

SKYEPHARMA PLC  
Form 20-F  
June 27, 2003

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

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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F

(Mark One)

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

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

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:

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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  No

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

Item 17  Item 18

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### 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.

	<u>High</u>	<u>Low</u>	<u>Period Average</u>	<u>Period End</u>
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
			<u>High</u>	<u>Low</u>
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.

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**SkyePharma PLC**

<i>Consolidated Income Statement Data</i>	Year ended December 31,					
	1998	1999	2000	2001	2002	2002
	(in thousands, except per share data)					
<b>U.K. GAAP<sup>(1)</sup></b>						
Turnover <sup>(2)(3)</sup>	£10,925	£17,739	£24,292	£46,126	£69,573	\$111,978
Cost of sales <sup>(4)</sup>	(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 <sup>(5)</sup>	(4,230)	(3,161)	(3,844)	(4,804)	(4,769)	(7,676)
Administration expenses <sup>(6)</sup>	(6,781)	(12,584)	(12,630)	(16,025)	(20,192)	(32,499)
Research and development expenses <sup>(7)</sup>	(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

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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)
<b>Net (loss)/profit<sup>(3)(8)</sup></b>	<b>£(22,096)</b>	<b>£(19,414)</b>	<b>£(19,690)</b>	<b>£(9,452)</b>	<b>£1,109</b>	<b>\$1,784</b>
Basic weighted average number of shares <sup>(9)</sup>	384,871	467,214	508,228	526,250	577,018	577,018
Diluted weighted average number of shares <sup>(9)</sup>	384,871	467,214	508,228	526,250	597,095	597,095
Basic and diluted (loss)/profit per ordinary share <sup>(9)</sup>	(5.7)p	(4.2)p	(3.9)p	(1.8)p	0.2p	\$0.003

## U.S. GAAP<sup>(1)</sup>

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 <sup>(9)</sup>	(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.

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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,						
<i>Consolidated Balance Sheet Data</i>	1998	1999	2000	2001	2002	2002
(in thousands, except number of shares)						
<b>U.K. GAAP</b>						
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 <sup>(1)</sup>	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
<b>U.S. GAAP</b>						
Total assets	169,788	197,557	290,317	306,121	330,907	532,593
Net Assets <sup>(1)</sup>	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.

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### 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

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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

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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.

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***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

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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, Muttentz, 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***

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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

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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.

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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

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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".

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## 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

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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.

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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

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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.

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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.

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### ***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.

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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.

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*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

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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:

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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:

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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.



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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

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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

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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 flashes.

*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

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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".

<b>Product</b>	<b>Modified Release</b>	<b>Therapeutic Category</b>	<b>Development Status</b>	<b>Geomatrix System</b>	<b>Collaborative Partner</b>
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.

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*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.

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*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

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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.

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#### *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".

<b>Product (Active Compound)</b>	<b>Therapeutic category</b>	<b>Development Status</b>	<b>Collaborative Partner</b>
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.

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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

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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

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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

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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".

<b>Product</b>	<b>Therapeutic Category</b>	<b>Development Status</b>	<b>Inhalation System</b>	<b>Collaborative Partner</b>
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

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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 equivalence with the CFC aerosol version. Phase III clinical studies in Europe commenced in June 2003.

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### *Formoterol-Combi*

The Company is developing a combination of formoterol, the long-acting beta-2 agonist, with fluticasone, an inhaled corticosteroid, to be used in metered dose inhalers to treat asthma. The combination product, known as "flutiform", is currently at the feasibility stage and is expected to enter Phase I trials towards the end of 2003.

## **Topical**

### *Topical Technologies*

#### *HA-Based Technologies*

The Company's HA-based technologies were acquired from Cade Struktur. They are topical drug delivery technologies based on HA, a natural polymer, which is designed to maintain efficacy and localize the delivery of drugs to the skin for the treatment of a variety of skin disorders. HA is a long-chained polysaccharide that is a major constituent surrounding cells in most animal tissues. In solution HA's coiled structure acts as a net which can entrap a wide variety of drug compounds. HA is attracted to and adheres to specific receptors on cell membranes which can be found in increasing numbers at sites of damage and disease in the body. This means that drugs can potentially be targeted to and held at the site where the drug is needed. HA's safety profile, its ability to carry drugs and its potential targeting characteristics make it an excellent vehicle for drug delivery. The Company anticipates that by enhancing the delivery of a specific drug, treatment with HA formulations might require less drug compared to treatment with the drug administered by itself. As a result the Company believes formulations employing HA based technologies may result in decreased systemic side effects or enhanced therapeutic effect.

*Crystalip*

Certain rights to the Crystalip technology were licensed from Bioglan in December 2000. The remaining rights were acquired by the Company in May 2002. Crystalip enhances stability of drugs by embedding them in lipid crystals. Suitable for hydrophilic or hydrophobic drugs, the drug is released as the lipid melts at skin temperature. The major advantage of Crystalip comes from its versatility, as it can be formulated as a spray, lotion, cream or paste. Additionally, it can stabilize lipophilic and hydrophilic actives, provide photostabilization, and, due to its anti-microbial effect, can be free from preservatives leading to a low risk of toxic or allergic reactions. There are no direct competitors to Crystalip in providing both stabilization of lipophilic and hydrophilic drugs combined with an anti-microbial effect.

*DermaStick*

The DermaStick technology was acquired from Bioglan in two stages together with the Crystalip technology. DermaStick presents the active ingredient in a wax stick, which facilitates controlled application to affected skin. A major advantage of DermaStick over existing stick technologies is that it avoids the problem of poor homogeneity of stick formulations. Poor homogeneity is experienced because the active is suspended in the vehicle, and during the solidification process the suspended active is allowed to sediment. The DermaStick avoids this issue by holding the active in solution and thereby allowing manufacture of homogeneous sticks.

*ES-Gel*

The ES-Gel technology was acquired from Bioglan in two stages, together with the Crystalip and DermaStick technologies. ES-Gel is a semi-solid formulation producing enhanced solubility of drugs and providing substantially increased bioavailability by the transdermal route. The system will primarily compete with transdermal patch technologies. Other than the avoidance of the need for a patch, the major advantage is ES-Gel's ability to deliver low water soluble compounds through the

skin and to do this without the use of penetration enhancers. The resultant products may also be significantly lower cost compared to patches and most other transdermal delivery systems.

*Approved Topical Products*

*Solaraze*

The first approved drug product using the Company's HA-based technology is Solaraze. Solaraze is a topical gel used to treat actinic keratosis, a pre-cancerous skin condition caused by over-exposure to the sun. It is a formulation of HA and the non-steroidal anti-inflammatory drug diclofenac. Solaraze has been shown to be an effective topical product for actinic keratosis. Compared to other actinic keratosis treatments, Solaraze is non-invasive, non-scarring and is well tolerated by patients.

In July 1997, Solaraze received regulatory approval for marketing in the U.K. Subsequently, in May 1998, Solaraze was approved for marketing in Germany, Sweden, Italy, France and Canada. In October 1998, the Company submitted an NDA for the marketing of Solaraze in the United States, which was filed by the FDA in December 1998. The Company received FDA approval for this product in October 2000.

In March 2000, the Company entered into an agreement with Bioglan for the manufacture, marketing and distribution of Solaraze in Europe for an up-front licensing fee and royalty payments. In December 2000, the Company entered into a further agreement with Bioglan for the license of marketing rights to the United States, Canada and Mexico for Solaraze for which Bioglan paid a \$14 million fee and agreed to pay further significant milestone payments upon commercialization of Solaraze.

On November 20, 2001, the Company announced that it had served notice to terminate all agreements with Bioglan concerning the licence of Solaraze for marketing in Europe, USA, Canada and Mexico. Bioglan was asked to provide redress for certain material breaches raised in the notice. In December 2001, SkyePharma announced the withdrawal of this termination notice following announcements from Bioglan concerning certain arrangements with its banks and Quintiles. Bioglan received £15 million from Quintiles in return for the U.S., Canadian and Mexican rights to market and sell Solaraze. To enable Bioglan to complete these arrangements, SkyePharma agreed, amongst other matters, to withdraw its notice to terminate all agreements concerning Solaraze. In addition, SkyePharma agreed the transfer of rights to market Solaraze in the United States, Canada and Mexico from Bioglan to Quintiles, in consideration of which Quintiles paid SkyePharma \$5 million. Bioglan agreed to pay SkyePharma \$12.5 million in settlement of monies owing under the license agreements between the two companies for the sales and marketing of Solaraze in United States, Canada and Mexico. Quintiles subsequently launched Solaraze in the United States in January 2002.

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On February 21, 2002, the affairs of Bioglan were placed into administration. On May 13, 2002, following negotiations with the Administrators of Bioglan, SkyePharma announced an agreement to transfer all rights to market Solaraze in Europe to Shire for a total consideration up to £15 million, plus royalties on European sales. Of this total consideration, £2.1 million is contingent on conditions, including Solaraze's launch in certain European countries.

In January 2001, SkyePharma PLC entered into an agreement with Meditech which included a license to commercialize Solaraze in Australia, New Zealand, Malaysia and Singapore. Under the agreement, SkyePharma was to receive a 15% share of all amounts Meditech received from either commercializing or licensing Solaraze and associated products in the above territories. After Australian regulatory approval was obtained, Solaraze was to be marketed by Meditech, or its sub-licensee, Faulding Limited. SkyePharma agreed to work with Meditech to expedite approval. Independently Meditech obtained a non-exclusive license over the HA-based technology to exclusively exploit its anti-cancer HyACT project worldwide. Meditech agreed to pay SkyePharma 10% of all net revenue it receives from the HyACT project. However, the first A\$5 million Meditech

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receives by way of reimbursement of development expenses would not be subject to the 10% royalty.

In May 2002, Jagotec AG, a wholly owned subsidiary of the Company, entered into an agreement with Meditech under which the previous agreement of January 2001 was declared null and void. In addition the parties agreed on new licensing terms for one Jagotec patent. That patent was exclusively licensed to Meditech for worldwide use for intratumoral and injection. Additionally, under the terms of the May 2002 agreement, Jagotec AG assigned to Meditech certain other patents acquired from Cade Struktur which would be of benefit to Meditech. In consideration for the exclusive license and assignment of patents, Meditech has agreed to pay Jagotec AG a lump sum together with a royalty of 8% of net sales or 12% of net sub-licensing proceeds received from the sales of its HyACT products.

In September 2002, the Company and Meditech entered into a reciprocal licensing agreement concerning Solaraze in certain Pacific Rim territories. The Company had acquired rights to Solaraze in 1999 from the administrators of Cade Struktur, excluding those relating to certain Pacific Rim territories which were owned by Meditech under a pre-existing agreement with Cade Struktur. Under the 2002 agreement the Company reacquired these territorial rights to Solaraze from Meditech in return for an upfront payment, a milestone payment payable on regulatory approval of the product in Australia or New Zealand, and a royalty on sales. Through this agreement, the Company gained the exclusive right to manufacture and market or sublicense Solaraze in Australia, New Zealand, Singapore and Malaysia whilst Meditech obtained equivalent rights in China, Taiwan, Indonesia and the Philippines, none of which were included in Meditech's original agreement with Cade Struktur. Each party will receive an identical royalty on sales made by the other party in its allocated territory.

In December 2002, the Company licensed to Shire the exclusive rights to manufacture, distribute and sell Solaraze in Australia, New Zealand, South Africa and certain other countries in the Pacific Rim not included in the Company's license to Meditech. In return for these rights, the Company will receive up to a total of £2.2 million pounds comprising an undisclosed upfront payment and additional milestone payments contingent on the product's successfully completing a Phase III clinical study in Australia and receiving regulatory approval in the licensed territories. The Company will also receive royalties on net sales and milestones as sales exceed certain levels.

### *Topical Products in Development*

<b>Product</b>	<b>Therapeutic category</b>	<b>Development Status</b>	<b>Topical System</b>	<b>Collaborative Partner</b>
Hyclinda	Acne	Phase III	HA	SkyePharma
Acyclovir	Anti-viral	Feasibility completed	ES-Gel	Sakai

#### *Hyclinda*

Hyclinda is a topical gel to treat acne, which was originally developed by Cade Struktur and latterly under license by Shire and for which pivotal Phase III trials have been completed. In 2002, the Company recovered the rights to Hyclinda from Shire. A new marketing partner is currently being sought.

#### *Acyclovir*

The Company has granted to Sakai an exclusive license, signed February 9, 2000 to its patented rights and know-how under the ES-Gel system in relation to Acyclovir to enable Sakai to develop, register and sell acyclovir in Japan for the treatment of Herpes Simplex and Herpes

Zoster infections. The use of the ES-Gel technology will allow the presentation of Acyclovir at the site of infection in a super saturated state which enhances the delivery and therefore the efficacy of the drug. In the case that the Company utilizes the results derived from the Sakai development programme outside Japan, the Company must pay a royalty on net sales to Sakai.

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## ***Solubilization***

### *Solubilization Technology*

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 acquisition of nano-particulate technology from Medac and the IDD technology from SkyePharma Canada provides the Company with access to important enabling technologies for the enhanced delivery of poorly water-soluble drugs.

Nano-particulate technology aims to improve a drug's solubility by reducing the size of the particles. 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 nano-particles are produced via a process of homogenization whereby a therapeutic compound dispersed in a solvent or a compound carrier system is subjected to size reduction forces in a homogenizer. A homogenizer is a device where material is pushed through a narrow chamber at very high pressure. The process breaks down the particles of the compound and generates particles in the nanometer size range.

The nano-particulate technology acquired from Medac was originally developed by a team of researchers at the Free University of Berlin in the early 1990s and was subsequently licensed to Medac which pursued the development of the technology. The nano-particulate technology acquired from Medac consists of three separate techniques:

Nano-suspensions, a dispersion of pure drug without any matrix;

Solid Lipid Nano-particles, solid solutions of drugs in a lipid matrix; and

Solid Polymer Nano-particles, solid solutions of drugs in a solid polymer matrix.

The IDD technology platform acquired with the acquisition of SkyePharma Canada has been developed since the early 1990s with over \$50 million having been invested in the technology and development of a proprietary product pipeline. To date, no products using the IDD technology have been approved. The IDD technology incorporates the following methods:

MicroParticle (IDD-P ), phospholipid stabilized sub-micron to micron sized water-insoluble drug particles. This approach can be used for a wide range of insoluble drugs to be administered via the oral, topical, injectable, implantable or inhaled routes; and

MicroDroplet (IDD-D ), phospholipid stabilized sub-micron to micron sized emulsions of water-insoluble drug particles. This approach is available also to a restricted range of drugs, limited by solubility in biocompatible oils, administered by the injectable route.

The IDD technology acquired with SkyePharma Canada is complementary to the Company's existing nano-particulate technology acquired from Medac, and, therefore, the Company expects to be able to provide customers with a wider range of patented solubilization technologies. It is intended that the SkyePharma solubilization technologies will also be used to complement and enhance the Company's other drug delivery systems.

### *Advantages of solubilization technologies*

The Company believes that its solubilization technologies acquired from Medac and SkyePharma Canada offer a number of potential advantages over other solubilization technologies being developed by pharmaceutical and biotechnology companies. These include the

following:

*A variety of solutions.* The SkyePharma technology encompasses five different approaches: nano-suspensions, solid lipid nano-particles and solid polymer nanoparticles, MicroParticle and MicroDroplet which offer a number of different methods to address solubility problems.

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*Simplicity of manufacturing process.* All particles are produced on the same relatively simple equipment, which may reduce the investment cost and complexity of the manufacturing operation.

*Rapid manufacturing process.* The homogenization part of the manufacturing process typically takes 1 to 2 hours which is significantly shorter than other processes used by competitors.

*Narrow particle size range.* The particles produced are within a narrow size range.

#### *Solubilization Products in Development*

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

<b>Product</b>	<b>Therapeutic Category</b>	<b>Development Status</b>	<b>Solubilization System</b>	<b>Collaborative Partner</b>
Propofol	Anesthesia/Sedation	Phase II	IDD-D	SkyePharma
Busulfan	Oncology	Phase II	IDD-P	SuperGen
Fenofibrate	Cardiovascular	Phase I	IDD-P	Undisclosed
Multiple	Undisclosed	Feasibility	IDD-P	Baxter

#### *Propofol*

Propofol is the active ingredient in AstraZeneca's Diprivan, a leading injectable anesthetic, which achieved sales in 2002 of \$443 million. The Company is developing an improved formulation of propofol using its IDD-D technology. Patents began to expire on Diprivan in 2000. Diprivan has problems with micro-organism growth if the product is not properly handled and also may cause the build up of fats in the body. The IDD-D formulation is inherently anti-microbial and offers significant improvement in both these areas. Propofol IDD-D entered Phase II trials during 2002 with a target launch date, on successful completion of clinical trials, in 2005.

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".

In December 2002, the Company entered into a development and commercialization agreement under which Endo received an exclusive license to the U.S. and Canadian marketing and distribution rights for two of the Company's patented development products, DepoMorphine, an injectable product, and Propofol IDD-D, 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 \$50 million for Propofol IDD-D, payable when the product successfully achieves certain regulatory milestones, including FDA approval. 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 any post-marketing studies and for selling and marketing expenses.

In the recently completed Phase II trial Propofol IDD-D 2% was shown to be similar to Diprivan in terms of pharmacokinetics, anaesthetic efficacy and safety. Propofol IDD-D 2% will commence Phase III trials by the end of 2003. The Phase III study will involve over 700 patients and is intended to support three target indications: general anesthesia in adults, monitored anesthesia care in adults and in the intensive care unit for the sedation of intubated, mechanically ventilated adults.

#### *Busulfan*

The Company has been developing an injectable formulation of Busulfan, for bone marrow transplants in pediatrics, in partnership with SuperGen, Inc. ("SuperGen"), using its IDD-P technology. Busulfan is currently marketed by SuperGen in oral form. The new formulation does not contain dimethyl acetamide ("DMA"), does not require refrigeration and is in Phase II trials.

#### *Fenofibrate*

The Company has been developing an improved formulation of fenofibrate, in partnership with an undisclosed pharmaceutical company. The Company and its partner are currently renegotiating the agreement. Depending on the results of these negotiations the Company will be reevaluating its position in respect of this product. Fenofibrate is a lipid-lowering drug launched by Abbott in the United States in 1998. Currently marketed forms of fenofibrate had sales in 2002 of over \$400 million. The IDD formulation is a lower dose product providing blood levels similar to the 200mg currently marketed form. The new formulation is currently in Phase I trials.

#### *Baxter*

SkyePharma Canada has signed an exclusive agreement with Baxter to collaborate on the use of the IDD technology for the formulation of injectable New Chemical Entity ("NCE") medications. Baxter will work with its pharmaceutical company clients to develop injectable formulations for insoluble medications utilizing the IDD technology and its expertise in formulating and manufacturing injectable drugs. One of the most challenging issues in the development of many pharmaceutical products is formulating a water-insoluble NCE a drug molecule that cannot be dissolved in water so that it can be administered to patients in an injectable form. Under the terms of the agreement, SkyePharma Canada will receive milestone payments from Baxter based on certain events leading to the commercialization of the first product under the collaboration. In addition, SkyePharma Canada will receive a proportion of license fees, milestone payments and royalties on net sales of the IDD formulated injectable medications developed by Baxter for Baxter's global pharmaceutical company partners. Baxter has exclusive manufacturing rights to these products. Where SkyePharma Canada develops products for Baxter's partners, SkyePharma will pay to Baxter a proportion of the milestones and royalties earned. In 2003 the agreement with Baxter was extended to incorporate the Medac nano-particulate technology.

#### *Undisclosed*

The Company had licensed its IDD technology to Blue Ridge Pharmaceuticals, Inc., a subsidiary of IDEXX Laboratories, Inc. ("IDEXX"), to be applied to a range of water insoluble veterinary drugs. IDEXX was to develop a number of products utilizing the IDD technology. In November 2002, the Company was notified by IDEXX that they had decided to discontinue any further efforts on this project.

#### *New Product Feasibility Programs*

In addition to the above described products, SkyePharma Canada has a number of deals for feasibility studies on third party compounds which are at an early stage of development. SkyePharma Canada has disclosed alliances with Schering Plough Corporation and other



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nondisclosed partners on drugs formulated using IDD technology. SkyePharma Canada owns or has exclusively licensed twenty two patents and has submitted twenty three patent applications on its IDD technology in the United States. SkyePharma Canada has also filed related patent applications on its IDD technology in other countries and regions.

### Research and Development

The Company's research and development activities are conducted at SkyePharma AG in Muttenz, Switzerland, SkyePharma Inc. in San Diego, United States, SkyePharma AB in Malmo, Sweden and SkyePharma Canada Inc. in Montreal, Canada. As of December 31, 2002, the Company had 338 employees at these four facilities, the majority of whom were engaged in research and development, including 219 scientists, 77 of whom hold Ph.D.s, masters or medical degrees. The Company has recently substantially reduced the staff of SkyePharma Canada by outsourcing its activities to other SkyePharma sites.

The Company conducts research and development both with respect to its own existing products as well as for third parties. The Company accounts for costs incurred in conducting internal research and development activities as research and development expenses and for costs incurred on development work for third party customers as cost of sales. The Company's self-sponsored research and development costs are expensed as incurred.

