytarabine is one of several drugs most commonly used for this therapy. Cytarabine acts by inhibiting a vital enzyme in DNA synthesis, resulting in death of a dividing cell. Therefore, the best results are obtained when the drug is localized in the vicinity of dividing cancer cells for an extended period.

Cytarabine does not last long in the fluid which surrounds the brain and spinal cord. The result is that neoplastic meningitis cannot be treated effectively without the use of repeated injections into the space between the brain and/ or spinal cord and the membrane which surrounds them. These injections are inconvenient and uncomfortable for patients, require physician supervision and increase the risk of infection. Because of these and other factors, the disease is often under-diagnosed and frequently left untreated. Without effective treatment, life expectancy for patients diagnosed with this disease is between two and four months. Clinical trials to date have shown that DepoCyt maintained concentrations of cytarabine in the fluid which surrounds the brain and spinal cord for up to two weeks after a single injection as compared to less than one day with traditional injections of cytarabine. As a consequence, the use of DepoCyt results in less frequent injections and may extend effective levels of the drug in the space between the brain and/ or spinal cord and the membrane which surrounds them.

Clinical Development

DepoCyt was developed in collaboration with Chiron Corporation in the United States and until June 2000 with Pharmacia & Upjohn S. p. A., an affiliate of Pharmacia Corporation. Since April 1994, SkyePharma Inc. has been conducting clinical trials of DepoCyt for the treatment of these cancers.

In April 1997, SkyePharma Inc. completed the filing of an NDA for the treatment of cancers which have spread to the fluid surrounding the brain and spinal cord from solid tumors with the FDA. In December 1997, an advisory committee to the FDA declined to recommend approval of DepoCyt for the treatment of these cancers. In April 1998, SkyePharma Inc. filed an amendment to

its NDA which provided information on twice the number of patients included in the original filing. In May 1998, the FDA informed SkyePharma Inc. that the amended new drug application did not contain adequate information to support approval for DepoCyt for the treatment of these cancers. In August 1998, the FDA sent a letter to SkyePharma Inc. inviting it to submit an NDA for DepoCyt for the treatment of cancers which have spread to the fluid surrounding the brain and spinal cord from the lymphatic system. This NDA was filed in October 1998. In April 1999, the FDA approved DepoCyt for the treatment of neoplastic meningitis from lymphomas and the product was launched in the United States in May 1999.

In October 1999, SkyePharma Inc. discovered that two lots of DepoCyt did not meet specifications and recalled these lots. Investigations identified that unannounced changes in a supplier's manufacturing process for a raw material resulted in product which did not meet all specifications throughout the shelf-life. SkyePharma Inc. and Chiron Corporation voluntarily withdrew DepoCyt from the market. There were no adverse events attributed to the recalled batches, and the product was made available to patients on a compassionate basis. In March 2001, the FDA gave clearance to return DepoCyt to the market.

In November 1999, SkyePharma Inc. received marketing approval for DepoCyt from the Canadian regulatory authorities for the treatment of neoplastic meningitis from lymphomas and solid tumours. The Canadian marketing and distribution rights were licensed to Paladin Labs Inc.

in June 2000.

Pharmacia Corporation filed for marketing approval of DepoCyt to be used in the treatment of cancers which have spread to the brain and spinal cord from both the lymphatic system and solid tumors in Europe but subsequently withdrew the application until additional data could be provided. In October 1999, Pharmacia Corporation refiled for marketing approval in Europe and its filing was accepted by the regulatory authority. In June 2000, Pharmacia Corporation notified the Company that it was terminating the marketing and distribution agreement with the Company for DepoCyt. Pharmacia Corporation assigned the European marketing application to the Company, and the Company continued to pursue European marketing approval.

In April 2001, the Company received notification that the European Committee on Proprietary Medicinal Products ("CPMP") had recommended the granting of marketing authorization for DepoCyt, marketed in Europe as DepoCyte , for the treatment of neoplastic meningitis from lymphomas. The CPMP suggested certain modifications to the DepoCyt manufacturing facility to improve personnel and materials flows. These modifications have been completed. The CPMP did not suggest any alterations to the DepoCyt manufacturing equipment or production process. In August 2001, the European Commission ratified the recommendation received from the CPMP by granting marketing authorization for DepoCyte throughout the European Union for the treatment of neoplastic meningitis from lymphomas.