The Company records amounts received from third parties under the Company's contract development arrangements within turnover, as contract development income. Contract development income represents amounts invoiced to customers for services rendered under development contracts or for milestone payments in accordance with the contract terms. Such amounts are only treated as revenue when the services have been rendered or the specified milestone has been met. Certain refundable income is treated as deferred income until the Company has no further obligations to make refunds. In each of 2000, 2001 and 2002, amounts reimbursed by collaborative partners, including milestone payments, were greater than the direct costs incurred in the provision of such services, representing the contribution to general and administrative costs. The Company generally attempts to break even on its development work for third party customers. Therefore, product development activities do not currently have a significant impact on the Company's operating profit/(loss).

Under the agreements with Paul Capital, announced in 2001 and 2002, Paul Capital have provided \$30 million, to fund the clinical development and regulatory submission of DepoMorphine by the Company, and \$30 million will be provided between 2002 and 2003 to principally fund the clinical development of Propofol and HFA-formoterol. These funds are recorded as Other Operating Income.

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The aggregate amount that the Company spent on research and development and the aggregate amount that was reimbursed by collaborative partners is shown in the table below.

	Consolidated Year ended December 31,		
	2000	2001	2002
	(in £ thousands)		
<b>Research and Development Expenses</b>			
Client sponsored research and development	6,986	7,917	12,649
Internal sponsored research and development	13,104	17,918	29,285
	20,090	25,835	41,934
<b>Contract Development Income</b>			
Client sponsored research and developments reimbursed by:			
Research and Development costs recharged	4,808	9,857	7,705
Milestone payments	11,997	28,379	47,736
	16,805	38,236	55,441
<b>Other Operating Income</b>	2,900	6,342	14,219

The Company's research and development efforts in respect of its drug delivery technologies are by their nature subject to risks and uncertainties. There can be no assurance that the products under development can be successfully formulated using the drug delivery technologies. In addition, even if such products can be successfully formulated, there can be no assurance that they will secure regulatory approval for the appropriate indication or that approved compounds would be capable of being produced in commercial quantities at reasonable costs and successfully marketed.

The Company's development processes are described below.

***Development Process for Brand-Name Pharmaceuticals***

The development of improved outcome or new pharmaceuticals using one of the Company's drug delivery technologies takes place in several steps. The first step, called the "preliminary assessment", is to assess the suitability of the drug candidate for a particular drug delivery system through various techniques including the use of sophisticated computer modeling. During the preliminary assessment, the Company will analyze product specifications provided by the client. If the preliminary assessment indicates that the drug candidate is suitable for formulation with the drug delivery technology, the project will proceed to development as follows:

*Feasibility* At this stage, the Company conducts an in vitro (laboratory) feasibility study to determine whether, under laboratory conditions, the formulation of the product candidate can be achieved. The Company may develop up to 20 prototype formulations for in vitro feasibility studies and selects the most promising two or three for further study and analysis.

*Pilot Trials* Once a successful feasibility study has been conducted, small batches of the selected prototypes are manufactured by the Company or its collaborative partners for in vivo (human) testing in pilot trials. Pilot trials involve approximately 12 patients. The purpose is to determine whether the in vitro results can be replicated in humans. Pilot trials are generally managed by the company and conducted by a clinical research organization (CRO). If the pilot trials demonstrate sub-optimal results, the product candidate may be reformulated and new pilot trials conducted.

*Scale-up/Bio-Batch* After a successful pilot trial, the Company or its collaborative partners will manufacture a commercial scale batch or a "bio-batch" (at least one tenth of the projected commercial batch size). The purpose of this stage is to develop and validate the process by which the product will be manufactured. If formulation changes are made during scale-up/

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biobatch, additional in vivo testing may be performed in pre-pivotal trials involving a small patient population.

The "pre-clinical" phase of development referred to in parts of this document means additional testing following initial feasibility studies and other studies, including additional animal studies, necessary to prepare and file an Investigational New Drug ("IND") application. For a more comprehensive description of the requirements of an IND, see "Government Regulation United States NDA Process" below.

*Phase I Trials* The first stage in the clinical development plan is to conduct Phase I clinical trials. These studies are usually performed to generate preliminary information on the chemical action of the compound, the activity or fate of the product in the human body over a period of time including adsorption, distribution, metabolism and elimination, and safety of the drug using normal healthy volunteers and patients. Phase I trials involve approximately 10-30 patients. These trials are generally managed by the Company and conducted by a clinical research organisation ("CRO") that has a Phase I clinical study unit.

*Phase II Trials* The second stage in the clinical development plan is to conduct Phase II clinical trials. These trials are generally carried out on patients with the disease or condition of interest. The main purpose is to provide preliminary information on: the positive effects of the treatment and whether the effects are correlated with the administered doses in one or more demographic groups, assess various measures of patient benefit as potential candidates for use in Phase III trials, and to supplement safety information obtained from Phase I trials. The Company, in collaboration with its partner, or the partner, manages the trial activities (from protocol development through to the writing of the study final reports). The Company may use a CRO to complete the trials. Phase II studies may not be required for improved outcome formulations of

an existing drug if the improved formulation is targeted at the same indication as the existing drug.

*Pivotal (Phase III) Trials* The last step of the development process is a pivotal (Phase III) trial of the product formulation in an expanded patient population to support the approval of marketing applications. Typically, the studies will be performed in the United States, Canada and Europe to facilitate a multi-national product registration process. The Company, in collaboration with its partner, or the partner manages the trial activities (from protocol development until the writing of the final study reports). The Company may use a CRO to complete the studies on schedule.

*Regulatory Filing* The Company, in collaboration with its partner, or the partner manages all regulatory activities during the product development phases until product approval. These activities included submissions, communication and meetings with health authorities and preparation of marketing approval applications.

## **Collaborative Arrangements**

### ***Overview***

The Company has collaborative arrangements with each of its pharmaceutical partners, the terms of which vary considerably. Pursuant to these arrangements, the Company's partners typically fund all or a large part of the research and development expenses incurred in the development of new formulations of their products. Most of the Company's development contracts either provide for a flat fee for the Company's research and development efforts or provide for an agreed research and development budget. Some agreements have involved equity investments in the Company by the Company's partners. In negotiating contracts with its partners, the Company's strategy generally has been to cover its costs in the research and development process. Substantially all potential profits are expected to be generated by royalty payments or manufacturing fees for successfully developed and marketed products. In some cases, the partners have agreed to make specified

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payments to the Company upon the achievement of certain milestones, which may be deducted from future royalty payments for successfully developed and marketed products.

In return, the Company gives each of its partners an exclusive license to market the products incorporating the Company's technologies. In some cases the licenses are worldwide. In others they are limited to specific territories. In all cases, however, partners are free to sublicense the technologies, although the Company's consent may be required and royalties on all sales must be paid to the Company. In addition, the majority of the collaborative agreements do not prohibit the Company from developing formulations of competitive products. In some cases, however, the Company will agree not to develop formulations of specified compounds for an agreed period of time. Most of the agreements do not prohibit partners from developing, either internally or in collaboration with the Company's competitors, controlled-release versions of the contract products.

The Company's collaborative partners generally take responsibility for conducting clinical trials and for preparing and pursuing all necessary regulatory approvals although more recently the Company has taken responsibility for managing clinical trials in some collaborations. The Company may assist its partners in the conduct of such trials and the preparation of regulatory filings, but its partners ultimately control the process, including the selection of the jurisdictions in which regulatory approval will be sought, if at all.

The collaborative agreements do not typically obligate the partners to market any successfully developed and approved products. The Company does not have any control over whether and to what extent a partner will elect to commercialize a product. A client may choose not to market a product for reasons wholly independent of the Company's technologies. In most cases if a client does not proceed to market the product once it has been successfully formulated and approved, the Company will not receive any additional income in respect of the product. In some more recent collaborations however, contracts have included certain commitments for the Company's partners to market the product or to pay a minimum royalty in lieu of sales of the product.

During the formulation and development stages, the Company's partners are generally free to terminate the collaborative relationship at any time and for any reason.

### ***Oral***

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The Company is currently receiving significant royalty revenues under two collaborative arrangements for its Geomatrix technology: Xatral OD and Paxil CR. Under the terms of these agreements, each of the development partners bore all of the costs of research and development according an agreed budget and are obligated to pay the Company continuing royalties of between 1.5% and 5% of net sales. In return, the Company granted the development partners exclusive licenses to use the Geomatrix technology in these products throughout the world. The license agreement for Xatral OD was signed in May 1999 with Sanofi-Synthelabo. The license agreement for Paxil CR was signed in March 1996 with SmithKline Beecham plc (now part of GlaxoSmithKline).

The only collaborative arrangement involving Geomatrix technology in which the Company is responsible for conducting clinical trials is the development and licensing agreement for a once-daily version of Requip (ropinirole) with GlaxoSmithKline, which was entered into in September 1999 with SmithKline Beecham (now part of GlaxoSmithKline). Under the terms of the agreement with GlaxoSmithKline the Company is responsible for all development activities for Requip oral controlled release tablets up to regulatory filing, in collaboration with GlaxoSmithKline. As part of the agreement, GlaxoSmithKline made an equity investment of £4.9 million in the Company and will pay milestone payments at intervals up to product approval, including an up-front payment. In December 2001 and June 2003, the Company and GlaxoSmithKline amended the 1999 license for Requip to take account of additional activities that had been undertaken by SkyePharma. Under the terms of the amendments, the timeline of certain milestone payments was renegotiated together with additional development revenues to reimburse SkyePharma for the additional activities. On commercialization of once-daily Requip, the Company will receive royalties on future product sales. GlaxoSmithKline will take responsibility for preparing and pursuing all

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necessary regulatory approvals. The once-daily version commenced Phase III clinical trials in June 2003.

The Company has a development and license agreement for Dilacor XR, signed in 1998 with Rorer, a member of the Rhône Poulenc Rorer Group (now part of Aventis Pharma). In 1997, Rorer granted to Watson Laboratories, Inc. (with the consent of the Company) exclusive rights to market, advertise, promote, sell and distribute Dilacor XR. The grant of rights to Watson Laboratories does not affect any entitlements of the Company or any of the material terms of the collaborative arrangement. The Company no longer receives royalties under this agreement.

In addition, the Company has entered into a technology access, license and development agreement with a Company based in the United States for the use of the Company's Geomatrix technology. In connection with the agreement the Company has been issued convertible preferred stock, which, assuming conversion, would give the Company a 14.2% stake in that company's ordinary share capital. This investment is recorded within fixed asset investments.

### ***Injectable***

In March 1994, SkyePharma Inc., formerly known as DepoTech, entered into a collaboration agreement with Chiron. The objective of the collaboration was to develop and commercialize DepoCyt for use in the treatment of neoplastic meningitis from lymphomas and solid tumors, and to explore the use of the Company's DepoFoam for certain other Chiron compounds. The Chiron agreement, as amended, granted Chiron rights to market and sell DepoCyt in the United States. Chiron funded, and was obligated to fund, 50% of the clinical development expenses in the United States. Canadian registration expenses and the cost of clinical trials required in Europe were funded by Chiron until June 1997, when the Chiron agreement was amended in connection with the agreement with Pharmacia Corporation described below. Under the Chiron agreement SkyePharma Inc. manufactured DepoCyt, Chiron marketed, sold, and distributed DepoCyt in the United States, and the parties shared all profits equally. The Company also funded 50% of the sales and marketing expenses incurred for DepoCyt. Chiron also had a right of first refusal to obtain a license to alternate DepoFoam formulations of cytarabine under terms and conditions to be negotiated. Following an evaluation of the markets and certain other factors, SkyePharma Inc. and Chiron mutually agreed not to further develop certain additional generic cancer compounds named in the Chiron agreement.

In June 1997, SkyePharma Inc. and Chiron amended their agreement, and SkyePharma Inc. repurchased rights to DepoCyt in Canada and Europe from Chiron for aggregate cash payments of up to \$13.7 million, of which \$2.0 million was expensed and paid to Chiron in December 1997. The remaining \$11.7 million originally was payable upon the earlier of six months following U.S. or European regulatory notification that the application to market or sell DepoCyt is approvable or approved. In March 1999, SkyePharma Inc. and Chiron further amended the agreement with Chiron, such that SkyePharma Inc. issued a note payable for \$9.7 million on receipt of FDA approval of DepoCyt on April 1, 1999. During 2000, SkyePharma and Chiron amended the March 1999 agreement whereby SkyePharma Inc. would have issued a note payable for \$3.5 million to Chiron upon the filing of an application for DepoCyt for pediatric indications in the United States. Under the amendment dated October 4, 2000, this note became payable on the earlier of the filing of an application for DepoCyt for pediatric indications in the United States or the date on which Phase IV clinical trials, required by the FDA as a condition of product approval, commenced. The \$3.5 million note was issued in December 2000. The notes were secured on the rights to DepoCyt and bore a floating rate of interest based on LIBOR. The remaining Chiron loan notes were repaid during 2002.

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In July 1997, SkyePharma Inc. entered into a marketing and distribution agreement with Pharmacia Corporation. Under the agreement, Pharmacia Corporation acquired rights to market and sell DepoCyt in countries outside the United States. Pharmacia Corporation was generally responsible for submitting regulatory filings, and for labeling, packaging, distributing, marketing and

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selling DepoCyt in this territory. SkyePharma Inc. agreed to manufacture DepoCyt and receive a share of the net sales of this product from Pharmacia Corporation, if any. SkyePharma Inc. received a cash payment of \$2.0 million when the agreement was signed. The agreement also provided for reimbursement by Pharmacia Corporation of certain clinical trial expenses and regulatory fees incurred by SkyePharma Inc. In February 2000, the Company and Pharmacia Corporation renegotiated certain aspects of this agreement relating to milestone payments and reimbursement of clinical trials expenses. In addition, the Company recovered the rights to DepoCyt for Japan and Canada. In June 2000, Pharmacia Corporation notified the Company that it was terminating the 1997 Marketing and Distribution Agreement. Subsequently, Pharmacia Corporation assigned the European marketing application to the Company and the Company continued to pursue the European marketing approval. In April 2001, the Company received notification that the CPMP had recommended the granting of marketing authorization for DepoCyt, for the treatment of neoplastic meningitis from lymphomas. The CPMP's recommendation was forwarded to the European Commission for ratification. In June 2001, the Company licensed the marketing and distribution rights for DepoCyt in Europe and the Philippines to Elan. In August 2001, the European Commission approved DepoCyt for marketing through the European Union.

In June 2000, the Company licensed the marketing and distribution rights for DepoCyt in Canada to Paladin Inc. and in June 2001, the Company licensed the marketing and distribution rights for DepoCyt in Japan and Taiwan to Nippon-Shinyaku. In association with an agreement with Elan for the return of rights to DepoCyt in Europe and the Philippines, the Company anticipates concluding a relicensing agreement for the European DepoCyt rights in the near future.

In November 2002, the Company re-acquired 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, Enzon Pharmaceuticals, Inc. licensed the North American rights to DepoCyt and 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 reduce 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. At December 31, 2002, the Company had a promissory note with Chiron of \$1 million which formed part of the consideration for the reacquisition of the DepoCyt marketing, distribution and sales rights. The promissory note is repayable in 2004 and bears interest at LIBOR plus 3%.

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. In respect of the first product launched under the agreement, the Company will pay Endo a fixed contribution in relation to marketing activities undertaken by Endo in respect of the first and second year of commercialization. Endo will be responsible for funding and conducting any post-marketing studies and for selling and marketing expenses. The agreement expires with respect to each product upon

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the later of the expiry of all relevant patents and the 15<sup>th</sup> anniversary of the date of first commercialization. The agreement may be terminated in various cases, including by Endo in the event the Company experiences delays in obtaining regulatory approval for the products or fails to achieve the target labeling and, without cause, upon sixty days' notice, provided that, in such an event, Endo shall pay an undisclosed termination fee to the Company.

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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. 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.

### ***Inhalation***

In November 1998, the Company and Novartis agreed to jointly develop a new formulation of Novartis' Foradil asthma drug using the Company's multi-dose dry powder inhaler. The Company is responsible for development of the drug in its finished form, to include supplying both the powder and the device as a product to Novartis. 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 December 2001, the Company signed exclusive agreements with AstraZeneca PLC to develop the next generation of AstraZeneca's Pulmicort metered dose inhaler. 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 approval. The Company received a signing fee of \$2 million and progress related payments could total up to \$10 million once marketing approval is granted. 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 Phase III clinical studies commenced in June 2003.

### ***Topical***

As set out above under "Drug Delivery Platforms Topical Approved Topical Products Solaraze", the Company entered into two agreements with Bioglan: for the manufacture, marketing and distribution of Solaraze in Europe and for the license of marketing rights to the United States, Canada and Mexico. As set out above, during 2001, SkyePharma agreed the transfer of rights to market Solaraze in the United States, Canada and Mexico from Bioglan to Quintiles. On May 13, 2002, following negotiations with the Administrators of Bioglan, SkyePharma announced an agreement to transfer all rights to market Solaraze in Europe to Shire for a total consideration up to £15 million, plus royalties on European sales. Of this total consideration, £2.1 million is contingent on conditions including Solaraze's launch in certain European countries.

On February 9, 2000, the Company granted Sakai an exclusive license its patented rights and know-how under the ES-Gel system in relation to acyclovir to enable Sakai to develop, register and

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sell acyclovir in Japan for the treatment of Herpes Simplex and Herpes Zoster infections. The project has recently completed the feasibility stage and it is anticipated that it will enter clinical trials in 2003. In the case that the Company utilizes the results derived from the Sakai development programme outside Japan, the Company must pay a royalty on net sales to Sakai.

In June 2000, SkyePharma entered into a research and development collaboration with Kings College London for the investigation of the use of HA as a carrier or vector for active substances in drug delivery applications, principally for administration by the topical route. The projects being pursued under this agreement are all at the pre-clinical stage of development.

### ***Solubilization***

In December 2002, the Company entered into a development and commercialization agreement under which Endo received an exclusive license to the U.S. and Canadian marketing and distribution rights for two of the Company's patented development products, DepoMorphine, an injectable product, and Propofol IDD-D, 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 \$50 million for Propofol IDD-D, payable when the product successfully achieves certain regulatory milestones, including FDA approval, except that, in the event the FDA-approved labeling fails to meet the parties' target labeling, only \$10 million becomes payable upon FDA approval,

with the remaining \$40 million being due upon the achievement of certain sales targets. 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. In respect of the first product launched under the agreement, the Company will pay Endo a fixed contribution in relation to marketing activities undertaken by Endo in respect of the first and second year of commercialization. Endo will be responsible for funding and conducting any post-marketing studies and for selling and marketing expenses. The agreement expires with respect to each product upon the later of the expiry of all relevant patents and the 15<sup>th</sup> anniversary of the date of first commercialization. The agreement may be terminated in various cases, including by Endo in the event the Company experiences delays in obtaining regulatory approval for the products or fails to achieve the target labeling and, without cause, upon sixty days' notice, provided that, in such an event, Endo shall pay an undisclosed termination fee to the Company.

SkyePharma Canada and Jagotec AG have signed an exclusive agreement with Baxter Healthcare Corporation to collaborate on the use of the IDD and nano-particulate technology for the formulation of injectable medications. Details of this collaboration are set out above under "Drug Delivery Platforms Solubilization Solubilization Products in Development New Product Feasibility Programs".

#### *Other Collaborative Arrangements*

In December 2000, SkyePharma entered into an agreement with Paul Capital. Under the agreement, Paul Capital has provided a total of \$30 million between 2000 and 2002, in return for the sale of a portion of potential future royalty and revenue streams from DepoMorphine, Xatral OD, Solaraze and DepoCyt. The monies will be used to fund the clinical development of DepoMorphine. Between January 2003 and December 2014, Paul Capital will receive 15% of the annual royalties and revenues from the stated products up to an agreed ceiling. Once the predetermined ceiling is reached, the percentage participation will fall to 3% for the remainder of the period until December 31, 2014.

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In March 2002, SkyePharma entered into a second 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. The nine products referred to are Propofol IDD-D and HFA-formoterol, the lipid-lowering drug fenofibrate, an anti-cancer agent busulfan, an intravenous formulation of the antibiotic oxytetracycline, oral budesonide to treat inflammatory bowel disease, HFA-budesonide and Foradil, for the treatment of asthma, and the anti-depressant Paxil CR. Between January 2002 and December 2015, Paul Capital could receive between 4% and 20% of the annual royalties and revenues from the total of nine products. The 20% rate applies first. The percentage then falls, when an agreed return is achieved, to 12.5% until a second ceiling is reached, before falling to 4% for the remainder of the period until December 31, 2015. During 2002 and 2003, the 20% rate will be reduced based on the percentage of the total \$30 million already funded. In addition, should the share of royalties received by Paul Capital not meet minimum returns, SkyePharma may issue SkyePharma ordinary shares up to a value of \$7.5 million. The number of ordinary shares to be issued is capped based upon a minimum price of 55 pence per share. Also under the terms of these agreements, Paul Capital has been issued warrants carrying rights to subscribe for 5 million SkyePharma Ordinary Shares at an exercise price of 73.75 pence, representing a 25% premium to the average trading price for the five trading days immediately prior to the closing date.

In December 2001, the Company entered into several agreements concerning the development of Astralis' novel injectable vaccine therapy, for the treatment of all forms of psoriasis, a chronic skin disorder. A first generation of Psoraxine, developed by Astralis, has completed clinical studies in Venezuela with encouraging results. Under the terms of a technology access agreement, the Company received from Astralis a \$5 million license fee, for access to DepoFoam and other relevant drug delivery technologies. In addition, through a service agreement, the company will provide all development, manufacturing, pre-clinical and clinical development services to Astralis for second generation Psoraxine, up to the completion of Phase II clinical studies. In the event that Phase II studies are successfully completed, Astralis will offer SkyePharma the option to acquire the worldwide licensing and distribution rights to Psoraxine. If SkyePharma does not exercise the option, Astralis will seek a marketing partner to fund Phase III clinical studies and to provide a sales and marketing infrastructure. Astralis filed an IND application to start Phase Ib clinical studies with the FDA in March 2003. The FDA has informed Astralis that, before clinical trials may proceed, Astralis will have to provide the FDA with additional information and address certain issues regarding the design of the pre-clinical studies. No assurance can be given that the FDA will release the hold placed on the study or whether or when Astralis may commence clinical trials.

In a separate transaction, the Company has made a total equity investment in Astralis of \$20 million in convertible preferred shares, and now owns 25.4% of Astralis assuming the Company was to convert its convertible preferred shares of Astralis into Astralis common stock. The Company made an initial investment of \$10 million on signing the agreement. The additional instalments of \$2.5 million were paid on January 31, 2002, April 30, 2002, July 31, 2002 and January 31, 2003.

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On May 14, 2002, SkyePharma announced its intention to enter a wide ranging strategic collaboration with Kowa Company Ltd., a leading Japanese company with substantial pharmaceutical interests, which proposed, under a Subscription Agreement signed on May 13, 2002, to make a strategic investment in SkyePharma. Kowa and SkyePharma also signed a separate non-binding Letter of Intent to evaluate Kowa's acquisition of a 50% interest in SkyePharma's manufacturing facility in Lyon. Kowa and the Company are still evaluating the proposal. On June 25, 2002, the Company announced that in accordance with the terms of an agreement dated May 13, 2002, and following shareholder approval at an Extraordinary General Meeting of the Company held on June 7, 2002, thirty million ordinary shares of 10p each in SkyePharma PLC had been allotted to Kowa Company Limited, for a total consideration of £25,320,000. This represented a holding of 5.01% after the investment. As part of its investment, Kowa had the right to appoint a non-executive director to the board of SkyePharma and on October 30, 2002, the Company confirmed the appointment of Mr. Torao Yamamoto as a Non-executive Director of SkyePharma.

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Kowa and SkyePharma have an active relationship involving the formulation development and scale-up for certain formulations of a new lipid-lowering agent NK-104 to support late-stage clinical development of the drug. The two parties now intend to strengthen their commercial relationship through manufacturing formulations of NK-104. Kowa and SkyePharma have also identified areas of synergy to exploit further their respective product and development pipelines. Kowa's sales and marketing experience should create opportunities to expand the market for SkyePharma's products into both Europe and Japan. In addition, SkyePharma's broad portfolio of drug delivery technology has the potential to create improved drugs from Kowa's marketed products and development pipeline. SkyePharma and Kowa are already cooperating on an undisclosed project using SkyePharma's enhanced solubilization technology.

In January 2003, the Company and Enzon Pharmaceuticals, Inc. agreed a strategic alliance based on a broad technology access agreement. The two companies will draw on their combined drug delivery technology and expertise to jointly develop up to three products for future commercialization. These products will be based on the Company's proprietary platforms in the areas of oral, injectable and topical drug delivery, supported by technology to enhance drug solubility and Enzon's proprietary PEG modification technology, for which Enzon received a US\$3.5 million technology access fee. The Company will receive a milestone payment for each product based on its own proprietary technology that enters Phase II clinical development. Research and development costs related to the technology alliance will be shared equally, as will future revenues generated from the commercialization of any jointly-developed products. PEG technology involves the attachment of polyethylene glycol to therapeutic proteins or small molecules, for the purpose of enhancing therapeutic value. Polyethylene glycol is a relatively non-reactive and non-toxic polymer that is frequently used in food and pharmaceutical products. The attachment of polyethylene glycol to a molecule increases its molecular weight, and for some proteins and small molecules can impart better solubility and stability, reduce immune responses, improve therapeutic and/or safety profiles and simplify or improve dosing regimens.

### **Patents and Proprietary Rights**

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.

### ***Geomatrix Technology***

The Company has two patent families in respect of its core Geomatrix technologies. The first patent family was issued in Australia, New Zealand, Italy, Europe, Japan, the United States and Canada. It expired in 2002 in Australia and New Zealand and will expire in 2005 in Italy, 2006 in the rest of Europe, Japan and the United States, and 2009 in Canada. A second patent family relating also to controlled rate release has been granted in Italy, the United States and Europe, Canada and Japan. These patents expire between 2009 and 2012.

In addition, the Company has several other granted patents, as well as applications filed in markets including Europe, the United States, Japan, Canada, Australia and New Zealand, which continue to protect the technology to 2015. Further applications have been filed as recently as spring 2003.

The patents and applications cover a variety of different tablet formulations containing an active drug core and various surface coatings covering the core. These cores and coatings contain excipients that enable a variety of release profiles to be achieved. Later applications cover recent innovations and/or improvements to the original inventions.

In 2001 the Company defended an opposition to one of its European Geomatrix patents. The European Patent Office ("EPO") upheld the decision. Following appeal by the Company, the patent

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was revoked. However the Company does not believe that this is material to its future commercialization of the Geomatrix technology.

In total the Company has 149 patents protecting the Geomatrix technology, which represents 21 patent families.

### ***DepoFoam Technology***

Through its acquisition of SkyePharma Inc. in 1999, the Company acquired a large portfolio of patents relating to the DepoFoam technology. There are in excess of 20 patent families relating to this technology, with patents granted in respect of these various families in the United States, Japan, Australia, New Zealand, Europe, Canada and many other countries. The majority of these patents will continue in force until 2014. Additional filings of patent applications have been made for improvements of the initial technology and for innovative technology relating to this subject matter. These applications have been filed in the United States, Australia, New Zealand, Canada, Japan and Europe and in many other countries throughout the world.

In addition, through a prior agreement entered into by SkyePharma Inc. with RDF, RDF granted certain rights, on an exclusive basis, relating to the DepoFoam technology to SkyePharma Inc. Under the agreement SkyePharma Inc. is obligated to prosecute certain patent applications and maintain issued patents relating to the licensed intellectual property. RDF retains the right to terminate the agreement or to convert the exclusive nature of the rights granted under the agreement, into a non-exclusive license in the event that SkyePharma Inc. does not satisfy its contractual obligations including making certain minimum annual payments. Additional termination events include bankruptcy and a material breach of the agreement which is not remedied within a specified period. The termination of this agreement or the conversion to a non-exclusive agreement would have a material adverse effect on the Company.

### ***Inhalation Technology***

The Company has twelve patent families in respect of this technology. One family covers the device itself as well as several of the structural elements and features incorporated therein, and has been granted in Switzerland, Europe, the United States, Australia, Canada, Japan and New Zealand and the first to expire of these patents, expires in 2015. Other patent families relate to a dry powder, for use with the Dry Powder Inhalers.

The Company has, together with other companies working in the same area, been involved in several European patent oppositions related to the use of environmentally friendly HFA as propellants. Of these oppositions three have been settled and the remaining five are in various stages within the European Patent Office. There is also a further opposition relating to the use of micronized powder for inhalation. There are currently six oppositions in which SkyePharma is participating in relation to various aspects of inhalation technologies.

### ***Topical Technology***

The Company acquired a wide range of intellectual property rights from Cade Struktur. Patents and applications covering many and varied uses of hyaluronic acid have been filed throughout the world. Following these filings, patents have been granted in, amongst others the United States, Europe, Australia, New Zealand and South Africa, expiring between 2010 and 2013. During the last twelve months the Company obtained two new U.S. patents regarding formulations containing hyaluronic acid. A further 18 patents were granted in non-U.S. territories. Following the acquisition of the Cade Struktur portfolio in 1999, the Company is continuing to pursue 81 pending patent applications. In order to rationalize the portfolio, the Company has assigned 4 patent families to Meditech, in return for a lump sum payment as well as royalties deferred from products sold which incorporate such assigned rights.

### ***Solubilization***

The Company previously acquired two patent families; these related to solid lipid nanoparticles and to nano-suspensions which are useful for drug delivery. The granted patents for this technology are in territories including Australia, Canada, Japan and Europe and will expire in 2012. There are also applications pending for this technology in the United States. In respect of the nano-suspension technology, there is a granted patent in the United States expiring in 2015 and corresponding applications filed in Europe, Australia, Canada and Japan as well as other countries. The Company also has an exclusive license under two further patent families: one relating to solid polymer nano-particulate technology and the other to further developments in the areas of solid lipid nano-particles and nano-suspensions.

As part of its recent acquisition of SkyePharma Canada, the Company acquired a large portfolio of patents and patent applications. The portfolio consists of three broad patent families relating to:

- i) Lipid stabilized microparticle technology (where the drug is a solid particle);
- ii) Lipid stabilized microdroplet technology (where the drug is a liquid); and
- iii) Omega-3 oil stabilized drug technology, which is useful for drug delivery.

The technology is protected by 15 U.S. patents and by 70 corresponding patents in countries outside the United States. In addition, the portfolio contains many pending applications, including 23 U.S., 35 outside of the United States and 23 regional (European and PCT) patent applications.

The granted patents will expire at various times. Those relating to U.S. rights for microparticle technology will expire in April 2010, and related non-U.S. patents will expire in April 2011. U.S. Patents related to microdroplet technology will expire in November 2003 and February 2005 respectively, related patents in Canada and Japan will expire in June 2004.

### ***Patent Protection***

There can be no assurance that the Company will be issued any additional patents or that if any patents are issued, they will provide the Company with significant protection or will not be challenged by third parties asserting claims against the Company concerning its existing products or with respect to future products under development by the Company. The Company, from time to time, may receive notification of alleged infringements. The Company may not, in all cases, be able to resolve any such allegations through licensing arrangements, settlement or otherwise. Furthermore, the Company anticipates that any attempt to enforce its patents would be time consuming and costly. Moreover, the law of some foreign countries does not protect the Company's proprietary rights in the products to the same extent, as does the United States. The U.S. Patent and Trademark Office has instituted changes to the U.S. patent law including changing the term to 20 years from the date of filing for applications filed after June 8, 1995. The Company cannot predict the effect that such changes on the patent laws may have on its business or on the Company's ability to protect its proprietary information and sustain the commercial viability of its products.

There can be no assurance that the Company's patents or any future patents will prevent other companies from developing similar or functionally equivalent products. Furthermore, there can be no assurance that (1) any of the Company's future processes or products will be patentable, (2) any pending or additional patents will be issued in any or all appropriate jurisdictions, (3) the Company's processes or products will not infringe upon the proprietary rights of third parties, or (4) the Company will have the resources necessary to protect its patent rights against third parties. The inability of the Company to protect its patent and proprietary rights or the infringement by the Company of the patent or proprietary rights of others could have a material adverse effect on the Company's business, financial condition or results of operations.

The Company also relies on trade secrets and proprietary know-how which it seeks to protect, in some cases through confidentiality clauses in agreements with its employees and consultants. There can be no assurance that these agreements will not be breached, that the Company would have adequate remedies from any breach or that the Company's trade secrets will not otherwise become known or be independently developed by competitors.

There has been substantial litigation in the pharmaceutical, biomedical and biotechnology industries with respect to the manufacture, use and sale of new products that are the subject of conflicting patent rights. Most of the brand name controlled-release products of which the Company is developing generic versions are covered by one or more patents. Under the Hatch-Waxman amendments, when a drug developer files an ANDA for a generic drug, and the developer believes that an unexpired patent, which has been listed with the FDA as covering that brand name product, will not be infringed by the developer's product or is invalid or unenforceable, the developer must so certify to the FDA. That certification must also be provided to the patent holder, who may challenge the developer's certification of non-infringement, invalidity or unenforceability by filing a suit for patent infringement. If a suit is filed within 45 days of the patent holder's receipt of such certification, the FDA can review and approve the ANDA, but is precluded from granting final marketing approval of the product until a final judgment in the action has been rendered or 30 months from the date the certification was received, whichever is sooner. Should a patent holder commence a lawsuit with respect to alleged patent infringement by the Company, the uncertainties inherent in patent litigation make the outcome of such litigation difficult to predict. The Company evaluates the probability of patent infringement litigation with respect to its ANDA submissions on a case by case basis. The delay in obtaining FDA approval to market the Company's product candidates as a result of litigation, as well as the expense of such litigation, whether or not the Company is successful, could have a material adverse effect on the Company's business, financial condition or results of operations.

## Manufacturing

### *Geomatrix and Inhalation Manufacturing*

The Company presently manufactures three Geomatrix products, Cordicant-Uno, Madopar DR and Diclofenac-ratiopharm-uno, and produces bio-batches for its collaborative partners.

Manufacturing operations take place at the Company's Lyon facility in France and Muttenz facility in Switzerland. In Muttenz the Company has a 9,647 square meter (103,826 square feet) facility. In Lyon the Company has an approximately 17,000 square meter (183,000 square feet) pharmaceutical manufacturing and production facility and an approximately 2,400 square meter (25,850 square feet) adjoining office complex. The Company acquired the Lyon facility in 1997 by acquiring 100% of the issued and outstanding share capital of Laboratories Novalis Production SAS ("Novalis"), a French company, from Wyeth-Ayerst International Inc., ("Wyeth"), a wholly-owned subsidiary of American Home Products Inc. ("AHP"), for a total consideration, excluding acquisition expenses, of two French francs and the assumption of liabilities in the amount of £891,000 arising out of a loan from Wyeth-Ayerst International, which is also a wholly-owned subsidiary of AHP. After the acquisition, Novalis changed its name to Jago Production SAS.

The terms of the acquisition allowed the Company to transfer its manufacturing activities gradually into the new facility over a three-year period from 1997 to 1999 without assuming all of the operating costs of the facility up front. The Company packaged certain pharmaceutical products and other products ("Contract Products") on behalf of certain subsidiaries of AHP. The current manufacturing space was sufficient to allow the Company to continue to package the Contract Products on behalf of AHP and to install the Company's own manufacturing suite. The facility is in compliance with cGMP with respect to the packaging operations and it had European regulatory approval to package the Contract Products. Under the original contract with AHP, AHP's subsidiaries compensated the Company on a sliding scale of 100%, 85% and 50% during the first, second and third year of the agreement, respectively, for the costs of operating the Lyon facility.

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AHP's subsidiaries were responsible for the registration of the Contract Products with all proper health, customs and other authorities under applicable law, but the Company furnished assistance to AHP's subsidiaries from time to time in connection with their filing of documentation as is necessary for such registrations. The Company's arrangements with AHP expired in 2001, and the Company no longer packages any products for AHP.

The Company has completed its Geomatrix manufacturing suite in the Lyon facility at a capital cost of approximately £7.1 million. This facility will be used to manufacture products for collaborative partners and for the Company. The facility will enable the Company to manufacture its own products in addition to contracting with third parties. The Muttenz facility will, however, remain the Company's principal research and development and laboratory facility for Geomatrix and inhalation products.

Currently, manufacturing operations for Cordicant-Uno, Madopar DR and Coruno take place at the Company's Muttenz site.

The Company is in the process of expanding its operations at the Lyon facility to include production activities for dry powder inhaler products pursuant to the Novartis development contract, see "Drug Delivery Platforms Inhalation Inhalation Products in Development" at a capital cost to date of approximately £8.1 million. Pending the successful outcome of an FDA pre-approval inspection, commercial production is expected to begin in late 2003.

The Lyon facility was designed and built for drug production in 1993 by American Cyanamid but was used instead for packaging activities. The Company believes that it has substantially brought the facility into compliance with cGMP and FDA standards at a cost of approximately £0.8 million. 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 XR. The Company is in the process of qualifying the facility as a second site of manufacture for Xatral. 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. 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.

On May 14, 2002 SkyePharma announced its intention to enter a wide-ranging strategic collaboration with Kowa Company Ltd., a leading Japanese company with substantial pharmaceutical interests, which proposes, under a Subscription Agreement signed on May 13, 2002, to make a strategic investment in SkyePharma. Kowa and SkyePharma have signed a separate non-binding Letter of Intent to evaluate Kowa's acquisition of a 50% interest in SkyePharma's manufacturing facility in Lyon. Kowa and the Company are still considering the proposal. Kowa and SkyePharma have an active relationship involving the formulation development and scale-up for certain formulations of a new lipid-lowering

agent NK-104 to support late-stage clinical development of the drug. The two parties now intend to strengthen their commercial relationship through manufacturing formulations of NK-104. For additional information, see "Item 7: Major Shareholders and Related Party Transactions Major Shareholders".

### ***DepoFoam Manufacturing***

In connection with its collaborative arrangements, the Company may elect to maintain exclusive formulation and manufacturing rights to any DepoFoam encapsulated drugs, or enter into a technology transfer agreement with corporate partners, which would allow the corporate partner to manufacture a DepoFoam formulation of the partner's drug under license from SkyePharma. Under these arrangements, the Company would receive compensation based on the manufacturing costs of the product or royalties, or both. The Company commenced manufacturing DepoCyt for commercial distribution and sale following approval of this drug in April 1999. Manufacturing is in an approximately 2,020 square meter (21,746 square feet) facility built for this purpose. This facility complies with cGMP regulations and has been approved for the manufacture of DepoCyt by the

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FDA and European Medicines Evaluation Agent ("EMA") and licensed for drug manufacturing by the State of California. Clinical trial materials are also manufactured in this facility. The Company must undergo and pass a preapproval inspection for many countries outside the United States in which applications to obtain marketing approval may be filed. Prior to marketing DepoCyt (and any other drugs) outside the United States, Canada and Europe, the Company will need to meet applicable regulatory standards, achieve prescribed product quality and reach necessary levels of production of such products and obtain marketing approvals.

In October 1999, SkyePharma Inc. discovered that two lots of DepoCyt did not meet specifications and recalled these lots. Investigations identified that changes in a supplier's manufacturing process for raw material resulted in product that 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 addition, SkyePharma Inc. leases an approximately 7,600 square meter (82,000 square feet) facility housing its administrative, research and development and future manufacturing activities. Effective June 2000, the Company subleased to a third party approximately 15,600 square feet of this facility. This lease expired on July 31, 2002. Prior to commencing commercial manufacturing operations from this facility, the Company will need to comply with additional and necessary validation, regulatory and inspection requirements.

To date, SkyePharma Inc. has relied on a particular method of manufacture for products based on its DepoFoam technology which involves processes known only to SkyePharma Inc. There can be no assurance that this method will be applicable to all pharmaceuticals the Company desires to commercialize. Further, the yield of DepoFoam product may be highly variable for different drugs. Finally, the Company will need to successfully meet any manufacturing challenges associated with the characteristics of the drug to be encapsulated. The physical and chemical stability of the DepoFoam formulation may vary with each drug over time and under various storage conditions. There can be no assurance that the manufacturing process will result in economically viable yields of product or that it will produce formulations of therapeutic products sufficiently stable under suitable storage conditions to be commercially useful.

In the event that the Company decides to pursue alternative manufacturing methods for some or all of its injectable drugs utilizing DepoFoam, there can be no assurance that these methods will prove to be commercially practical or that the Company will have or be able to acquire rights to use such alternative methods.

### ***Manufacturing Partners***

While the Company has its own manufacturing sites for Geomatrix, inhalation and DepoFoam manufacturing, for the manufacture of certain of its existing products, and certain of those currently in development, the Company will depend on manufacturing partners.

Under the terms of the development and commercialization agreement with Endo for DepoMorphine, a DepoFoam product, and Propofol IDD-D, a product using the Company's IDD solubilization technology, signed in December 2002, the Company is primarily responsible for the clinical development of the products 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. The Company currently has no internal manufacturing site equipped to manufacture its IDD solubilization products and is therefore seeking to conclude a supply agreement with a manufacturing partner for Propofol. The Company has also agreed to qualify and obtain final regulatory approval for a second manufacturing site for DepoMorphine and Propofol, either internally or through a third party manufacturing partner, within a specified period from the date of first

commercial sale.

### **Supplies and Raw Materials**

The Company and its collaborative pharmaceutical company partners rely on certain suppliers of key raw materials. Certain of those materials are purchased from single sources and others may be purchased from single sources in the future. Although the Company has no reason to believe that it and its collaborative pharmaceutical company partners will be unable to procure adequate supplies of such raw materials on a timely basis, and at commercially reasonable rates, disruptions in supplies, including delays due to the inability of the Company's pharmaceutical company partners, the Company or its manufacturers to procure raw materials, would have a material adverse effect on the Company's business.