Marketing Partners and Licensing

In November 2002, the Company re-acquired the DepoCyt marketing, distribution and sales rights for the United States from Chiron Corporation in return for an undisclosed cash payment, and for Canada from Paladin Labs Inc for a nominal sum. In December 2002, the Company licensed the North American rights to DepoCyt to Enzon. Enzon paid a license fee of $12 million. The Company will manufacture DepoCyt and Enzon will purchase finished product at 35% of net sales, which will be reduced should a defined sales target be exceeded. The Company is also entitled to milestone payments based on the achievement of certain sales levels and the approval of additional indications.

In June 2001, the Company licensed the marketing rights for DepoCyte in Europe and the Philippines to Elan and the rights for DepoCyt in Japan and Taiwan to Nippon-Shinyaku. In association with an agreement with Elan for the return of rights to DepoCyte in Europe and the Philippines, the Company anticipates concluding a relicensing agreement for the European DepoCyte rights in the near future.

Additional Territories and Indications

The Company is currently conducting a Phase IV clinical trial, the results of which should provide data to support a claim for treatment of neoplastic meningitis associated with solid tumours in the United States and Europe.

DepoFoam Injectable Products in Development

The table below summarizes DepoFoam products currently under development. The stages of the development process: pre-clinical, Phase I, Phase II and Phase III are explained under "Research and Development Development Process for Brand-Name Pharmaceuticals".

Product (Active Compound)	Therapeutic category	Development Status	Collaborative Partner
DepoMorphine (morphine)	Acute Pain	Phase III completed	SkyePharma
DepoBupivacaine (bupivacaine)	Local Anesthetic	Phase I E.U. completed	SkyePharma
Interferon alpha-2b	Anti-viral/Oncology	Pre-clinical	GeneMedix

DepoMorphine

The Company is developing DepoMorphine for use in moderating acute pain following surgery. This product is intended for administration into a space surrounding the spinal cord (the epidural space) and may provide up to two days of pain relief following surgery. DepoMorphine may replace repeated administration of pain medicines and use of patient controlled analgesia devices.

In December 1996, SkyePharma Inc. filed an investigational new drug application with the FDA to begin human studies of DepoMorphine for the management of acute pain following surgery. In December 1997, SkyePharma Inc. completed a Phase I dose-escalation study that assessed the safety and level of drug exposure in the blood of single doses of DepoMorphine administered to healthy volunteers.

In February 2000, the Company announced that in Phase II clinical trials, DepoMorphine, when given to patients as a single pre-operative epidural injection using hip replacement surgery as the pain model, showed a statistically significant dose-related reduction in post-operative fentanyl usage and pain intensity scores relative to placebo for up to 48 hours. For patients requesting post-operative fentanyl, pain intensity at time of first request was rated "severe" in 57% of placebo patients but rated "severe" in only 21%, 9% and 4% in the patients dosed with 10mg, 20mg and 30mg of DepoMorphine respectively.

In January 2001, the Company announced that it had started its Phase III clinical trials for DepoMorphine. The last Phase III study was completed in March 2003. The clinical development program for DepoMorphine involved four separate pain models involving nearly 1000 patients. In the two pivotal trials, in hip surgery and lower abdominal surgery, DepoMorphine demonstrated sustained dose-related analgesia and achieved its primary endpoint (superiority over study comparators in terms of total demand for opioid analgesics after surgery) with a high degree of statistical significance. DepoMorphine also achieved statistical significance on several secondary endpoints such as patient perception of pain intensity and adequacy of pain relief. In two related Phase IIb trials, DepoMorphine was significantly better than study comparators in a caesarean section study and approached statistical significance in a knee arthroplasty study. In the latter study, the primary endpoint was recalled pain intensity. DepoMorphine did achieve a high degree of statistical significance in total demand for opioid analgesics after surgery, a secondary endpoint in the knee arthroplasty trial but the primary endpoint in the three other studies. SkyePharma expects to file DepoMorphine with the FDA in mid 2003 and with the European agency in late 2003.