Regulatory requirements for pharmaceutical products tend to make the substitution of suppliers costly and time-consuming. The inability to develop alternative sources could have a material adverse effect on the Company's ability to manufacture and market its products.

One of the DepoFoam Injectable products in development, DepoMorphine, has morphine sulphate as its active ingredient. Morphine sulphate is classified as a Scheduled Drug by the DEA. The DEA has determined that these drugs have a high potential for abuse and could lead to severe psychological or physical dependence. The DEA controls the national production and distribution of certain Scheduled Drugs in the United States by allocating production quotas based, in part, upon the DEA's view of national demand. SkyePharma Inc. has a DEA license to use morphine sulphate in its research and manufacturing of DepoMorphine. While the Company expects that adequate quantities of the drug will be available to it to meet future research and commercial requirements, there can be no assurance to that effect.

### **Sales and 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. However, in some more recent collaborations, contracts have included certain commitments for the Company's partners to market products developed in collaboration with the Company.

### **Competition**

The pharmaceutical industry is highly competitive and is affected by new technologies, governmental regulations, health care legislation, availability of financing and other factors. Many of the Company's competitors have longer operating histories and greater financial, marketing and other resources than the Company.

The Company is and will continue to be subject to competition from numerous other entities that currently operate, or intend to operate, in the pharmaceutical industry. These include companies that are engaged in the development of controlled-release technologies and products, as well as other pharmaceutical manufacturers that may decide to undertake in-house development of these products.

As the pharmaceutical industry continues to consolidate and as pressures increase for cost-effective research and development, some pharmaceutical companies have reduced and may continue to reduce their funding of research and development. Competition for limited client financing may therefore increase, and this competition could include the clients' internal research and development programs, other drug delivery programs and other technologies and products of third parties.

### **Government Regulation**

All drugs and medical devices, including the Company's products under development, are subject to extensive regulation in the United States and Europe, the Company's two principal

markets. In the United States, the primary regulatory body is the FDA, although to a lesser extent state and local authorities are also involved in the regulatory process. In Europe, there are two regulatory systems. There is a European Union system that is the responsibility of the EMEA. In addition, each country has its own regulatory agency. In both the United States and Europe, the applicable regulations govern or influence the development, testing, manufacture, safety, labeling, storage, record keeping, approval, advertising, promotion, sale and distribution of prescription pharmaceutical products. Pharmaceutical manufacturers are also subject to certain record keeping and reporting requirements, establishment registration and product listing and agency inspections. In addition, acts of foreign governments may affect the price or availability of raw materials needed for the development or manufacture of generic drugs.

#### *United States*

The federal Food, Drug and Cosmetics Act ("FDCA"), the Public Health Services Act, the Controlled Substances Act and other federal statutes and regulations govern or influence all aspects of the Company's business. Noncompliance with applicable requirements can result in fines and other judicially imposed sanctions, including product seizures, injunctive actions and criminal prosecutions. In addition, administrative or judicial actions can result in the recall of products, and the total or partial suspension of the manufacturing of products, as well as the refusal of the government to approve pending applications or supplements to approved applications. The FDA also has the authority to withdraw approvals of drugs in accordance with statutory due process procedures.

FDA approval is required before any dosage form of any new unapproved drug, including a generic equivalent of a previously approved drug, can be marketed. All applications for FDA approval must contain information relating to evidence of safety and efficacy or bio-equivalence to a listed reference drug, product formulation, stability, manufacturing processes, packaging, labeling and quality control.

#### *ANDA Process*

The Drug Price Competition and Patent Restoration Act of 1984, known as the Hatch-Waxman Act, established abbreviated application procedures for obtaining FDA approval for those drugs which are off-patent and whose non-patent exclusivity under the Hatch-Waxman Act has expired and which are shown to be bioequivalent to brand-name drugs. Approval to manufacture these drugs is obtained by filing an ANDA. An ANDA is a comprehensive submission which generally must contain data and information pertaining to the bioequivalence of the drug covered by the ANDA to a referenced listed drug, formulation specifications, stability data, analytical data, methods and manufacturing validation data and quality control procedures. As a substitute for clinical studies, the FDA requires data indicating that the ANDA drug formulation is bioequivalent to a previously approved NDA drug. In order to obtain an ANDA approval of a strength or dosage form which differs from the referenced brand-name drug, an applicant must file and have granted an ANDA Suitability Petition. A product is not eligible for ANDA approval if it is not bioequivalent to the referenced brand-drug or if it is intended for a different use. However, such a product might be approved under a Section 505(b)(1) or (b)(2) NDA with supportive data from clinical trials.

The advantage of the ANDA approval process is that an ANDA applicant generally can rely upon bioequivalent data in lieu of conducting pre-clinical testing and clinical trials to demonstrate that a product is safe and effective for its intended use(s). While the FDCA provides for a 180-day review period, the Company believes the average length of time between initial submission of an ANDA and receiving FDA approval is at least two years.

While the Hatch-Waxman Act established the ANDA, it has also fostered pharmaceutical innovation through such incentives as market exclusivity and patent restoration. The Hatch-Waxman Act provides two distinct market exclusivity provisions which either preclude the submission or delay the approval of a competitive drug application. A five-year marketing exclusivity period is

provided for new chemical compounds and a three-year marketing exclusivity period is provided for applications containing new clinical investigations essential to the approval of the application. The non-patent marketing exclusivity provisions apply equally to patented and non-patented drug products. Any entitlement to patent marketing exclusivity under the Hatch-Waxman Act is based upon the term of the original patent plus any patent extension granted under the Hatch-Waxman Act as compensation for reduction of the effective life of a patent as a result of time spent by the FDA in reviewing the innovator's NDA. The patent and non-patent marketing exclusivity provisions do not prevent the filing or the approval of a full Section 505(b)(1) NDA. Additionally, the Hatch-Waxman Act provides 180-day marketing exclusivity against effective approval of another ANDA for the first ANDA applicant who submits a certification challenging a listed patent as being invalid or not infringed and successfully defends in court any patent infringement action based on such certification.

#### *NDA Process*

An NDA is a filing submitted to the FDA to obtain approval of a new drug or a new formulation of an existing drug and must contain complete pre-clinical and clinical safety and efficacy data or a right of reference to such data. Before dosing a new drug in healthy human subjects or patients may begin, stringent government requirements for pre-clinical data must be satisfied. The preclinical data, typically obtained from studies in animal species, as well as from laboratory studies, are submitted in an Investigational New Drug application, or its equivalent in countries outside the United States, where clinical trials are to be conducted. The pre-clinical data must provide an adequate basis for evaluating both the safety and the scientific rationale for the initiation of clinical trials.

Clinical trials are typically conducted in three phases, Phase I, II and III. A description of each of these phases of development is included in "Research and Development Development Process for Brand-Name Pharmaceuticals". Data from pre-clinical testing and clinical trials are submitted to the FDA as an NDA for marketing approval. The process of completing clinical trials for a new drug is likely to take several years and require the expenditure of substantial resources. Preparing an NDA or marketing authorization application involves considerable data collection, verification, analysis and expense, and there can be no assurance that approval from the FDA will be granted on a timely basis, if at all. The approval process is affected by a number of factors, primarily the risks and benefits demonstrated in clinical trials as well as the severity of the disease and the availability of alternative treatments. The FDA may deny an NDA or marketing authorization application if the regulatory criteria are not satisfied, or such authorities may require additional testing or information.

Even after initial FDA approval has been obtained, further studies, including Phase IV post-marketing studies, may be required to provide additional data on safety and will be required to provide approval for the use of a product as a treatment for clinical indications other than those for which the product was initially tested. Also, the FDA or other regulatory authorities require post-marketing reporting to monitor the adverse effects of the drug. Results of post-marketing programs may limit or expand the further marketing of the products. Further, if there are any modifications to the drug, including changes in indication, manufacturing process or labeling or a change in manufacturing facility, an application seeking approval of such changes must be submitted to the FDA or other regulatory authority. Additionally, the FDA regulates post-approval promotional labeling and advertising activities to assure that such activities are being conducted in conformity with statutory and regulatory requirements. Failure to adhere to such requirements can result in regulatory actions which could have a material adverse effect on the Company's business, results of operations and financial condition.

The FDCA provides for NDA submissions that may rely in whole or in part on publicly available clinical data on safety and efficacy under section 505(b)(2) of the FDCA. The Company and its collaborative partners may be able to rely on existing publicly available safety and efficacy data in filing NDAs for extended-release products when such data exist for an approved immediate-release

version of the same chemical entity. However, there is no guarantee that the FDA will accept such applications under section 505(b)(2), or that such existing data will be publicly available or useful. Further, utilizing the section 505(b)(2) application process is uncertain, because neither the Company nor the FDA have had significant experience with it. Additionally, under the Prescription Drug User Fee Act of 1992 (the "PDUFA"), all NDAs require the payment of a substantial fee upon filing, and other fees must be paid annually after approval. Under the PDUFA, there are circumstances when waivers may be granted to the payment of user fees. No assurances exist that, if approval of an NDA is required, such approval can be obtained in a timely manner, if at all.

### *Other Regulation*

The Prescription Drug Marketing Act ("PDMA"), which amends various sections of the FDCA, imposes requirements and limitations upon drug sampling and prohibits states from licensing wholesale distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include, among other things, state licensing of wholesale distributors of prescription drugs under federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations of these and other provisions. Various sections of the PDMA are still being implemented by the FDA and the states. Nevertheless, failure by the Company's distributors to comply with the requirements of the PDMA could have a material adverse effect on the Company's business, results of operations and financial condition.

Manufacturers of marketed drugs must comply with cGMP regulations and other applicable laws and regulations required by the FDA, the Environmental Protection Agency, the DEA, the HPB in Canada, the EMEA in the European Union and other regulatory agencies. Failure to do so could lead to sanctions, which may include an injunction suspending manufacturing, the seizure of drug products and the refusal to approve additional marketing applications. The Company seeks to ensure that any third party with whom it contracts for product manufacturing will comply with cGMP. The FDA conducts periodic inspections to ensure compliance with these rules. However, there can be no assurance that any such third parties will be found to be in compliance with cGMP standards. Any such non-compliance could result in a temporary or permanent interruption in the development and testing of the Company's planned products or in the marketing of approved products, as well as increased costs. Such non-compliance could have a material adverse effect on the Company's business, results of operations and financial condition. In addition, SkyePharma Inc.'s manufacturing facility located in San Diego, California is regulated by the State of California, Department of

Health Services, Food and Drug Branch, and the DEA.

**European Union Regulation**

The European drug registration system is based on co-operation between the EMEA, established in London, and competent national authorities of the member states of the European Union.

Since 1995, two new registration procedures have been available throughout the European Union.

The first of these is a centralized procedure which is compulsory for medicinal products derived from biotechnology, and available at the request of companies for other innovative new products. Marketing Authorization Applications (MMA's) are submitted to the EMEA in London. At the conclusion of the EMEA's internal scientific evaluation, the opinion of the EMEA's scientific committee is transmitted to the European Commission, the approval of which will form the basis of a single market authorization applying to the whole European Union.

The second procedure is 'mutual recognition' which is mandatory for most conventional medicinal products. It is based upon the principle of mutual recognition of national authorizations and it provides for the extension of an MAA granted by one member state of the European Union to one or more other member states identified by the applicant. Should the original national

authorization not be recognized in another member state the points in dispute are submitted to EMEA's scientific committee for arbitration.

In both cases, the final decision is adopted by the European Commission, with the assistance of the EMEA or, in the event of serious disagreement between the member states, by the European Council. In addition, certain European countries outside the European Union follow the decisions of the European Commission.

In addition to the above forms of regulation, price constraints on pharmaceutical products exist in most countries either through governmental regulation or pressure from healthcare organizations. In some countries, governments or governmental agencies are substantial purchasers of human healthcare products and this also imposes an indirect form of regulation on the industry.

**Environmental Matters**

The Company's operations are subject to a number of environmental laws and regulations in each of the jurisdictions in which it operates governing, among other things, air emissions, wastewater discharges, the use, handling and disposal of hazardous substances and wastes, soil and groundwater contamination, as well as employee health and safety. Environmental compliance obligations and liability risks are inherent in many of the Company's manufacturing activities.

The Company believes that its operations are currently in material compliance with all applicable environmental laws and regulations. In many jurisdictions, environmental requirements may be expected to become more stringent in the future, which could affect the Company's ability to obtain or maintain necessary authorizations and approvals and result in increased environmental compliance costs. While the Company's management does not believe that environmental compliance or remedial requirements are likely to have a material effect on the Company, there is no assurance that future material environmental compliance or remedial obligations will not arise in connection with the Company's operations or facilities or that such obligations will not have a material adverse effect on its business, financial condition or results of operations.

**ORGANIZATIONAL STRUCTURE**

SkyePharma PLC is an international pharmaceutical company and has a number of wholly-owned principal subsidiary undertakings as detailed below:

Company	Country of incorporation	% Held <sup>(1)</sup>
SkyePharma Canada Holding Inc.*	Canada	100%
SkyePharma Canada Inc.	Canada	100%
SkyePharma Production SAS*	France	100%
Krypton Limited	Gibraltar	100%



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Company	Country of incorporation	% Held <sup>(1)</sup>
SkyePharma Holding AG*	Switzerland	100%
Jago Holding AG	Switzerland	100%
SkyePharma AG	Switzerland	100%
Jagotec AG <sup>(2)</sup>	Switzerland	100%
SkyePharma Holding Inc.*	U.S.	100%
SkyePharma US Inc.	U.S.	100%
SkyePharma Inc.	U.S.	100%
SkyePharma AB*	Sweden	100%

\*  
Directly held by SkyePharma PLC

(1)  
Portion of ownership interest equals portion of voting power held.

(2)  
Jago Research AG and Jagotec AG are currently being merged, effective as of January 1, 2003. Jagotec AG will be the surviving entity.

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### Property, Plants and Equipment

The Company's principal executive offices are located in an approximately 850 square meter (9,150 square feet) facility in London, England. The premises are occupied pursuant to a lease expiring in December 2005 at a total annual rent of approximately £522,000 per year. The Company also leases a small office space in New York City, New York, for a total annual rent of approximately \$420,000 pursuant to a leasing agreement renewed in February 2001 for two years based on an independent valuation. The Company is currently negotiating an extension to this lease. Following expiry of the Company's short-term lease on its office in Exton, Pennsylvania in December 2002, the Company's U.S. business development operations were moved to the New York office.

In January 1997, the Company acquired an approximately 17,000 square meter (183,000 square feet) pharmaceutical manufacturing and production facility and an approximately 2,400 square meter (25,850 square feet) adjoining office space near Lyon, France by acquiring 100% of the issued and outstanding share capital of Novalis from Wyeth for a total consideration of two French francs and the assumption of certain liabilities. See "Business Operations Manufacturing Geomatrix and Inhalation Manufacturing" above.

In addition, the Company owns a 3,435 square meter (36,961 square feet) facility in MuttENZ, Switzerland in which its principal research and development, production, small-scale manufacturing, laboratory and workshop operations are housed. In February 1999, the Company purchased a warehousing and administration facility in MuttENZ, Switzerland, of approximately 6,138 square meters (66,045 square feet), including approximately 2,040 square meters (22,000 square feet) previously occupied by the Company under a leasing agreement. The purchase price of Chf 10.2 million was financed by a bank mortgage at fixed interest rate of 3% per annum with repayments of Chf 100,000 semi-annually. Interest and repayment terms will be renegotiated at the end of the five-year period. The building has since been extended and refitted to house additional administrative, research and laboratory operations, and the building was officially re-opened on April 7, 2001.

On March 10, 1999, the Company acquired SkyePharma Inc., which maintains its principal operations in a leased 7,600 square meter (82,000 square feet) building in San Diego, California. The facility houses production, research and development and administrative functions. The future minimum annual rental commitment ranges from \$2.9 million to \$4.3 million per year over the balance of the remaining lease term of approximately 13 years based upon pre-established annual rent increases. Effective June 2000, the Company subleased to a third party approximately 15,600 square feet of this facility. Sublease income totaled approximately \$998,000 over the term of the lease, which expired July 31, 2002. Upon expiry, the Company began to use the additional space for its own operations. With the acquisition of SkyePharma Inc., the Company also acquired the leasehold of a 2,020 square meter (21,746 square feet) purpose built facility, approved by the FDA for the commercial manufacture of DepoCyt. The lease expires in January 2006 and annual rental fees range from \$653,000 to \$720,000 in this period. Additionally, the Company maintains a leased facility containing primarily office space, with lease terms expiring in January 2006. The facility was subleased effective January 1, 2001 with annual rental income ranging from \$317,000 to \$352,000 for the terms of the sublease, which expires on January 31, 2006. At the end of February 2003, the Company was notified that the sublessee was discontinuing operations, and would discontinue rental payments due under the sublease arrangement effective April 1, 2003. The Company is actively seeking a new tenant for the space, while seeking to enforce its rights under the existing sublease.

On December 27, 2001, the Company reached agreement to acquire the majority of the outstanding voting shares in RTP, now SkyePharma Canada. SkyePharma Canada maintains its principal operations in a leased 36,000 square foot building located in Montreal, Québec, Canada. The building houses an 18,000 square foot purpose built facility, including laboratories, approved GMP clean-room, and offices with the remaining 18,000 square feet space being used for research & development, storage and administrative functions. The future minimum rent commitments are Cdn\$ 385,000 per year until December 2005, with an additional 5 year renewal option. The Company is currently in the process of renegotiating this lease.

On May 13, 2002, the Company acquired the entire drug delivery business of Bioglan AB, and formed SkyePharma AB which maintains its operations in 1,925 square meter leased facilities in Malmö, Sweden. The facility houses research and development and administrative functions. The annual rental commitment for the first term of the rental agreement to November 30, 2003 is SKr 4,930,000. After the first term of the rental agreement SkyePharma AB has the option to prolong the rental agreement for a further 12 months with a 6 month notice period. Thereafter the agreement is automatically renewed annually. The annual rent will increase at 3% per year from November 30, 2003.

The Company believes that its current facilities are adequate to meet its anticipated needs for the foreseeable future.

#### **Item 5: Operating and Financial Review and Prospects**

*The following discussion contains forward-looking statements that involve risks and uncertainties. The Company's actual results may differ materially from the results discussed in such forward-looking statements as a result of various factors, including those set forth under the caption "Risk Factors".*

The following discussion and analysis of the financial condition and results of the operations of the Company should be read in conjunction with the Consolidated Financial Statements of the Company, including related Notes, and other financial information included in this annual report. For the Company's Consolidated Financial Statements as of and for the three years ended December 31, 2002 see the information set forth beginning on page F-1. SkyePharma prepares its consolidated financial statements in accordance with U.K. GAAP, which differ in certain 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 is set out in Note 30 of the Notes to the Consolidated Financial Statements.

#### **CRITICAL ACCOUNTING POLICIES AND ESTIMATES**

The preparation of the Consolidated Financial Statements requires the Company to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. On an on-going basis, the Company evaluates its estimates, including those related to revenue recognition, intangible assets, deferred consideration and other contingent liabilities. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable. Actual results may differ from these estimates under different assumptions or conditions.

#### **Revenue Recognition**

The Company's revenues comprise contract development and licensing, royalty, and contract manufacturing and distribution income. Contract development and licensing income represents amounts invoiced to customers for services rendered under development and licensing agreements, including milestone payments and technology access fees. Under U.K. GAAP, contract revenue is recognized when earned and non-refundable and to the extent that there are no future obligations pursuant to the revenue, in accordance with the contract terms. Refundable contract revenue is treated as deferred until such time as it is no longer refundable. Royalty income represents income as a percentage of product sales. Advance royalties received are treated as deferred income until earned, when they are recognized as income. Manufacturing and distribution revenues principally comprise contract manufacturing fees invoiced to third parties and income from product sales. See discussion of revenues under "Operating Results - Year ended December 31, 2002 compared with the year ended December 31, 2001" below.

Under U.S. GAAP, the Company recognizes revenue in accordance with SEC Staff Accounting Bulletin No. 101 (SAB 101). The Company recognizes up-front fees and milestone payments when

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they are non-refundable and when performance obligations are completed based on the criteria of SAB 101. In situations where those criteria are not met, the Company defers and recognizes up-front non-refundable fees ratably over the performance period. The application of SAB 101 criteria to complex collaboration agreements requires significant estimates and judgment. In addition, in arrangements with multiple deliverables, there may be significant judgment in separating the different revenue generating activities and in determining whether each is a separate earnings process. Milestone payments, if any, related to scientific or technical achievements are recognized in income when the milestone is accomplished. The terms of such arrangements may cause our operating results to vary considerably from period to period. Due to the significant portion of our revenue that we currently receive from up-front fees, milestone payments and certain contract development reimbursements in which recognition criteria differ between U.K. and U.S. GAAP, our results from operations will continue to differ, at times significantly.

The Directors believe that the Group's revenue recognition policy is appropriate, reflecting the appropriateness of recording revenue under U.K. GAAP where costs associated with the revenue have been expensed and the deferral of revenue when it is subject to future obligations on the part of the Company connected with the revenue.

During 2002, the Group deferred a further net £6.3 million of turnover and other income under this policy, including amounts relating to the licensing agreements with Endo, Enzon and Shire, in addition to the £11.7 million deferred at the end of 2001. This results in total deferral of £18.0 million at the end of 2002 comprising:

### *Deferred Income*

	At December 31, 2001	Received <sup>(1)</sup>	Recognized <sup>(2)</sup>	At December 31, 2002
	(in £ thousands)			
Contract development and licensing revenue	6,959	58,682	(55,441)	10,200
Other operating income	4,731	17,317	(14,219)	7,829
Total	11,690	75,999	(69,660)	18,029

(1) Amounts 'received' consist of amounts received in cash pursuant to the contract terms and amounts included within debtors during 2002. Deferred income at December 31, 2002 will be released under U.K. GAAP in later years in line with the related costs or as associated obligations under the relevant contracts are satisfied.

(2) Amounts 'recognized' consist of amounts received and not deferred as well as amounts released from deferred income under U.K. GAAP during 2002 and recorded in the income statement.

### **Intangible Fixed Assets**

The Company's intangible fixed assets comprise goodwill, intellectual property and capitalized development costs. The Directors estimate the useful economic life of such assets and the assets are amortized over this period. Future events could cause the Directors to amend their view of the estimated economic life of these assets.

Under U.S. GAAP, if appropriate, the Company allocates a portion of the consideration paid to purchase other businesses to acquired in-process research and development with no alternative future use, which is written off directly to net income in the period in which the acquisition is made. The valuation of acquired in-process research and development requires significant management estimates and judgment as to expectations for various products and business strategies. Significant changes to the assumptions and judgments used in the purchase price allocation could result in different valuations for acquired in-process research and development and goodwill.

### **Impairment of Fixed Assets**

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The Company reviews the carrying value of fixed assets when there is an indication that the assets may be impaired. First-year impairment reviews are conducted for acquired goodwill and intangible assets. Impairment is determined by reference to the higher of net realisable value and value in use, which is measured by reference to discounted future cash flows. Any provision for impairment is charged to the income statement in the year concerned. Judgments regarding the existence of impairment indicators are based on legal factors, market conditions and operational performance of our acquired businesses. Future events could cause the Company to conclude that impairment indicators exist and assets may have been impaired. Any resulting impairment loss could have a material adverse impact on the Company's financial condition and results of operations.

Under U.S. GAAP, the Company adopted SFAS No. 142, Goodwill and Other Intangible Assets ("FAS 142") on January 1, 2002. Under FAS 142, goodwill is no longer amortized but will be tested for impairment at least on an annual basis in accordance with the provisions of FAS 142.

The goodwill impairment test involves a comparison of the fair value of each of our reporting units as defined under FAS 142, with the carrying amounts of net assets, including goodwill, related to each reporting unit. If the carrying amount exceeds a reporting unit's fair value, the second step of the impairment test is performed to measure the amount of impairment loss, if any. The impairment loss is measured based on the amount by which the implied fair value of goodwill exceeds the carrying amount of goodwill in the reporting unit being tested. Fair values are determined based on valuations that rely primarily on the discounted cash flow method. This method uses future projections of cash flows from each of our reporting units and includes, among other estimates, projections of future revenues and expenses, projected capital spending and an assumption of our weighted average cost of capital. If the fair value of the asset determined is less than its carrying amount, a loss is recognized for the difference between the fair value and its carrying value.

Changes in any of these estimates, projections and assumptions could have a material effect on the fair value of these assets in future measurement periods and result in an impairment of goodwill with a material effect on the Company's future net income and shareholders' funds under U.S. GAAP.

### **Deferred Consideration**

Provisions for deferred consideration comprise the fair value of contingent consideration arising from acquisitions. The eventual outcome is subject to the Group's future performance and certain contractual terms. Provisions are reviewed annually by the Directors, who make significant judgments as to, and changes to, the estimated fair value of the contingent consideration. Based on these judgments, changes to the estimated fair value are recorded as an adjustment to goodwill or the underlying asset value. Where the effect of the time value of money is material, provisions are reflected at their present value, and the interest element arising on discounting the liability is recorded as interest payable in the profit and loss account as it unwinds. At December 31, 2002, the main judgments on balances recorded for deferred consideration related to the 1996 acquisition of Krypton and the 2001 acquisition of SkyePharma Canada.

The deferred consideration of Krypton was revised on April 26, 1996, such that a maximum of 37.5 million Ordinary Shares would be issued contingent on a change in control of the Company at a share price of not less than 80 pence compounded at an annual rate of 10%, or satisfaction of a potential four hurdles related to product approval and sales. As no Krypton products are currently being marketed and no licensing partners have been identified for any of these products, the Directors have taken the view that the above product approval and sales-related hurdles can no longer be reasonably expected to be met. Consequently no provision for deferred consideration has been recognized as at December 31, 2002 under U.K. GAAP.

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In consideration for the loss of the former SkyePharma Canada shareholders' certain option rights, which were agreed on July 19, 2001 when the Group acquired an initial 40.2% interest in SkyePharma Canada, deferred consideration was 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 under U.K. GAAP as of 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. See "Item 4: Information on the Company History and Development Corporate Acquisitions" for more information this transaction.

### **Contingent Liabilities**

Provisions for contingent liabilities are dependent upon estimates and assessments of whether the criteria for recognition have been met, including estimates by the Directors as to the probable outcome and the amount of the potential cost of resolution. The Company follows the

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strict rules for identification and recognition of such provisions in accordance with U.K. GAAP. The Company is currently involved in certain legal proceedings as discussed in "Item 8: Financial Information - Legal Proceedings". As at December 31, 2002, no costs have been accrued in relation to these proceedings because the Company does not believe that the proceedings will have a material adverse effect on the Company's consolidated financial position. Any estimate for such an accrual would be developed in consultation with external legal advisors handling the Company's defense in these matters and would be based upon an analysis of potential outcomes. It is possible that future results of operations could be materially affected by changes in our assumptions.

### OPERATING RESULTS

The following table sets forth selected items of the Company's consolidated income statement for the three years ended December 31, 2002:

	Year Ended December 31,		
	2000	2001	2002
	(in £ thousands)		
<b>Results</b>			
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

The Company has only one segment: pharmaceuticals. This reporting system is in compliance with the U.K. GAAP Statement of Standard Accounting Practice ("SSAP") rule SSAP 25 "Segmental Analysis" and also reflects the Company's internal financial reporting and the predominant sources of risks and returns in its business.

The Company's revenues are principally generated from three sources: (1) contract development and licensing, including milestone payments and technology access fees, (2) royalties from sales by third parties of products developed by the Company, and (3) contract manufacturing and distribution.

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The table below provides a breakdown of turnover by revenue source for the three years ended December 31, 2002:

	Year Ended December 31,		
	2000	2001	2002
	(in £ thousands)		
<b>Turnover by Revenue Source</b>			
Contract development and licensing <sup>(1)</sup>	16,805	38,236	55,441
Royalties	4,011	1,468	6,751
Contract manufacturing and distribution	3,476	6,422	7,381
<b>Total</b>	<b>24,292</b>	<b>46,126</b>	<b>69,573</b>

(1) Contract development and licensing comprises milestone payments and cost reimbursements for research and development services performed by the Company for third parties.

Historically, the revenue contribution of each of the Company's revenue sources has varied from period to period. This is especially true of contract development and licensing revenues, the level of which may fluctuate, depending on, among other things, scientific developments, the timing of regulatory approvals, and the market introduction of new products. As a result, year-to-year comparisons of the Company's revenues

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may be materially distorted. See "Item 3: Key Information Risk Factors The Company's results of operations tend to fluctuate" for more information on factors influencing the level of the Company's revenues.

Each of the Company's revenue sources yields significantly different gross margins. Accordingly, the comparability of gross margins from period to period is materially affected by the revenue mix in each period. For example, royalty revenues generally result in higher gross margins than contract development and licensing revenues. The Company pursues different strategies with respect to its various revenue sources. In respect of contract development and licensing revenue, the Company generally endeavors to recover its direct costs, its objective being to generate long-term profits from royalties on successful product commercializations.

After cost of sales, the Company's costs principally comprise research and development expenses, administration expenses, selling and marketing expenses, the costs of the corporate offices and interest expense. As the majority of the Company's expenses are incurred in Switzerland, France and the United States, whereas the Company's revenues are substantially denominated in U.S. dollars, the Company's results of operations, as reported in pounds sterling, may be materially influenced by exchange rate movements. Foreign currency exchange movements did not have a material impact on the results of operations during any of the periods presented below.

Inflation did not have a significant impact on the Company's operations during any of the periods presented.

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### Year Ended December 31, 2002 compared with the Year Ended December 31, 2001

The following table sets forth selected items of our consolidated income statement for the two years ended December 31, 2002.

	Year ended December 31,	
	2001	2002
	(in £ thousands)	
<b>Consolidated Income Statement</b>		
Turnover	46,126	69,573
Cost of sales	(18,820)	(24,830)
	27,306	44,743
Gross profit		
Selling, marketing and distribution expenses	(4,804)	(4,769)
Administration expenses	(16,025)	(20,192)
Research & development expenses	(17,918)	(29,285)
Other operating income	6,342	14,219
	(5,099)	4,716
Operating (loss)/profit		
Associated undertaking	(578)	
	(5,677)	4,716
(Loss)/profit on ordinary activities before interest and taxation		
Interest receivable	1,251	1,081
Interest payable	(4,951)	(4,464)
	(9,377)	1,333
(Loss)/profit on ordinary activities before taxation		
Taxation	(75)	(224)
	(9,452)	1,109
Retained (loss)/profit		

### Turnover

Turnover increased by 51%, from £46.1 million in 2001 to £69.6 million in 2002. This increase was primarily driven by a substantial increase in milestone payments, the effects of which were partially offset by lower cost reimbursements from third parties for research and development services rendered pursuant to contract development arrangements. In geographic terms, the increase in turnover was due mainly to

higher turnover in the United States. The acquisition of SkyePharma Canada Inc. (formerly RTP Pharma Inc.) contributed revenue of £3.9 million.

*Contract Development and Licensing*

Contract development and licensing revenue represents amounts invoiced to customers for client-sponsored research and development and milestone payments in accordance with the terms and conditions of the relevant collaborative arrangement. Such amounts are treated as revenue when the relevant services have been rendered or the specified milestones have been met, to the extent that there are no obligations pursuant to the revenue. Contract development and licensing revenue increased by 45%, from £38.2 million in 2001 to £55.4 million in 2002, mainly reflecting higher levels of milestone payments and upfront payments received on the signing of agreements. In 2002 milestone payments and payments received on the signing of agreements included revenue from Shire for the rights to market Solaraze in Europe, Endo for the U.S. and Canadian marketing and distribution rights for DepoMorphine and Propofol IDD-D and Enzon for the rights to DepoCyt in North America. Additionally a key milestone payment was received from GlaxoSmithKline for the completion of Phase II clinical trials for Ropinirole in November 2002.

*Royalties*

Royalty income represents amounts paid by third parties for the sale of therapeutics based on the Company's drug delivery technologies. Royalties are typically calculated as a percentage of the third parties' net sales of the relevant drugs. Advance royalty payments are treated as deferred

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income until earned, at which point they are recognized in income. Royalty income increased substantially, from £1.5 million in 2001 to £6.8 million in 2002, reflecting principally revenues from Paxil CR, which was launched in the United States in April 2002, and an increase in revenues from Xatral OD and Solaraze.

*Contract Manufacturing and Distribution*

Contract manufacturing and distribution revenue principally comprises contract manufacturing fees invoiced to third parties and revenue from the sale of products. Contract manufacturing and distribution revenue increased by 15%, from £6.4 million in 2001 to £7.4 million in 2002. The 2002 figure comprises contract manufacturing revenues of £5.4 million and SkyePharma's share of DepoCyt sales, which amounted to £2.0 million. Included in contract manufacturing revenue in 2002 is some £1.8 million in respect of Foradil DPI for Novartis and £1.0 million from Kowa under our collaboration on formulations of NK-104.

*Expenses*

*Cost of Sales*

Cost of sales consists primarily of the costs of the Company's research and development activities performed on behalf of third parties, including:

the costs of clinical trials conducted on behalf of the Company's collaborative partners,

the direct costs of contract manufacturing, and

the direct costs of licensing arrangements and royalties payable.

Cost of sales increased by 32%, from £18.8 million in 2001 to £24.8 million in 2002, reflecting the higher level of activity and increased number of projects currently being undertaken. As a percentage of turnover, cost of sales decreased from 41% to 36%. The decrease of costs of sales relative to turnover reflects an increase in the proportion of milestone payments and royalty revenue which typically offer higher margins than other types of revenue.

*Selling, Marketing and Distribution Expenses*

Selling, marketing and distribution expenses comprise the costs of marketing the Company's services and the Company's share of marketing and distributing DepoCyt. Selling, marketing and distribution expenses were £4.8 million in 2002, unchanged compared to 2001, of which, £2.8 million related to product sales such as DepoCyt and £2.0 million related to the expenses of the business development offices in New York, Muttentz and Japan.

*Amortization Expenses*

Amortization expenses include the amortization of intangible fixed assets, including goodwill and intellectual property. Amortization of intangible assets increased by 50%, from £4.3 million in 2001 to £6.5 million in 2002, which includes an increase in the amortization of goodwill of £1.5 million relating to the acquisition of SkyePharma Canada Inc. and the drug delivery business of Bioglan AB. In addition, the increase reflects increased amortization charges on intellectual property with respect to DepoCyt licenses.

*Other Administration Expenses*

Other administration expenses include the non-product related general and administration costs of the Company. Other administration expenses increased by 12%, from £12.2 million in 2001 to £13.7 million in 2002. The increase mainly reflects the administration costs of SkyePharma's new operations in Canada and Sweden, which were fully consolidated for the first time in 2002 and increased professional fees for transactions undertaken during the year.

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*Research and Development Expenses*

Research and development expenses comprise only costs incurred by the Company in conducting its own research and development projects on existing formulations. Costs incurred in conducting research and development projects for third parties are booked as Cost of sales. Research and development expenses increased by 63%, from £17.9 million in 2001 to £29.3 million in 2002, due to increased expenditure on projects such as DepoMorphine, HFA-formoterol, Budesonide-HFA and Propofol.

*Other Operating Income*

Other operating income comprises income recognized by the Company under its transactions with Paul Capital. Income is recorded on a 'cost to complete' basis over the life of each individual project. This means that the Company takes the risk of project costs exceeding the projections underlying the agreements with Paul Capital.

In December 2000, the Company entered into an agreement with 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.

In March 2002, the Company announced that it had entered into a further 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 Company's agreements with Paul Capital are explained under "Item 4: Information on the Company Business Operations Collaborative Arrangements Other Collaborative Arrangements."

Other operating income increased by 124% from £6.3 million in 2001 to £14.2 million in 2002. During 2002, SkyePharma received £6.4 million of cash under the 2001 agreement and recognized income of £9.7 million on a cost to complete basis which was in line with expenditure on the project. Royalty payments are not required to be made to Paul Capital under this agreement until 2003. In addition, SkyePharma received £11.6 million of cash and recognized income of £4.5 million under the 2002 agreement on a cost to complete basis. During the year royalty payments of £0.7 million were made to PCP under this agreement. Further details are provided in Note 3 in Item 18 of this Form 20-F; Other Operating Income.

*Operating (Loss)/ Profit*



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As a result of the factors described above, the Company achieved an operating profit of £4.7 million in 2002, compared with an operating loss of £5.1 million in 2001.

Comparing the first half of 2002 with the second half, the Group recorded an operating profit of £6.8 million in the second half compared to an operating loss of £2.0 million in the first half. The periods compare as follows:

	<b>Six months ended June 30, 2002</b>	<b>Six months ended December 31, 2002</b>	<b>Year ended December 31, 2002</b>
(in £ thousands)			
Turnover	27,676	41,877	69,573
Gross profit	15,408	29,335	44,743
Operating (loss)/profit	(2,044)	6,760	4,716
Net (loss)/profit before tax	(4,000)	5,333	1,333
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The trend shown in the table continues a trend seen in previous years where there is higher income in the second half compared to the first, and this trend is expected to continue in the near term.

The Company has stated that while its internal forecasts indicate that it may achieve profitability in 2003, the Company may make a loss in the first half of 2003. The extent of that loss will depend, amongst other factors, on the timing of the licensing deals and receipt of milestone payments. See "Item 3: Key Information Risk Factors".

### ***Retained (Loss)/Profit***

In 2002, SkyePharma achieved its first full year profit after tax of £1.1 million, compared to a net loss of £9.5 million in 2001. The Group also achieved a profit on ordinary activities before tax of £1.3 million in 2002, after a net interest payable charge of £3.4 million (2001: £3.7 million), which compares to a loss on ordinary activities before tax of £9.4 million in 2001. The earnings per share for the year increased by 2.0 pence per share to 0.2 pence per share (2001: 1.8 pence loss per share). Earnings before Interest, Tax, Depreciation and Amortization ("EBITDA") for 2002 is £17.3 million compared to £3.4 million in 2001. Foreign currency exchange movements did not have a material impact on the results of operations in 2002 compared with 2001. Under U.S. GAAP, the Company recorded a loss of £45.3 million in 2002, compared with £43.9 million in 2001.

<b><i>Reconciliation of retained (loss)/profit to EBITDA</i></b>	<b>Year ended December 31, 2001</b>	<b>Year ended December 31, 2002</b>
(in £ thousands)		
Retained (loss)/profit	(9,452)	1,109
Interest receivable	(1,251)	(1,081)
Interest payable	4,951	4,464
Taxation	75	224
Depreciation of tangible fixed assets	4,778	6,101
Amortization of intangible fixed assets and deferred expenditure	4,327	6,506
EBITDA	3,428	17,323

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Year Ended December 31, 2001 compared with the Year Ended December 31, 2000

	Year ended December 31,	
	2000	2001
	(in £ thousands)	
Turnover	24,292	46,126
Cost of sales	(15,598)	(18,820)
Gross profit	8,694	27,306
Selling, marketing and distribution expenses	(3,844)	(4,804)
Administration expenses	(12,630)	(16,025)
Research & development expenses	(13,104)	(17,918)
Other operating income	2,900	6,342
Operating loss	(17,984)	(5,099)
Associated undertaking		(578)
Loss on ordinary activities before interest and taxation	(17,984)	(5,677)
Interest receivable	1,806	1,251
Interest payable	(3,508)	(4,951)
Loss on ordinary activities before taxation	(19,686)	(9,377)
Taxation	(4)	(75)
Retained loss	(19,690)	(9,452)

Turnover in the year ended December 31, 2001 increased by 90% to £46.1 million, compared to £24.3 million in 2000.

Contract research and development revenue, including milestone payments, increased by 128% to £38.2 million. Milestone payments in 2001 included £12.4 million in respect of Solaraze and £9.0 million following receipt of the DepoCyt European approval. Contract development income excluding milestones also more than doubled during the year to £9.9 million. Manufacturing and distribution revenues increased by 85% to £6.4 million mainly due to the return of DepoCyt to the market in March 2001. Royalty income of £1.5 million is comprised of approximately £1.1 million from Xatral OD and Solaraze, with £0.4 million from generics. This contrasts with 2000 where £3.7 million came from generics and £0.3 million from non-generics. The Company also recognized income of £6.3 million during the year under its agreement to finance the development of DepoMorphine shown as 'Other operating income'. See Note 30 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F for the accounting treatment of this transaction under U.S. GAAP.

SkyePharma recognizes revenue only when it is earned and non-refundable, and when there are no future obligations pursuant to the revenue, in accordance with the contract terms. During 2001 some £11.7 million (2000: £Nil) of turnover and other income was deferred under U.K. GAAP using this policy:

	Year ended December 31, 2001
	(in £ thousands)
Contract development revenue	6,959
Other operating income	4,731
	11,690

Cost of sales consists of research and development expenditures, including: the costs of certain clinical trials incurred on behalf of our collaborative partners; the direct costs of contract manufacturing; and the direct costs of licensing arrangements and royalties payable. Cost of

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sales were £18.8 million in 2001 compared to £15.6 million in 2000. However, gross profit trebled to £27.3 million compared to £8.7 million in 2000, primarily as a result of the increased milestone payments received.

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Selling, marketing and distribution expenses were £4.8 million compared to £3.8 million in 2000, reflecting primarily SkyePharma's share of expenses for DepoCyt under its collaboration agreement with Chiron Corporation. Research and development expenses increased by £4.8 million to £17.9 million, due to increased expenditure on DepoMorphine, DepoCyt and on expanding and maintaining the Group's patent portfolio. Amortization of intangible assets increased by £0.5 million to £3.8 million in 2001 and other administration expenses were £12.2 million in 2001 compared to £9.3 million in 2000. The increase in administration costs reflects the growth of the business and increased professional fees for significant transactions entered into during the year.

Under an agreement with Paul Capital, signed in December 2000, Paul Capital has provided a total of \$30 million between 2000 and 2002 in return for the sale of a portion of potential future royalty and revenue streams from DepoMorphine, Xatral OD, Solaraze and DepoCyt. The monies will be used to fund the clinical development of DepoMorphine. During 2001 £11.0 million (2000: £2.9 million) was received of which £6.3 million (2000: £2.9 million) has been recognized as other operating income which essentially offsets the R&D expenses associated with DepoMorphine during the period. The remaining £4.7 million (2000: nil) was deferred.