In December 2000, the Company entered into an agreement with the Paul Capital Royalty Acquisition Fund, L. P. ("Paul Capital"). Under the agreement, Paul Capital has provided $30 million between 2000 and 2002 in return for the sale of a portion of potential future royalty and revenue streams from four products from the Company's pipeline. The monies will be used to fund the

clinical development of DepoMorphine. Details of the agreement with Paul Capital are explained under "Collaborative Arrangements Other Collaborative Arrangements" below.

In December 2002, the Company entered into a development and commercialization agreement under which Endo Pharmaceuticals Inc. received an exclusive license to the U.S. and Canadian marketing and distribution rights for two of the Company's patented development products, DepoMorphine and Propofol IDD-D, a product using the Company's IDD solubilization technology, with options for other development products. In return the Company received a $25 million upfront payment in respect of DepoMorphine. In addition, the Company may receive further milestone payments totaling $95 million which include total milestones of $10 million for DepoMorphine through FDA approval. The total further comprises a $15 million milestone payment when net sales of DepoMorphine reach $125 million in a calendar year, and a $20 million milestone payment when net sales of DepoMorphine reach $175 million in a calendar year. The Company will also receive a share of each product's sales revenue that will increase from 20%, to a maximum of 60% of net sales as the products' combined sales achieve certain thresholds in any given year. The agreement provides for the parties to work together and complete the necessary clinical, regulatory and manufacturing work for regulatory approval of DepoMorphine and Propofol IDD-D in the United States and Canada. The Company will be primarily responsible for clinical development up to final FDA approval and for product manufacture, including all associated costs. Upon approval, Endo will market each product in the United States and Canada with the Company as supplier. Endo will be responsible for funding and conducting and post-marketing studies and for selling and marketing expenses.

DepoBupivacaine

The Company is developing DepoBupivacaine, a DepoFoam formulation of the widely used local pain medicine bupivacaine for controlling post-surgical or post-injury pain. Pain associated with surgery or injury is often treated with local anesthetics. However, the usefulness of local anesthetics is frequently limited by their short period of effectiveness following administration which results in recurrence of pain and the need for repeated drug administration by a medical professional. One dose of DepoBupivacaine is expected to provide more than 24 hours of regional pain relief, compared to two to six hours following conventional bupivacaine administration.

SkyePharma Inc. has successfully encapsulated bupivacaine into DepoFoam. Initial studies have shown that DepoBupivacaine is released slowly from the site of injection, resulting in prolonged duration (more than 24 hours) of pain relief following a single-dose administration. The Company completed a Phase I clinical trial in Europe for DepoBupivacaine during 2001.

The Company believes that a DepoFoam formulation of a local anesthetic may complement its current DepoMorphine program and that the DepoMorphine and local anesthetic formulations may give physicians improved drugs to manage post-operative pain.

Under the development and commercialization agreement with Endo Pharmaceuticals Inc. for DepoMorphine and Propofol IDD-D signed in December 2002, Endo has an option to obtain commercialization rights for DepoBupivacaine, when the Company successfully completes its

Phase II trials, as well as other of the Company's products formulated using the DepoFoam technology successfully developed for the prophylaxis or treatment of pain.

Interferon alpha-2b

In June 2002, the Company signed a Joint Agreement with GeneMedix plc to develop an extended release formulation of interferon alpha-2b using the Company's DepoFoam technology. Interferon alpha-2b is already accepted as a part of the standard therapy in the treatment of Hepatitis C and Hepatitis B infection, and as an adjunct to chemotherapy in certain forms of cancer. Therapeutic proteins are easily degraded inside the body. An extended release DepoFoam formulation of interferon alpha-2b has the possibility to deliver therapeutic doses of the protein in a controlled manner for a period up to 28 days from a single injection. This would represent a

considerable benefit to patients with Hepatitis C whose current treatment may require injection of interferon alpha-2b up to every seven days.

The Company had already formulated interferon alpha-2b with its DepoFoam technology. Reflecting this, and the value of DepoFoam licensing rights, SkyePharma received non- refundable consideration of £3.25 million. The consideration was in the form of an unsecured Convertible Loan Note, issued by GeneMedix, carrying a 5% coupon, which is convertible at any time into between approximately 8.3 million and 11.2 million fully paid, ordinary GeneMedix shares. GeneMedix has the option to redeem the Note for cash in certain circumstances. In addition, SkyePharma will receive undisclosed milestones payable against progress through clinical development. The two companies will assume equal shares of further development and manufacturing costs and will also share potential milestones and royalties received from a third party on the eventual out-licensing and sales of the product.

New Product Feasibility Programs

The Company is also evaluating with undisclosed corporate partners, DepoFoam formulations of several additional compounds including macromolecules. These projects are all at the pre-clinical stage of development. The objectives of these programs are to:

- determine whether DepoFoam can be combined with the candidate drugs;
- evaluate drug release characteristics in the lab and in animal tissue; and
- conduct initial effectiveness and/ or safety studies in animal models to demonstrate potential clinical utility and advantages of the DepoFoam formulations.

Biosphere Technologies

The Company believes that the Biosphere injectable technology will complement its DepoFoam sustained-release injectable expertise by providing additional delivery options for proteins and peptides. Proteins and peptides cannot be given orally because they will not survive passage through the digestive system. However the short half-life of most protein and peptides means that injections usually need to be given frequently and as injections are unpopular with patients, compliance tends to be poor.

The Biosphere drug delivery system, acquired in May 2002, provides sustained-release of injectable proteins and peptides. The technology encapsulates the drug substance in highly purified starch in microscopic spheres that are then coated with a copolymer of lactic and glycolic acid. After injection, the coating and core erode and the drug content is released over a period that can be controlled from days to months. In contrast with conventional microspheres, the coating used in Biosphere does not contain any drug so there is a low "burst" even at high drug loadings. The Biosphere technology achieves encapsulation of protein drugs under gentle conditions that avoid exposure of the protein to organic solvents that can often cause structural changes.

The first human administration of coated and uncoated starch Biosphere microspheres containing no active drug took place in 2001. The study involved 16 subjects and no significant adverse reactions were reported. In February 2003 the Company announced that the Biosphere technology had been successfully used to deliver a protein drug over an extended period of time. A paper in Drug Delivery Systems & Sciences (Vol. 2, No. 4, 103-109) by scientists from the Company's research unit in Malmo, Sweden describes pre-clinical studies on the release of human growth hormone over a period of two weeks from a single injection. In the study, the human growth hormone was encapsulated with high efficiency and released evenly throughout the period. Importantly the gentle encapsulation process and the inert conditions within the Biosphere

particles preserved protein structure and function. It is anticipated that the human growth hormone, utilizing Biosphere technology, will enter clinical trials by the end of 2003. In addition to the human growth hormone, the Company is also evaluating, with Chugai, and other undisclosed corporate partners, Biosphere formulations of other proteins and peptides.

Inhalation

Inhalation Technologies

The Company is developing advanced inhalation drug delivery technologies that are designed to deliver medicines via a patient's lungs without relying on CFC-based propellants which are considered environmentally harmful. The 1997 Montreal protocol signed by more than 140 countries aims to eliminate the manufacture, use and sale of CFC propellants by 2005. This pressure for the phasing out of CFCs has led to an increased focus on the development of both non-CFC MDIs and dry powder inhaler DPIs. The Company is currently working with two types of inhalation drug delivery systems: non-CFC MDIs using hydro-fluoro-alkane ("HFA") as a propellant and DPIs that require no propellant and are breath-activated. In its MDI development work, the Company focuses on the formulation of drugs for use in MDIs manufactured by third parties. In its DPI development work, the Company focuses both on the development of the device and on formulating of drugs for use with the device.