Operating losses for the 12 months to December 31, 2001 fell by 72% to £5.1 million from £18.0 million in 2000. The Group's loss on ordinary activities before tax was £9.4 million in 2001, after a net interest payable increase of £2.0 million, compared to £19.7 million in 2000.

The Group made its first operating profit and net profit in the second half of 2001. The two half years compare as follows:

	<b>Six months ended June 30, 2001</b>	<b>Six months ended December 31, 2001</b>	<b>Year ended December 31, 2001</b>
(in £ thousands)			
Turnover	14,799	31,327	46,126
Gross profit	5,549	21,757	27,306
Operating (Loss)/Profit	(9,919)	4,820	(5,099)
Net (Loss)/Profit	(11,603)	2,151	(9,452)

The acquisition of SkyePharma Canada negatively impacted the second half results by £0.6 million. The loss per share for the year fell by 54% to 1.8 pence compared to 3.9 pence in 2000.

### LIQUIDITY AND CAPITAL RESOURCES

#### Cash Flow

	<b>Year ended December 31,</b>	
	<b>2001</b>	<b>2002</b>
(in £ thousands)		
Net cash inflow from operating activities	5,909	1,552
Returns on investments and servicing of finance	(1,799)	(3,100)
Taxation	(75)	(224)
Purchase of tangible and intangible fixed assets	(7,983)	(6,273)
Purchase of fixed asset investment	(8,273)	(6,285)
Acquisitions	1,318	(3,595)
	(10,903)	(17,925)
Cash outflow before use of liquid resources and financing	(10,903)	(17,925)
Management of liquid resources	14,668	(3,872)

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	Year ended December 31,	
	2002	2001
Financing	(4,891)	21,621
Decrease in cash	(1,126)	(176)

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The Company finances its operations primarily by the sale of equity and debt securities, funding provided by collaborative partners and, in 2002 and 2001, cash generated from operations.

Net cash inflow from operating activities was £1.6 million in 2002, versus £5.9 million in 2001. The reconciliation of operating profit/(loss) to net cash flow from operating activities shows an increase in debtors between 2002 and 2001 of £21.6 million. This reflects the amounts received from Endo and Enzon on January 3, 2003 in respect of contracts signed at the end of December 2002.

During 2002 £6.4 million (\$9.6 million) (2001: £11.0 million (\$16.0 million)) in cash was received under an agreement with Paul Capital by which Paul Capital has provided a total of \$30 million between 2000 and 2002 in return for the sale of a proportion of potential future royalty and revenue streams from DepoMorphine, Xatral OD, Solaraze and DepoCyt. The monies will be used to fund the clinical development of DepoMorphine.

In March 2002, SkyePharma entered into a second agreement with Paul Capital. Under the agreement, Paul Capital will pay SkyePharma \$30 million during 2002 and 2003, in return for a portion of the potential 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 SkyePharma's Propofol IDD-D and HFA-formoterol. Between January 2002 and December 2015, Paul Capital could receive between 4% and 20% of the annual royalties and revenues from the total of nine products. Based on management's current projections, the 20% rate will apply from 2004 to 2008. The percentage then falls, when an agreed return is achieved, to 12.5% until a second ceiling is reached, before falling to 4% for the remainder of the period until December 31, 2015. During 2002 and 2003, the 20% rate will be reduced based on the percentage of the total \$30 million already funded. In addition, should the share of royalties received by Paul Capital not meet minimum returns, SkyePharma may issue SkyePharma Ordinary Shares up to a value of \$7.5 million. The number of Ordinary Shares to be issued is capped based upon a minimum price of 55 pence per share. Also under the terms of these agreements, Paul Capital has been issued warrants carrying rights to subscribe for 5 million SkyePharma Ordinary Shares at an exercise price of 73.75 pence, representing a 25% premium to the average trading price for the five trading days immediately prior to the closing date on March 7, 2002. During 2002 under this second agreement, SkyePharma received £11.6 million (\$17.5 million) and royalty payments of £0.7 million (\$1.0 million) were made to Paul Capital under this agreement.

On May 14, 2002 SkyePharma announced its intention to enter a wide-ranging strategic collaboration with Kowa Company Ltd., a leading Japanese company with substantial pharmaceutical interests, which proposes, under a Subscription Agreement signed on May 13, 2002, to make a strategic investment in SkyePharma. Kowa and SkyePharma have signed a separate non-binding Letter of Intent to evaluate Kowa's acquisition of a 50% interest in SkyePharma's manufacturing facility in Lyon. At an Extraordinary General Meeting on June 7, 2002, shareholder approval was obtained for Kowa to acquire 30 million ordinary shares of 10p each in SkyePharma for a total consideration of approximately £25.3 million. This represents a holding of around 5% after the investment. As part of its investment, Kowa exercised the right and appointed Mr. Torao Yamamoto, the senior managing director of the Pharmaceutical Division of Kowa Company Limited in Japan, as a non-executive director to the board of SkyePharma on October 30, 2002.

Financing also includes £3.9 million of repayment of loans, which represents the repayment, in full, of the Chiron loan note which was settled during the year in July and December.

Total cash outflow before use of liquid resources and financing in 2002 was £17.9 million (2001: £10.9 million). Purchases of fixed asset investments totaled £6.3 million (2001: £8.3 million) of which £5.2 million related to the acquisition of a further 750,000 series A convertible preferred shares in Astralis and £1.1 million purchase of SkyePharma ordinary shares for the SkyePharma PLC General Employee Benefit Trust for the Deferred Share Bonus Plan as part of the Group's hedging strategy.

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Purchases of tangible and intangible fixed assets totaled £6.3 million (2001: £8.0 million). The Company's cash position including short-term bank deposits at December 31, 2002 amounted to £28.1 million (2001: £25.3 million), net of bank overdrafts of £nil (2001:

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£1.6 million). The receipts from the licensing deals with Endo and Enzon signed in late December 2002 were received on 3 January 2003. Taking these receipts into account, net cash amounts to £51.0 million, an increase of £25.7 million from December 31, 2001.

Based upon the Company's business plan and the cash balances described above, the Directors believe, taking into account the amounts of cash available, the Company has sufficient working capital for the requirements of the foreseeable future. The current cash balances will enable the Company to selectively develop a number of key projects to a later stage of development prior to licensing out, thereby potentially increasing its share of the profits. The Company is an emerging pharmaceutical company and expects to absorb cash until products are fully commercialized. Much of the Company's cash requirement is of an investment nature and is to a great extent discretionary. Funds will be used for the Company's own product development efforts and capital expenditure. Capital commitments as at December 31, 2002, amounted to £0.2 million (2001: £0.3 million).

As part of the RTP acquisition, deferred consideration may be due to former RTP shareholders in consideration for the loss of certain option rights. 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.

Future acquisitions or investments, a material decrease in our cash flow from operations or the failure of our collaborative partners to provide funding are circumstances which could affect our liquidity and working capital. The Company is reliant on collaborative partners and upon its ability to continue to obtain new development contracts from third parties to further develop and commercialize its drug delivery technologies. See "Item 3: Key Information Risk Factors". The Company is dependent on Geomatrix and DepoFoam technologies as to which further successful development is uncertain; however, the failure by the Company's collaborative partners to provide funding, obtain regulatory approvals and conduct marketing activities could adversely affect the Company's business.

### **Borrowings**

At December 31, 2002, the Company had short-term borrowings, including obligations under finance leases, amounting to £3.6 million (2001: £6.4 million) and long-term borrowings, including obligations under finance leases and Convertible Bonds (the "Bonds"), amounting to £66.1 million (2001: £66.8 million).

At December 31, 2002, the Group had an overdraft facility of £1.3 million (CHF 3 million) (2001: £1.2 million) with the Basellandschaftliche Kantonbank, secured on the assets of Jago and guaranteed by SkyePharma PLC.

At December 31, 2002, the Group also had an overdraft facility with Societe Generale of £0.3 million (Euro 0.5 million), secured by the trade debtors of SkyePharma Production SAS and guaranteed by SkyePharma PLC.

Included within bank loans, the Basellandschaftliche Kantonbank has extended a loan of £0.9 million (CHF2 million) and a fixed credit facility of £0.7 million (CHF1.5 million). These loans are renewable annually and bear interest at 6.5% and 6.0%, respectively. The bank loans are all secured on the assets of Jago and the credit facility is guaranteed by SkyePharma PLC.

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At December 31, 2002, the Group had a property mortgage facility with the Basellandschaftliche Kantonbank of £7.8 million (CHF 17.3 million). The mortgage is in two tranches, both secured by the assets of Jago, and guaranteed by SkyePharma PLC. The first tranche of £3.3 million (CHF 7.4 million) bears interest at 4.25% and is repayable by installments over 21 years semi-annually. The second tranche of £4.5 million (CHF 9.9 million) bears interest at 3.0% and is repayable in 2004.

At December 31, 2002, the Group had a promissory note with Chiron of £0.6 million (\$1 million) which formed part of the consideration for the reacquisition of the DepoCyt marketing, distribution and sales rights. The promissory note is repayable in 2004 and bears interest at LIBOR plus 3%. It is guaranteed by SkyePharma PLC. The Chiron loan note, which was included within creditors at December 31, 2002, was payable upon the filing of an application for DepoCyt for pediatric indications in the United States. As part of the re-acquisition of the U.S. DepoCyt marketing, distribution and sales rights from Chiron, the Company settled the loan note.

On June 16, 2000, the Company issued £59.4 million 6% Bonds due 2005. The Bonds are convertible at the option of the holder into fully paid 10 pence Ordinary Shares in the Company at an initial conversion price of 132 pence at any time up to June 19, 2005. The initial conversion

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price was recalculated to the minimum 83 pence on June 19, 2001. Unless previously redeemed or converted, the Bonds will be redeemed by the Company at their principal amount on June 19, 2005.

### Financial Instruments

The Group holds financial instruments to finance its operations and to manage the currency risks that arise from these operations. Further information on these financial instruments is set out in Note 25 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F.

The following is a summary of the Group's contractual cash obligations as of December 31, 2002:

	Payments Due by Period				
	Total	< 1 year	1-3 years	4-5 years	After 5 years
	(in £ thousands)				
Bank loans	1,572	1,572			
Secured mortgage	7,772	270	4,717	359	2,426
Chiron loan notes	621		621		
Finance leases	1,320	1,085	151	84	
Operating leases	40,508	3,038	6,567	4,663	26,240
Convertible bonds	58,377		58,377		
Non-equity Deferred 'B' shares	11,310			11,310	
Provisions	201			201	
	121,681	5,965	70,433	16,617	28,666
<b>Total Contractual Cash Obligations</b>	<b>121,681</b>	<b>5,965</b>	<b>70,433</b>	<b>16,617</b>	<b>28,666</b>

Capital commitments, contracted for but not provided in the accounts, were £0.2 million at December 31, 2002 and £0.3 million at December 31, 2001.

In December 1999 SkyePharma Production SAS entered into a leasing arrangement with Lombard North Central PLC by which certain pharmaceutical manufacturing and laboratory equipment was the subject of a four-year sale and leaseback arrangement. The Company has guaranteed the obligations of the lessee under this lease to an amount of Euro 4.6 million (£2.8 million).

### PRINCIPAL DIFFERENCES BETWEEN U.K. AND U.S. GAAP

The Company's financial statements have been prepared in accordance with U.K. GAAP, which differs in certain respects from U.S. GAAP. See Note 30 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F for a reconciliation of the Company's net income for the three years ended December 31, 2002 and shareholders' funds as of December 31, 2001 and 2002 from U.K. GAAP to U.S. GAAP.

The reconciliation of the Company's net income for 2002 primarily reflects differences in the accounting principles under U.K. GAAP and U.S. GAAP with respect to revenue recognition and the sale of royalty interests. The reconciliation of the Company's net income for 2001 mainly reflects differences in the accounting treatment under U.K. GAAP and U.S. GAAP governing write-offs of acquired in-process research and development costs and revenue recognition. The reconciliation of the Company's net income for 2000 mainly reflects differences in the accounting rules under U.K. GAAP and U.S. GAAP in respect of the amortization of goodwill and other intangibles.

The reconciliation of the Company's shareholders' funds as of December 31, 2002 is principally the result of the different treatment under U.K. GAAP and U.S. GAAP of goodwill, funding liabilities, and deferred revenue. The reconciliation of the Company's shareholders' funds as of December 31, 2002 primarily reflects differences in the accounting principles under U.K. GAAP and U.S. GAAP in respect of goodwill, differences in the accounting for shares and warrants to be issued, deferred shares and shares issued to Dr. Gonella, and the different treatment of

contingent consideration charged to goodwill reserve.

#### **NEW ACCOUNTING STANDARDS NOT YET ADOPTED**

SFAS 146 'Accounting Costs Associated with Exit or Disposal Activities', which was issued at the end of June 2002, addresses issues regarding the recognition, measurement, and reporting of costs associated with exit and disposal activities, including restructuring activities. This standard will be implemented with effect from January 1, 2003. The Group does not expect the adoption of this standard will have a material impact on its financial position or results of operations.

In November 2002, the FASB issued Interpretation No. 45 (FIN 45), 'Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others'. FIN 45 expands on the accounting guidance of other SFASs FIN 45 elaborates on the existing disclosure requirements for most guarantees, including loan guarantees such as standby letters of credit. It also clarifies that at the time a company issues a guarantee, it must recognize an initial liability for the fair value, or market value, of the obligations it assumes under that guarantee and must disclose that information in its interim and annual financial statements. FIN 45 will be implemented on a prospective basis to guarantees issued or modified after December 31, 2002. The disclosure requirements in this Interpretation are effective for financial statements of periods ending after December 15, 2002. The Group is currently evaluating the impact of this interpretation on its financial position and results of operations.

In January 2003, the FASB issued Interpretation No. 46, 'Consolidation of Variable Interest Entities' (FIN 46). Under this interpretation, certain entities known as 'Variable Interest Entities' (VIE), must be consolidated by the 'primary beneficiary' of the entity. The primary beneficiary is generally defined as having the majority of the risks and rewards arising from the VIE. For VIE's in which a significant (but not majority) variable interest is held, certain disclosures are required. The measurement principles of this interpretation will be effective for the Group's December 31, 2003 financial statements. The Group is currently assessing the impact of this interpretation on its financial position and results of operations.

In November 2002, the Financial Accounting Standards Board issued Emerging Issues Task Force Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" (EITF 00-21). EITF 00-21 addresses certain aspects of the accounting by a company for arrangements under which it will perform multiple revenue-generating activities. EITF 00-21 addresses when and how an

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arrangement involving multiple deliverables should be divided into separate units of accounting. EITF 00-21 provides guidance with respect to the effect of certain customer rights due to company nonperformance on the recognition of revenue allocated to delivered units of accounting. EITF 00-21 also addresses the impact on the measurement and/or allocation of arrangement consideration of customer cancellation provisions and consideration that varies as a result of future actions of the customer or the company. Finally, EITF 00-21 provides guidance with respect to the recognition of the cost of certain deliverables that are excluded from the revenue accounting for an arrangement. The provisions of EITF 00-21 will apply to revenue arrangements entered into in fiscal years beginning after June 15, 2003. The Group is currently evaluating the impact of EITF 00-21 on its financial position and results of operations.

#### **RESEARCH AND DEVELOPMENT, PATENTS AND LICENSES**

For a discussion of the Company's research and development activities, see "Item 4: Information on the Company Business Operations Research and Development" and information on patents and licenses, see "Item 4: Information on the Company Business Operations Patents and Proprietary Rights".

#### **TREND INFORMATION**

The Company's results of operations have fluctuated materially on a monthly, semi-annually and yearly basis, partly as a result of acquisitions and partly due to the timing of contract revenues. Therefore, period-to-period and period-on-period comparisons are not meaningful at this stage in the Company's development. The Company believes that it will continue to experience fluctuations in its results of operations in the near to medium term.

The Company has stated that while its internal forecasts indicate that it may achieve profitability in 2003, the Company may make a loss in the first half of 2003. The extent of that loss will depend, amongst other factors, on the timing of the licensing deals and receipt of milestone payments. See "Item 3: Key Information Risk Factors".

**Item 6: Directors, Senior Management and Employees****DIRECTORS AND SENIOR MANAGEMENT**

Name	Age	Position
Ian Gowrie-Smith <sup>(1)(4)</sup>	55	Executive Chairman
Michael Ashton <sup>(1)</sup>	57	Chief Executive Officer
Donald Nicholson <sup>(1)</sup>	45	Finance Director and Executive Director
Air Chief Marshal Sir Michael Beavis <sup>(2)(3)</sup>	73	Senior Independent Non-executive Director
Dr. David Ebsworth <sup>(2)(3)</sup>	48	Non-executive Director
R. Stephen Harris <sup>(3)(4)</sup>	60	Non-executive Director
Dr. Keith Mansford <sup>(3)</sup>	71	Non-executive Director
Dr. Argeris (Jerry) Karabelas <sup>(2)(4)</sup>	50	Non-executive Director
Tora Yamamoto	60	Non-executive Director

(1) Member of Executive Committee.

(2) Member of Audit Committee.

(3) Member of Remuneration Committee.

(4) Member of Nomination Committee.

The above information is correct as at June 24, 2003, the latest practicable date prior to the filing of this Report.

*Ian Gowrie-Smith* has been Executive Chairman of the Board of the Company since January 1995. From January 1995 to November 1998 he was also Chief Executive Officer of the

Company. Mr Gowrie-Smith has more than 16 years of management experience in the pharmaceutical industry, most recently as Chief Executive Officer of Medeva plc. He is non-executive chairman of Tiberon Metals Limited and Micap PLC. He graduated with a Bachelor of Commerce degree from the University of Melbourne in 1970.

*Michael Ashton* was named Chief Executive Officer of the Company in November 1998. He joined the Company in January 1997 as Chief Executive Officer of Jago, was appointed to the Board in March 1997 and was named Chief Operating Officer of the Company in May 1998. He has over 31 years of experience in the pharmaceutical industry. Prior to joining the Company, he was Chairman, President and Chief Executive Officer of Faulding Inc. He is a non-executive director of Transition Therapeutics Inc. and Astralis Limited. He obtained a B. Pharm degree from Sydney University in 1968 and an MBA from Rutgers University in 1974.

*Donald Nicholson* was named Finance Director in March 1997. He joined the Company in February 1996 as Chief Financial Officer and was appointed to the Board in March 1997. He has more than 13 years of experience in the healthcare industry. Prior to joining the Company, he was the Corporate Strategy and Finance Director at Corange Group. He is a member of the Institute of Chartered Accountants of Scotland and obtained a B.Com (Hons) degree from the University of Edinburgh in 1980.

*Air Chief Marshal Sir Michael Beavis* was appointed to the Board in 1989 and was appointed Senior Independent Non-executive Director in May 2001. He retired from the Royal Air Force in 1987 as an Air Chief Marshal. His last appointment was Deputy Commander-in-Chief Allied Forces Central Europe, NATO. He became a defense consultant with Burdeshaw Associates, USA, in 1987. He graduated from the Royal Air Force Staff College in 1963 and from the Royal College of Defense Studies in 1974. He is a Companion of the Chartered Management Institute, a Freeman of the City of London and a Liveryman in the Guild of Air Pilots and Navigators.



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*Dr. David Ebsworth*, was appointed to the Board in April 2002. Dr. Ebsworth has over 20 years of pharmaceutical industry experience. Prior to his last position as president and general manager of the Pharmaceutical Business Group for Bayer AG in Leverkusen, Germany, Dr. Ebsworth held a series of global positions within the same group in Canada, Europe and the United States. Dr. Ebsworth is a non-executive director of Clal Biotechnology Industries and CuraGen Corporation and held the same office, until 1998, with Schein Pharmaceutical, Inc. (now known as Watson Pharmaceuticals, Inc.). He was chief executive officer of Oxford GlycoSciences PLC up until May 2003.

*R. Stephen Harris* was appointed to the Board in November 1995. He has over 36 years' commercial experience in the pharmaceutical industry, having worked for ICI Pharmaceuticals, Merck, Eli Lilly, Boots, Reckitt & Colman and Gensia and was director of Development and Licensing with Medeva plc. He is non-executive chairman of Proteome Sciences plc and a non-executive director of Advanced Medical Solutions Group plc, Microscience Ltd, Prophilian plc, Sinclair Pharma Limited and GeneMedix plc. He is a member of the Pharmaceutical Society of Great Britain and graduated with a B.Sc in Pharmacy from the University of London in 1964.

*Dr. Argeris (Jerry) Karabelas* was appointed to the Board in November 2000. Dr. Karabelas has more than 21 years' experience in the pharmaceutical industry having spent the majority of his career with SmithKline Beecham plc. Dr. Karabelas is a partner at Care Capital LLC. He was previously the CEO of Novartis Pharma AG where he had responsibility for pharmaceuticals, R&D, consumer products, and the generics business. He is also an external director of Human Genome Sciences, Fox Chase Cancer Center, The University of the Sciences in Philadelphia, and a member of the Scientific Advisory Committee of the Massachusetts General Hospital, Boston. He is also a director of NitroMed Inc., Halsey Pharmaceuticals, Anadys, Renovo and a member of the scientific advisory board of Epigenesis. He received a Ph.D in Pharmacokinetics from the Massachusetts College of Pharmacy in 1979.