In both its MDI and DPI development work, the Company's objective is to maximize the efficiency of the delivery system while addressing commercial requirements for reproducibility, formulation, stability, safety and convenience. The Company has assembled a team of researchers with substantial experience in both powder and aerosol science and is applying this expertise to develop proprietary techniques and methods that it believes will produce stable and reproducible dry powder and aerosol formulations. To achieve this goal, the Company is combining an understanding of lung biology, aerosol science, chemical engineering and mechanical engineering.

MDI Technologies

Metered dose inhalers, the most widely used systems for inhalation drug delivery, have been in existence for more than 40 years and are primarily used to deliver asthma medications and other small molecule drugs to the lung, although significant advances have been made in recent years in the delivery of large molecule drugs, such as peptides and proteins, via the lung. The drugs are typically packaged in a portable canister as a suspension or solution in a volatile propellant. The primary technical challenge in developing a non-CFC MDI results from the fact that the two most widely used non-CFC propellants, HFA 134a and HFA 227, behave differently from CFC gases because of their physio-chemical characteristics. This has resulted in a need for a complete reengineering of the MDI device rather than a simple substitution. Among other things, this means that the mechanical components of the MDI device, especially the valves and gaskets, must be completely reformulated to work properly with non-CFC gases. The Company's work in this area has resulted in a high level of expertise in the evaluation of valves and gaskets utilized in the MDI device. The Company is currently developing aerosol formulations of a range of generic or off-patent drugs for the treatment of asthma. In its formulation work, the Company is working with both the HFA 134a and HFA 227 propellants.

DPI Technologies

Dry powder inhalation technology has emerged as an effective means of delivering asthma medications to the pulmonary system without the use of CFC propellants. DPIs rely on the patient's own lung power to deliver a fine dry powder suspension to the lung. DPI drug compounds are formulated in solid form and packaged in portable containers. Most DPIs currently on the market provide medicine in a pre-metered single dose form, such as a gelatine capsule or blister pack. Under the brand name "SkyeHaler" the Company is developing a DPI with a drug reservoir with the capacity to deliver up to 300 doses.

The primary technical challenge in developing a DPI device is to design a product that offers accurate and uniform dosing at variable flow rates of inhalation. Although additional testing remains to be performed, the Company believes that it has solved this problem by designing and incorporating valves in its DPI that make it flow-rate independent at inhalation rates of between 25 and 60 litres per minute. The Company's DPI is fully breath-actuated and offers an easy-to-use

mechanism that is capable of delivering uniform doses. In addition, the device benefits from a counter that keeps track of how many doses remain in the device.

Each drug designed for use with a DPI poses different formulation challenges due to varying physical and chemical characteristics and dosing requirements. These challenges require significant optimization work for each drug. The Company has assembled a team with substantial experience in formulation, dry powder science and aerosol science and is applying this expertise to develop proprietary techniques and methods that it believes will produce stable, fillable and dispersible dry powder drug formulations. Through its development work, the Company is developing an extensive body of knowledge of dry powder formulations, including knowledge relating to powder flow characteristics and solubility within the lung, as well as physical and chemical properties of various excipients.

The Company's SkyeHaler has completed Phase III clinical trials with a new formulation of Novartis' Foradil asthma drug, together referred to as the Foradil Certihaler. On December 20, 2002 the Company announced the submission by Novartis of a NDA for the Foradil Certihaler to the FDA and to health authorities in EU. Although the device has not yet been approved, the Company believes that its DPI benefits from the following features:

Flow Rate Independent. The Company's DPI offers accurate and uniform dosing at variable flow rates of inhalation of between 25 and 60 litres per minute.

Breath Activated. The Company's DPI relies on the patient's own lung power to deliver a fine powder suspension to the lung.

Uniform Delivery. The Company's DPI offers an easy-to-use mechanism to deliver consistent and uniform doses to the lung.

Dose Counter. The Company's DPI incorporates an easy-to-read dose counter that keeps track of how many doses remain in the device.

The Company is continuing to seek additional collaborative partners to further develop and commercialize its inhalation drug delivery technologies. The Company's strategy is to enter into development contracts with established pharmaceutical companies. In entering into collaborative arrangements, the Company's goal is to cover all or a large part of its research and development costs and receive milestone payments upon the achievement of specified objectives. The Company would expect to receive royalties from its partners based on sales of products incorporating the Company's pulmonary drug delivery technologies.