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*Dr. Keith Mansford* was appointed to the Board in March 1996. He has over 45 years' experience in the pharmaceutical and biotechnology sectors principally with Beecham Group and SmithKline Beecham plc. From 1984 to 1992 he was chairman of Research and Development at Beecham Group and subsequently SmithKline Beecham plc. He is an external director of Sepracor Inc. He is also chairman of Mansford Associates, an international healthcare consultancy; non-executive Chairman of Convè Limited and professor of Biochemistry at the University of Buckingham. He obtained a B.Sc in Chemistry and a M.Sc in Biochemistry from the University of Durham and a Ph.D. in Biochemistry from the University of London.

*Torao Yamamoto* was appointed to the Board in October 2002. Mr. Yamamoto is the senior managing director of the Pharmaceutical Division of Kowa Company Limited in Japan. Mr. Yamamoto has been with Kowa, a Japanese conglomerate with interests in pharmaceuticals, textiles, electronics, optics and chemicals, since 1965. He has held management positions in Japan and the US, where he was general manager of all Kowa's operations for four years until June 1998. He currently serves on the board of directors of Kowa Company Limited, Kowa Pharmaceutical Europe, Ltd., and Kowa Research Europe, Ltd. He graduated in March 1965 with a Bachelor's Degree in Business Administration from Kobe University of Commerce in Japan.

Mr. Yamamoto was appointed a Non-executive Director in October 2002 pursuant to an agreement between the Company and Kowa.

There are no other arrangements or understandings with major shareholders, customers or suppliers or others pursuant to which any person was selected to serve as a director or senior manager.

There are no provisions within the directors' service contracts that provide for any benefit to accrue to any director upon termination of employment save that salary may be paid in lieu of notice.

### COMPENSATION

In 2002 the Company paid £1,889,000 in aggregate to its directors as a group (10 persons).

The following table provides certain information regarding the compensation paid to directors and officers of the Company in 2002.

Name	Salary	Bonus	Pension Benefits	All Other Compensation <sup>(1)</sup>
(in £ thousands)				
Ian Gowrie-Smith	426	144	53	29

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Name	Salary	Bonus	Pension Benefits	All Other Compensation <sup>(1)</sup>
Michael Ashton <sup>(2)</sup>	367	179	46	55
Donald Nicholson	189	92	24	10
Air Chief Marshal Sir Michael Beavis	53			
Dr. David Ebsworth (appointed April 11, 2002)	21			
Stephen Harris	51			
Dr. Keith Mansford	50			
Walter Zeller <sup>(3)</sup>	61			
Dr. Argeris (Jerry) Karabelas	35			
Torao Yamamoto (appointed October 30, 2002)	4			

- (1) All other monetary compensation includes company car allowance and medical insurance for directors, officers and their families.
- (2) All other monetary compensation additionally includes living allowance.
- (3) Mr. Zeller retired as a Director on May 28, 2003.

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The fees paid to Non-executive Directors include a cash amount of fees and a one-off additional payment of fees in shares.

For further information on share options granted, see "Outstanding Options" below.

The Remuneration Committee of the Board of Directors administers a bonus plan for the Company's executive directors and officers. Bonuses are paid at the discretion of the Remuneration Committee, in recognition of the individual's contribution to the success of the Company and the achievement of specified objectives. In 2002 the primary performance targets were a combination of objective corporate, divisional and specific individual targets. A fundamental part of the annual bonus plan is the requirement that a stated proportion of any cash bonus awarded under the bonus plan each year be deferred through the Company's Deferred Share Bonus Plan introduced in 2001. The Plan is designed to align the interests of participants with those of the shareholders by encouraging executive directors and officers to build up and maintain shareholdings which are meaningful in the context of their remuneration. The mandatory deferred proportion of the bonus is currently set at 50%. The Company currently provides one matching share for each executive share acquired (calculated on the gross bonus deferral). These matching shares will be released after three years provided that the executive director or officer remains in employment and the corresponding executives shares have not been sold. The release of matching shares is not subject to additional performance criteria because the maximum potential level of annual bonus including matching shares for 2002 was 112.5% of salary and the performance conditions for earning this bonus were challenging.

### PENSION AND SAVINGS PLANS

The Company operates various defined contribution plans for its employees in the U.K., Switzerland, the United States, Canada and Sweden. The Company's contributions to these plans are charged to the income statement in the year to which they relate, and the assets are held in separate trustee administered funds. In 2002, the Company contributed £1,525,000 (2001: £822,000) to pension and savings plans and a provision of £201,000 (2001: £51,000) is included within provisions for liabilities and charges. See Note 18 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F.

The Company operates an unfunded defined benefit scheme in respect of its employees in France, based on the national collective agreement of the pharmaceutical industry.

At December 31, 2002, a valuation was performed by professionally qualified actuaries on the present value of the accrued liabilities calculated under the projected unit credit actuarial cost method.

### BOARD PRACTICES

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The Company's Articles of Association provide that, except as otherwise provided in the Articles or unless otherwise determined by ordinary resolution of the Company, the Board of Directors shall consist of not less than three directors. Directors of U. K. companies do not generally have fixed terms of office. The Articles provide that at each Annual General Meeting, a number of directors equal to as close as possible (but not exceeding) one-third of the directors must retire from office by rotation, based principally on length of term of office, and are eligible for re-election. Directors may be appointed by the Company by ordinary resolution of the shareholders. In addition, the Board of Directors may appoint directors to fill vacancies or as additional directors. Any director so appointed by the Board of Directors must retire from office at the next Annual General Meeting but is then eligible for re-appointment by the shareholders at that meeting. In accordance with best practice in the United Kingdom, Sir Michael Beavis was appointed Senior Independent Non-executive Director in May 2001.

The Board has an Executive Committee, an Audit Committee, a Remuneration Committee and a Nomination Committee. The Executive Committee is responsible for the executive management of

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the Company. It is chaired by the Chief Executive Officer and is comprised of the executive directors. The Executive Committee generally meets monthly between Board meetings.

The Audit Committee is responsible for pre-approving all audit and non-audit services, reviewing and appraising the Company's financial reporting practices and procedures, the adequacy of its system of internal accounting control, reviewing the auditor's report describing all critical accounting policies and practices, all alternative treatments within GAAP for material items discussed with management and other material written communications and any matters raised by its independent auditors. It also is responsible for reviewing the half-year and full-year results of the Company and its Interim and Annual Reports and Accounts prior to their submission to the full Board. The Committee reviews the cost-effectiveness, independence and objectivity of the external auditors and also pre-approves all permitted non-audit expenditure incurred with them. It meets formally at least twice a year.

The Remuneration Committee is responsible for approving the remuneration and other benefits, including pension contributions, bonus payments, share options and severance payments, of the executive directors and other members of senior management. The Remuneration Committee is comprised of the Non-executive directors identified above and is chaired by Sir Michael Beavis.

The Nomination Committee is responsible for making recommendations to the Board on any appointment to the Board. The Nomination Committee is comprised of the Chairman and the Non- Executive Directors identified above.

### EMPLOYEES

The following table shows the distribution of the year end number of employees for the last three fiscal years by activity and geographic location:

	Year ended December 31,		
	2000	2001	2002
<b>By category of activity:</b>			
Corporate Management and Administration	50	68	92
Marketing operations	10	11	13
Research and Development	169	215	239
Manufacturing Operations	146	151	155
	375	445	499
<b>By geographic location:</b>			
U.K.	15	18	18
Switzerland	131	133	126
France	120	124	131
Sweden			38
U.S. and Canada	109	170	186

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	Year ended December 31,		
	375	445	499
Number of employees with scientific qualifications:			
PhD's, masters or medical degrees	68	74	89
Scientists (including PhD's, masters or medical degrees)	166	229	267

The Company believes that it has good relations with its employees and labor unions.

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### SHARE OWNERSHIP

The following table sets out the interests of Directors in the ordinary shares of the Company (including the interests of their immediate families and persons connected with the Directors) as at June 24, 2003.

Name	Number of ordinary shares	Percentage of issued share capital
Ian Gowrie-Smith	19,281,339	3.143%
Michael Ashton	300,130	0.049%
Donald Nicholson	234,199	0.038%
Air Chief Marshal Sir Michael Beavis	210,297	0.034%
Dr. David Ebsworth	30,000	0.005%
Stephen Harris	131,083	0.021%
Dr. Argeris (Jerry) Karabelas <sup>(1)</sup>	26,667	0.004%
Dr. Keith Mansford	67,943	0.011%

(1) Includes ordinary shares represented by ADSs. Each ADS represents ten ordinary shares.

In addition to the interests shown above Mr. I. R. Gowrie-Smith had a beneficial interest in 20,000 convertible bonds, all issued by the Company. Subject to the satisfaction of certain conditions, Mr. Gowrie-Smith has agreed in principle to a divorce settlement that would include 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.

The aggregate number of ordinary shares held by the Directors listed in the table above at June 24, 2003 was 20,281,658, representing 3.3% of the total ordinary shares outstanding.

The aggregate number of ordinary shares underlying the Company's outstanding options and warrants as of June 24, 2003 was 61,186,281.

### Share Option Plans

The Company has five share option schemes: grants between 1996 and 1998 were made under the 1988 Executive Share Option Scheme and the European and North American Scheme and grants from April 1999 were made under the SkyePharma PLC 1999 Share Option Scheme, the European and North American 1999 Scheme and the SkyePharma Holding Inc 1999 Stock Option Plan for SkyePharma Inc. Employees.

Executive Directors and senior executives participate in the SkyePharma PLC 1999 Share Option Scheme, the European and North American Scheme and the SkyePharma Holdings Inc. 1999 Share Option Plan as appropriate. Following publication in March 2001 of revised Association of British Insurers guidelines for Share Incentive Schemes, the Board gained shareholder approval to make certain changes to the SkyePharma PLC 1999 Share Option Scheme and the SkyePharma Holdings Inc. 1999 Share Option Plan at the Annual General Meeting of the Company in June 2001. In particular, the individual participation limits of 200% of remuneration and the performance conditions were amended so that exercise is dependent upon total shareholder return performance against a peer group of companies. All options granted to Executive Directors and senior executives during 2002 were made on this basis and vest after three years on a scale between 0% and 100% depending on

the Company's performance relative to the performance against the comparator group of companies (in France, options granted during 2002 will still vest according to this three year performance period but they will not be exercisable until four years from date of grant). A further change approved by shareholders at the Annual General Meeting in June 2001 was that future options will not be subject to re-testing. Accordingly, options granted in 2002 and subsequent years will not be re-tested. If the stringent performance requirements are not met at the end of the performance period, all options will lapse.

There are two types of options, options and Super Options. With respect to options, prior to 2001 individual participation limits under the schemes were set at four times individual remuneration. Options granted under the schemes are granted at the market price ruling at the date of grant, are exercisable after three years and up to a maximum of 10 years from date of grant. Options granted under each of the schemes may be exercised only if, over a period of three consecutive years, the shareholder return of the Company exceeds the growth in FTSE All Share Index over the same period. Prior to 2001, the individual participation limits for Super Options were set at eight times remuneration. Super Options, also granted at the market price ruling at the date of grant, are exercisable after five years and are subject to more challenging performance conditions based upon top quartile performance in the FTSE 250 Index.

The Company has decided within the current rules of the SkyePharma PLC 1999 Share Option Scheme to normally transfer the employer's national insurance contributions on the gain on the exercise of unapproved options to the option-holder.

#### ***SkyePharma PLC 1999 Share Option Scheme***

The SkyePharma PLC 1999 Share Option Scheme (the "Scheme") is divided into two parts, the first of which is approved by the Inland Revenue and the second of which is unapproved. The unapproved part is designed for the grant of options to employees, the value of which may exceed the approved limit of £30,000. Except to the extent required to obtain Inland Revenue approval, the two parts of the Scheme are similar in all material respects.

The Scheme is governed by the Rules of the Scheme and is administered by the Board of Directors of the Company. Eligibility for participation in the Scheme is limited to those employees of SkyePharma, including Directors, who work for SkyePharma at least 25 hours per week, as may from time to time be invited to participate by the Board. No Director or employee will be entitled as of right to participate in the Scheme.

Options may be granted under the Scheme within six weeks of the day on which the Company first announces its annual or interim results in any year in which the Scheme is in operation or any date on which the Directors determine that exceptional circumstances exist which justify the grant of options at that date. Initially, offers to participate also had to be made within six weeks of May 19, 1999, the date of approval of the Scheme by shareholders. No consideration is payable on the grant of an option. An option may not be granted to an individual selected to participate if the total subscription price thereunder would exceed 200% of the participant's remuneration in that year. Remuneration includes salary, commission and bonuses, but excludes benefits in kind. In the case of the approved part of the Scheme, participants may only be granted options up to a value of £30,000. The Directors will only grant options to replace those already exercised if they are satisfied that there has been sustained improvement in the performance of the Company over not less than a two to three year period prior to such grant. Benefits under the Scheme are not pensionable.

The price per ordinary share at which a participant may acquire ordinary shares (the "Option Price") on the exercise of an option will be at the discretion of the Board, but shall not be less than the market value (as defined in the Rules) of an ordinary share at the date of grant and shall not in any event be less than the nominal value of an ordinary share.

Options granted pursuant to the Scheme may not be exercised prior to the third anniversary of their grant and must be exercised before the expiry of ten years from the date of grant. Super options may not be exercised prior to the fifth anniversary of their grant and must be exercised before the expiry of ten years from the date of grant. Options may be exercised in whole or in part in respect of any number of ordinary shares subject to a minimum of 1,000 ordinary shares. An option granted under the Scheme may not be exercised unless the relevant condition, as specified by the Directors or a committee thereof and notified to the participant no later than the date of grant, is satisfied. In the case of a super option, the performance condition specified by the Directors will be more challenging and in accordance with criteria recommended by the Association of British Insurers.

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If a participant leaves the service of the Company by reason of injury, disability, redundancy or normal retirement, or because the company by which such participant is employed ceases to be a member of the Company, such participant will be entitled to exercise any options in accordance with the rules of the Scheme. If a participant leaves the service of the Company by reason of death, such participant's personal representative will be entitled to exercise any options within 12 months following the date of such participant's death. If a participant leaves the service of the Company for any reason other than the foregoing, in respect of option grants prior to 2001 such participant will be entitled to exercise any options within six months of leaving the service of the Company. For options granted during 2001 and subsequently, the options would normally lapse.

If an offeror obtains control of the Company on the occurrence of (i) a general offer to acquire the whole of the ordinary share capital of the Company, (ii) pursuant to an offer, an offeror becoming entitled to acquire the shares under Sections 428-430 of the Companies Act 1985 (the "Act") or (iii) a compromise or arrangement being sanctioned by the Court under Section 425 of the Act, then an option holder and the offeror may agree that the options held can be exchanged for equivalent options in the offeror. Alternatively, if an offeror gains control pursuant to either a general offer or a compromise or arrangement pursuant to Section 425 of the Act, then the option holder may in the case of a general offer, exercise his options within six months following the later of the date of the acquisition or the date upon which the offer becomes unconditional, or in the case of a court order sanctioning a compromise or arrangement, within six months of that date.

### *The European and North American Scheme*

The European and North American Scheme is in all material aspects identical to the SkyePharma PLC 1999 Share Option Scheme, except that eligibility is restricted to employees in Europe and North America. No further grants will be made under this Scheme.

### *The SkyePharma Holdings Inc 1999 Stock Option Plan for SkyePharma Inc. Employees*

The SkyePharma Holdings Inc. 1999 Stock Option Plan (the "Plan") is governed by the rules of the Plan and is administered by the Board of Directors of the Company acting through the Remuneration Committee. The Plan will be available to all officers and key employees of SkyePharma Holdings Inc. and its subsidiaries who render services which contribute to its management growth or financial success, at the discretion of the Remuneration Committee. No Director or employee will be entitled as of right to participate in the Plan.

Options may be granted under the Plan within six weeks of the day on which the Company first announces its annual or interim results in the year which the Plan is in operation or any date on which the Remuneration Committee determines that exceptional circumstances exist which justify the grant of options at that date. An option could not be granted to an individual selected to participate if the total subscription price thereunder exceeds 200% of his remuneration in that year. Remuneration includes salary, commission and bonuses, but excludes benefits in kind.

If an option is to qualify for tax benefits under certain provisions of the U.S. Internal Revenue Code of 1986 as amended, ("Incentive Options") then the aggregate exercise price of options first becoming exercisable in any one calendar year may not exceed U.S.\$100,000.

The price per ordinary share at which a participant may acquire ordinary shares (the "Option Price") on the exercise of an option will be at the discretion of the Remuneration Committee, but shall not (in the case of Incentive Options) be less than the market value (as defined in the rules of the Plan), or (in the case of options which are not Incentive Options) 85% of the market value (as so defined) of an ordinary share at the date of grant and shall not in any event be less than the nominal value of an ordinary share.

Options must be exercised before the expiry of ten years from the date of grant. The earliest date at which an option may be exercised is at the discretion, in each case, of the Remuneration Committee. The Remuneration Committee may, but is not obliged, to impose conditions on the

exercise of an option. In exercising its discretion in these respects, the Remuneration Committee will seek to act in the best interests of the Company, having regard to the conflicting requirements of, on the one hand, the custom and practice in the United States with regard to the grant of share options, and the expectations of U.S.-based employees, and on the other hand, the need to operate the Plan in such a way as complies with best U. K. practice.

The lapsing provisions and those relating to change of control under the Plan are in all material respects similar to the provisions of the SkyePharma PLC 1999 Share Option Scheme, as described on page 92.

### **Outstanding Options**

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The table below sets forth certain information concerning the options issued to certain directors and officers of the Company pursuant to the Company's share option plans as of June 24, 2003. The remaining directors and officers of the Company have no outstanding ordinary or Super Options.

### *Ordinary Options*

Name	Number of ordinary shares underlying Options Granted	Exercise Price	First Exercise Date	Last Exercise Date
Ian Gowrie-Smith <sup>(1)(2)</sup>	1,234,568	81.0p	December 6, 1999	December 6, 2006
	575,539	69.5p	April 19, 2002	April 19, 2009
	1,008,313	80.6p	June 12, 2004	June 12, 2011
	1,178,022 <sup>(4)</sup>	72.3p	April, 12 2005	April 12, 2012
	1,935,484 <sup>(5)</sup>	46.5p	April 7, 2006	April 7, 2013
Donald Nicholson <sup>(1)</sup>	533,333	75.0p	April 29, 1999	April 29, 2006
	86,022	93.0p	March 31, 2001	March 31, 2008
	172,662	69.5p	April 19, 2002	April 19, 2009
	446,650	80.6p	June 12, 2004	June 12, 2011
	521,826 <sup>(4)</sup>	72.3p	April, 12, 2005	April 12, 2012
Michael Ashton <sup>(3)</sup>	946,237 <sup>(5)</sup>	46.5p	April 7, 2006	April 7, 2013
	639,077	93.0p	March 31, 2001	March 31, 2008
	871,451	69.5p	April 19, 2002	April 19, 2009
	868,486	80.6p	June 12, 2004	June 12, 2011
	1,014,661 <sup>(4)</sup>	72.3p	April 12, 2005	April 12, 2012
	1,703,226 <sup>(5)</sup>	46.5p	April 7, 2006	April 7, 2013

- (1) 1,234,568 options in respect of Ian Gowrie-Smith and 533,333 in respect of Donald Nicholson were issued pursuant to the Executive Share Option Scheme. This scheme has subsequently expired in respect of further grants and the remainder of these options were granted under the SkyePharma PLC 1999 Share Option Scheme.
- (2) Also held 'B' Warrants. See "Warrants" below.
- (3) 639,077 issued pursuant to the European and North American Scheme. The remainder of Michael Ashton's options are granted under the SkyePharma PLC 1999 Share Option Scheme.
- (4) Options granted during 2002.
- (5) Options granted during 2003.

### *Super Options*

Name	Number of Ordinary Shares Underlying Options Granted	Exercise Price	First Exercise Date	Last Exercise Date
Ian Gowrie-Smith	2,385,009	56.67p	May 25, 2004	May 25, 2009
Donald Nicholson	1,022,147	56.67p	May 25, 2004	May 25, 2009
Michael Ashton	2,044,293	56.67p	May 25, 2004	May 25, 2009

The aggregate number of ordinary shares underlying all of the outstanding options as of June 24, 2003 was 55,894,504. Such options have exercise prices ranging between 44.8 pence and 93 pence and expire between April 29, 2006 and April 7, 2013.