Inhalation Products in Development

The table below summarizes inhalation products currently under development. The stages of the development process: Feasibility, Phase I, Phase II and Phase III are explained under "Research and Development Development Process for Brand-Name Pharmaceuticals".

Product	Therapeutic Category	Development Status	Inhalation System	Collaborative Partner
Foradil	Asthma	NDA submitted	DPI	Novartis
HFA-formoterol	Asthma	Phase II	HFA - MDI	SkyePharma
Pulmicort® MDI	Asthma	Phase III	HFA - MDI	AstraZeneca
Formoterol Combi	Asthma	Feasibility	HFA - MDI	SkyePharma

Foradil

In November 1998, the Company and Novartis agreed to jointly develop a new formulation of Novartis' Foradil asthma drug using the Company's SkyeHaler, together referred to as the Foradil Certihaler. Foradil (formoterol fumarate) is a beta-agonist bronchodilator used for the preventative treatment of asthma. It is currently marketed in over 60 countries and achieved worldwide sales in 2002 of $262 million. The Company will be responsible for development of the drug in its finished form, to include supplying both the powder and the device as a product to Novartis. The Company plans to produce the product at its Lyon facility. Under the arrangement, Novartis has paid the Company a technology access fee of £0.4 million and has made an equity investment in the Company amounting to £6.1 million. Novartis has also agreed to

pay the Company royalty income on future worldwide sales of the drug. In return, the Company has granted Novartis an exclusive worldwide license to market Foradil in the new delivery form.

In October 1999, the Company and Novartis announced that this new formulation of Foradil had entered clinical trials. Phase III clinical trials commenced in the second half of 2000 and were completed in 2002. The Company produced DPI devices for the clinical trials, filled with the new formulation of Foradil, at its Lyon production facility. On December 20, 2002, the Company announced the submission by Novartis of a NDA to the FDA and to health authorities in the European Union for the Foradil Certihaler. In December 2002, Novartis licensed the Foradil franchise in the United States to Schering Plough. This licensing does not affect the Company's commercial agreement on royalties or manufacturing with Novartis.

HFA-formoterol

The Company's HFA formulation of formoterol, "HFA-formoterol" is a long-acting beta-agonist and will be used in metered dose inhalers to treat asthma. The Company's Phase II trial data has confirmed that its HFA aerosol inhaler is equivalent to the dry powder version of formoterol in terms of effect on patient lung function. HFA-formoterol is expected to enter Phase III clinical studies in the second half of 2003, and to be filed for approval in 2004.

In March 2002, the Company announced that it had entered into an agreement with Paul Capital. Under the terms of the agreement, Paul Capital will pay SkyePharma $30 million during 2002 and 2003, in return for a portion of the future royalty and revenue streams from nine products from the Company's pipeline. The monies will be used principally to fund the clinical development of Propofol IDD-D and HFA-formoterol. Details of the agreement with Paul Capital are explained below under the caption "Collaborative Arrangements".

Pulmicort MDI

In December 2001, the Company signed exclusive agreements with AstraZeneca PLC to develop the next generation of AstraZeneca's Pulmicort (budesonide) metered dose inhaler for the European market. The Company will apply one of its inhalation delivery technologies using HFA as propellant to replace CFC's in the currently marketed MDIs. Under the terms of the agreement, the Company will be responsible for all pre-clinical and clinical development, as well as compiling regulatory filings for marketing in Europe. SkyePharma retains the U.S. marketing rights. The Company received a signing fee of $2 million and payments under the agreement total up to $10 million, payable on the achievement of certain development and regulatory milestones up to the granting of marketing approval. AstraZeneca has also agreed to pay the Company royalty income on future net sales of the HFA-based product. The Company has already developed an internal formulation of budesonide, the active ingredient in Pulmicort that is pharmaceutically stable and suitable for use in an HFA-MDI. Phase II clinical studies on the AstraZeneca formulation have been completed and successfully demonstrated equiv