## Deferred Share Bonus Plan

The Deferred Share Bonus Plan, introduced in 2001, operated for the whole year. Approximately 25 senior executives (including all Executive Directors) participate in the Deferred Share Bonus Plan. It is designed to align the interests of participants with those of the shareholders by encouraging executives to build up and maintain shareholdings which are meaningful in the context of their remuneration. The Deferred Share Bonus Plan requires that there is a mandatory deferral of part of each annual bonus, in the form of Company shares ("Executive Shares"), for a period of normally three years. The mandatory deferred proportion of the bonus is currently set at 50%. The Company currently provides one Matching Share for each Executive Share acquired (calculated on the gross bonus deferral). Currently, as set by a Committee of Directors, these matching shares will be released after three years provided that the executive remains in employment and the corresponding executive shares have not been sold.

The Deferred Share Bonus Plan is operated by the Directors of the Company (the "Committee"). The Remuneration Committee, the members of which are Non-executive Directors, supervise the operation of the Deferred Share Bonus Plan in respect of the executive directors of the Company. Eligible participants are any employees of the Company selected by the Committee, or a trustee acting on behalf of such employees ("Eligible Employee").

Awards may be granted in the form of Matching Shares or Deferred Shares ("Award"). Awards will be made as a deferred and conditional grant of shares. Shares will normally be purchased by executives with the amount of the bonus (net of tax) mandatorily deferred. Matching Shares will always be granted in consideration for the purchase of Executive Shares. Deferred Shares may be granted subject to such terms and conditions as the Committee determines. It is the current intention of the Committee that only Awards of Matching Shares will be granted.

For the year ended December 31, 2003, the Committee has determined that 50% of bonus earned will be subject to a mandatory deferral and that the ratio of Matching Shares granted to Executive Shares purchased shall be 1:1. Unless the Committee so determines, there will normally be no further performance requirements relating to the release of awards unless the ratio of Matching Shares to Executive Shares proposed exceeds 1:1 when the Committee may attach additional performance conditions to the release of the Matching Shares (the maximum matching ratio is three Matching Shares for each Executive Share).

The maximum value of shares subject to an Award for financial year 2003 is 50% of the relevant Eligible Employee's salary. It is the current intention of the Committee that the maximum value of an Award will not exceed 50% of the relevant Eligible Employee's salary and/or bonus after the deduction of tax.

The Company may issue 10% of its shares within a ten year period to satisfy Awards to employees under the Deferred Share Bonus Plan and any other share scheme operated by the Company under which shares are issued. Where Awards are granted to executives which will be satisfied by the issue of shares no more than 5% of the Company's shares will be issued under the Deferred Share Bonus Plan or any other share scheme operated by the Company where shares are issued provided that this limit may be exceeded if the executives are required to satisfy more stretching performance requirements. The Remuneration Committee will be monitoring the issue of shares during the ten year period.

If the Company decides to grant Deferred Shares, the maximum value that may be granted to an individual in any year is 100% of the participant's salary and/or bonus. This type of Award will normally be subject to the attachment of performance conditions. Participants shall have no rights to vote or receive dividends in respect of the shares subject to the Award during the holding period.

Shares subscribed will not rank for dividends payable by reference to a record date falling before the date on which the shares are acquired but will otherwise rank pari passu with existing shares. Application will be made to the relevant exchange on which the shares are listed for

admission to trading on the relevant exchange for new shares that are to be issued following the release of an Award.

If a participant disposes of his Executive Shares during the holding period or ceases employment, his award will lapse unless the Committee in its absolute discretion determines otherwise. Awards are not transferable and will lapse if the participant attempts to do so. If a participant leaves employment prior to the expiration of the holding period, then the Award will lapse unless the Committee in its absolute discretion determines otherwise. In the event of a takeover, reconstruction, amalgamation or winding up of the Company then all Awards will be released unless in certain circumstances they are exchanged for Awards over shares in the acquiring company. In the event of a merger or demerger of the Company, the Committee may determine that all Awards will be released or the number of shares comprised in an Award may be adjusted.



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On a variation of the capital of the Company, the number of shares subject to an Award may be adjusted in such manner as the Committee determines and a professional advisor of the Company confirms to be fair and reasonable.

The Committee may not grant Awards under the Deferred Share Bonus Plan more than five years after its adoption unless the Deferred Share Bonus Plan is extended pursuant to shareholder authority for a further period of up to five years.

Amendments to the rules may be made at the discretion of the Committee. However, the provisions governing eligibility requirements, equity dilution, share utilization and individual participation limits and the adjustments that may be made following a rights issue or any other variation of capital and the limitations on the number of shares that may be issued cannot be altered to the advantage of participants without prior shareholder approval, except for minor amendments to benefit the administration of the Deferred Share Bonus Plan, to take account of a change in legislation or to obtain or maintain favorable tax, exchange control or regulatory treatment for participants or for the Company and any subsidiary.

Shares acquired, awards and any other rights granted pursuant to the Deferred Share Bonus Plan are non-pensionable.

The Company has the ability to use new issue shares under the Deferred Share Bonus Plan. Any shares issued under this Deferred Share Bonus Plan would be subject to the limits set out above for the Option Schemes (i.e., the shares issued under this Deferred Share Bonus Plan would be aggregated with the shares issued under the Option Schemes when calculating the number of shares issued against the limits). In addition, the provision of matching shares may be subject to the satisfaction of performance conditions. The attachment of performance conditions to matching shares means that the Deferred Share Bonus Plan would be classified as a long-term incentive plan requiring shareholder approval. It is the Company's current intention to provide additional performance conditions to matching shares where the ratio of matching shares to executive shares is greater than 1:1.

### Share Purchase Plan

The Company's intention is to encourage share ownership at all levels of the business, thereby aligning all employees' interests with those of the shareholders. Accordingly, the Company introduced the SkyePharma International Share Purchase Plan ("the Employee Plan") and the Employee Stock Purchase Plan in February 2002.

All employees (including all the Executive Directors) are eligible to participate in the Employee Plan under the arrangements introduced in their respective countries.

The Employee Plan complements the Option Schemes as it is more focused on employee retention and enables the same remuneration policy applied to executives under the Deferred Share

Bonus Plan to be applied to all employee levels, i.e., awarding matching shares on the basis of the number of employee purchased shares.

Under the Employee Plan, employees are given the opportunity of purchasing Company shares up to a maximum of £1,500 per year (or local currency equivalent). The Company will then match each share purchased with an award of 'Matching Shares'. The maximum ratio of Matching Shares to employee purchased shares is two to one although the current ratio adopted by the Company is one Matching Share for each share purchased. The Matching Shares are subject to a three year holding period. Normally, the Matching Shares will only be released at the end of this holding period of the corresponding employee purchased shares have not been sold and the employee is still in employment at that time. Awards under this Employee Plan lapse if the holder is adjudicated bankrupt or when the holder sells his or her shares or ceases to be in the Company's employment during the restricted period determined by the Directors. Matching Shares cannot be released later than ten years after the date of the purchase of the shares.

The shares required for the Employee Plan are currently being purchased in the market rather than being issued by the Company. The Company does, however, want to have the flexibility to issue new share for the purposes of the Employee Plan if this becomes necessary or desirable in the future and hence shareholder approval was obtained for this amendment to the Employee Plan at the Company's Annual General Meeting held on May 30, 2002.

### Warrants

*'B' Warrants*

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In January 1996, in connection with the Krypton acquisition, the Company issued 59,443,235 "B" Warrants. The warrants entitled the holders to subscribe for ordinary shares at any time during the period beginning six months after the date of issue and ending on December 31, 2002 at a predetermined price. On December 31, 2002 all outstanding "B" Warrants lapsed.

### *Other Warrants*

Warrants were issued by the Company in December 1999 as part of the acquisition of DepoTech. These warrants entitle their holders to subscribe for 291,777 ordinary shares at any time during the period beginning December 31, 1999 and ending on February 25, 2005 at an exercise price of \$1.453 per ordinary share.

### *'D' and 'E' Warrants*

The Company has issued warrants to Paul Capital giving rights to subscribe for 5 million SkyePharma ordinary shares at an exercise price of 73.75 pence, representing a 25% premium to the average trading price for the five trading days immediately prior to the closing date. At June 24, 2003 should the warrants be converted, they represented 0.8% of the Company's ordinary share capital. The warrants are divided into 2,500,000 Series D and 2,500,000 Series E warrants. The terms are identical save for the exercise dates. The Series D Warrants can be exercised at any time from the date of creation of the warrants until December 31, 2008 and the Series E Warrants can be exercised at any time from June 30, 2002 until December 31, 2008. There are standard provisions in the deed polls creating the warrants relating to provision for adjustment of the warrant rights in certain circumstances such as a capital reorganisation and relating to certain restrictions on the Company such as capital distributions and there are a number of provisions in the deed polls designed to comply with U.S. Securities Act.

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## **Item 7: Major Shareholders and Related Party Transactions**

### **MAJOR SHAREHOLDERS**

As far as the Company is aware, it is neither directly nor indirectly owned or controlled by another corporation or any government, and there are no arrangements in place the operation of which may result in the change in its control.

As of June 24, 2003, the Company had notice or was aware that the following persons owned more than 3% of the outstanding ordinary shares:

	<b>Number of Ordinary Shares</b>	<b>% Holding</b>
Dr. Jacques Gonella	54,037,706	8.8%
Oppenheimer Funds	38,202,850	6.2%
Kowa Company Limited	30,000,000	4.9%
Jupiter Asset Management	22,793,015	3.7%
Legal & General Investments Management	20,863,108	3.4%
Mr. I. R. Gowrie-Smith	19,281,339	3.1%
Standard Life Investments	18,891,384	3.1%

The Company's major shareholders do not have different voting rights, except for Kowa's right to appoint a non-executive director pursuant to its investment agreement with the Company in May 2002.

Dr. Jacques Gonella also has an interest in 12 million 'B' Deferred Shares which do not confer upon the holder the right to receive notice of or attend or vote at any general meeting of the Company. The Deferred Shares automatically convert into ordinary shares on the occurrence of certain events. The contingencies determining the conversion of the Deferred Shares into ordinary shares are set out in Note 22 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F. Following the April 2002 U.S. launch of Paxil CR by GlaxoSmithKline and the first commercial sale of Paxil, Dr. Gonella's 12 million 'A' Deferred Shares were converted into 12 million ordinary shares in August 2002. Since June 19, 2002, the date when the Company filed its Annual Report on Form 20-F for the year ended December 31, 2001, Dr. Gonella's stake in the Company has declined by 3,390,298 shares.

On May 14, 2002 SkyePharma announced its intention to enter a wide ranging strategic collaboration with Kowa Company Ltd., a leading Japanese company with substantial pharmaceutical interests, which proposes, under a Subscription Agreement signed on May 13, 2002, to make a strategic investment in SkyePharma. Kowa and SkyePharma have signed a separate non-binding Letter of Intent to evaluate Kowa's acquisition of a 50% interest in SkyePharma's manufacturing facility in Lyon. At an Extraordinary General Meeting on June 7, 2002, shareholder approval was obtained for Kowa to acquire 30 million ordinary shares of 10p each in SkyePharma for a total consideration of approximately £25.3 million. This represents a holding of around 5% after the investment. As part of its investment, Kowa have the right to appoint a non-executive director to the board of SkyePharma, and Mr. Torao Yamamoto was appointed to the Board on October 30, 2002.

As of June 24, 2003, there were 20,775 holders of record of ordinary shares and 40 of such holders were beneficial U.S. holders representing 15.5% of the ordinary shares. In addition, at June 24, 2003 there were 134 holders of record of American Depositary Shares ("ADSS") representing 5.7% of the ordinary shares.

## RELATED PARTY TRANSACTIONS

### Certain Arrangements in Respect of the Jago Acquisition

The Company acquired Jago from Dr. Jacques Gonella, the sole shareholder of Jago, on May 3, 1996 at an initial purchase price of approximately £101 million in cash (plus a prepayment of \$6 million) and 30,711,856 ordinary shares (valued at 75 pence per share or approximately £23 million). In the fund-raising associated with the transaction, Dr. Gonella purchased 84,789,463 ordinary shares of the Company, at a purchase price of 75 pence per share. In addition, the Company agreed to pay Dr. Gonella up to \$5 million of any license income, royalties, milestones and contract fees received by the Company from the Joint Venture. The Company also agreed to pay Dr. Gonella up to \$5 million in connection with any licensing, contract fees or other compensation payable by a third party to the Company (under the terms of a joint venture agreement or otherwise) in respect of the pulmonary drug delivery technologies acquired in the Jago acquisition.

The Company agreed to pay additional consideration in respect of the Jago acquisition pursuant to an earn-out arrangement. The agreement provides that the Company would pay Dr. Gonella an earn-out of the lesser of

(1) \$250 million; or

(2) the aggregate of (A) 20% of the Company's consolidated gross Geomatrix license income (which is generally defined to include all income received by the Company relating to its Geomatrix technologies, but excludes intracompany payments, reimbursements from third parties relating to the Company's contract research and development expenses, and any royalty payments from sales of Dilacor XR) and (B) 2% of its consolidated gross Geomatrix sales revenues (which is generally defined to include any income received by the Company relating to the sale of any products that directly or indirectly use the Geomatrix technologies, but excludes intra-company sales), over a period of 10 years commencing May 1996.

The Company was obligated to make any payments due under the earn-out arrangement on a semi-annual basis over a period of 10 years, subject to the sum of the Company's consolidated gross Geomatrix license income and 10% of the Company's consolidated gross Geomatrix sales revenues reaching a threshold of \$30 million in any given year. Each installment was to be equal to 20% of the Company's consolidated gross Geomatrix license income and 2% of the Company's consolidated gross Geomatrix revenues during the six months preceding the date of the semiannual payment. The Company had the option to prepay the earn-out arrangements in cash for the present value of \$250 million, discounted from 2006 at an annual rate of 8.5%, less any amount paid under the amount prior to the exercise of this option. Additionally, the Company had the option to pay \$123 million to Dr. Gonella when the first \$30 million threshold was reached, in full satisfaction of its earn-out obligation.

Under U.K. GAAP, the Directors are obliged to provide a reasonable estimate of the fair value of the earn-out likely to be payable in preparing the accounts. Having regard to these matters at December 31, 1998 a provision of approximately £40 million was recognized based upon the Directors' then estimate of the maximum amount likely to be due under a proposed Settlement Agreement with Dr Gonella.

The Directors believed that it was in the best interests of the Company to settle the deferred consideration to remove a significant uncertainty that complicated the evaluation of the Group. As a result, at March 31, 2000, the following amendments were made to the 1996 Acquisition Agreement for Jago as set out below:

1. An amendment was signed by which the Company obtained the right to satisfy the deferred consideration in shares rather than cash.

2. A Settlement Agreement was signed establishing the full and final settlement, in shares, of the deferred consideration payable to the vendor of Jago, Dr. Gonella. The

Settlement Agreement received shareholder approval on July 11, 2000 and the following shares were issued on July 20, 2000:

(i) 6 million ordinary shares;

(ii) 12 million 'A' Deferred Shares. These Deferred Shares automatically convert into 12 million ordinary shares on the first commercial sale of Paroxetine/Paxil in combination with Geomatrix technology under the current Licence Agreement. This condition was satisfied in April 2002; and

(iii) 12 million 'B' Deferred Shares. These Deferred Shares automatically convert into 12 million ordinary shares on the Company's receipt of a royalty statement under the current License Agreement stating that reported sales of Paroxetine/Paxil in combination with the Geomatrix technology have exceeded \$1,000 million during any calendar year prior to January 1, 2006, or exceeded \$337 million between January 1, 2006 and May 3, 2006.

In the event that this third condition set out above is not satisfied prior to May 3, 2006, the Deferred 'B' Shares will not be converted and will be cancelled. The vendor shall not be entitled to any other compensation nor additional compensation.

As a result of the above agreement, the deferred consideration payable was re-classified and recorded as 'Shares and warrants to be issued', at December 31, 1999. In the Directors' opinion, 30 million ordinary shares were likely to be issued under the terms of the Settlement Agreement. This represented a settlement valued at £33 million based upon a closing share price of 110 pence on March 31, 2000, the date of the agreement.

The 6 million Ordinary Shares and 12 million Deferred 'A' and 'B' shares were issued on July 20, 2000. On issue, the Ordinary Shares were recorded as share capital and share premium at a price of 94.25 pence. The Deferred Shares were recorded within non-equity share capital and non-equity share premium at a price of 94.25 pence, the fair value of those shares, on July 20, 2000.

Following the U.S. launch and first commercial sale of Paxil CR by GlaxoSmithKline in April 2002, the 12 million 'A' Deferred Shares were converted into 12 million ordinary shares.

In the years ended December 31, 1998 and 1999 the Company made no payments to Dr. Gonella in respect to the foregoing earn-out arrangement. In the year ended December 31, 2000, no payments were made to Dr. Gonella except the issue of shares described above. Given the above amendment and agreements, no further payments will ever be made to Dr. Gonella.

#### **Certain Arrangements in Respect of the Krypton Acquisition**

The Company acquired Krypton on January 8, 1996 from a series of trusts in which Ian Gowrie-Smith, Richard Stewart and Joseph Bozman (each of whom was then a director or officer of the Company), Amy Ikerd (an employee of the Company) and an unrelated third party had interests. At the time of the acquisition, Gowrie-Smith held a 64% interest, Stewart held a 3.8% interest and Bozman held a 11.7% interest in Krypton through their respective trusts. The total consideration paid by the Company (as adjusted to reflect the Company's 1996 reverse stock split) was 30 million ordinary shares and 30 million 'B' Warrants that entitle the holders to subscribe for an additional 3 million ordinary shares at an effective exercise price of 40 pence per share. The Company agreed to pay additional consideration pursuant to an earn-out arrangement of up to 37.5 million additional ordinary shares and 37.5 million additional 'B' Warrants that would entitle the holders to subscribe for 3.75 million ordinary shares at an effective exercise price of 40 pence per share. All outstanding 'B' Warrants lapsed on December 31, 2002.

The agreement provides that these be issued contingent on a change in control of the company at a share price of not less than 80 pence compounded at an annual rate of 10%, or on satisfaction of the following conditions and hurdles:

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(a) for each of the first three Krypton Products (as defined below) that obtains ANDA approval before December 31, 2003, an additional 2.5 million ordinary shares shall be issued;

(b) in the event that the aggregate annual sales of the Krypton Products exceed \$50 million and the Company is profitable in respect of these products before December 31, 2003, 10 million additional ordinary shares shall be issued;

(c) in the event that the aggregate annual sales of the Krypton Products and the annual revenues of the Company exceed \$200 million and the Company is profitable in respect of these products before December 31, 2003, an additional 10 million ordinary shares shall be issued; and

(d) in the event that the aggregate annual sales of the Krypton Products and annual revenues of the Company exceed \$275 million and the Company is profitable in respect of these products before December 31, 2003, an additional 10 million ordinary shares shall be issued.

In the event that two of hurdles (b), (c) and (d) are satisfied in relation to any single year's sales, only the first such hurdle will be considered as having been satisfied. For purposes of this paragraph, the term "Krypton Products" refers to glipizide, glyburide, ISMN, midazolam HCL and vecuronium bromide.

Immediately prior to the acquisition of Krypton, Gowrie-Smith held 13.9%, Stewart held 0.5% and Bozman held 1.6% of the ordinary shares of the Company. At that time, if all of the outstanding Convertible Preference Shares and then existing 'A' Warrants had been exercised, Gowrie-Smith would have held an interest of 19.58%, Stewart an interest of 0.4% and Bozman an interest of 1.35% in the Company. Immediately after the acquisition, Gowrie-Smith held 24.7%, Stewart held 1.2% and Bozman held 3.9% of the ordinary shares of the Company. At that time, if all of the outstanding Convertible Preference Shares, 'A' Warrants and 'B' Warrants had been exercised, Gowrie-Smith would have held an interest of 26.38%, Stewart an interest of 1.17% and Bozman an interest of 3.63% in the Company.

Certain of the hurdles relating to the Krypton acquisition were not formulated to take account of the detailed arrangements currently envisaged by the Company. Should the annual revenues of the Company approach the amounts specified in hurdles (c) and (d), the Company may need to renegotiate elements of the Krypton acquisition agreement.

As no Krypton products are marketed and no licensing partners have been identified for the products the Directors have taken the view that the above hurdles can no longer be reasonably expected to be met. Consequently no provision for deferred consideration has been recognized as at December 31, 2002.

In January 1996, the Company repaid an amount of approximately £1 million that had been loaned interest-free to Krypton by the Ian Gowrie-Smith Family Trust to fund certain drug development and milestone payments.

### Other Arrangements

At the end of December 1998, Ian Gowrie-Smith (through a family-owned trust) acquired a 50% interest in 10 East 63<sup>rd</sup> Street Inc., the company which owns 10 East 63<sup>rd</sup> Street, a property in New York. In December 2002, Mr. Gowrie-Smith acquired the remaining 50% interest. SkyePharma PLC has been in occupation of that property since January 1997, subject to a tenancy agreement renewed in February 2001 at which time the annual rent was increased to \$360,000 per annum based upon an independent valuation. On April 1, 2002, the company took additional space within

the property at which time the annual rent was increased to \$420,000 per annum. Until April 1, 2002, approximately one-third of the premises was subleased to Fifth Avenue Capital Inc.

In December 2001, the Company entered into several agreements concerning the development of Astralis' novel injectable vaccine therapy, for the treatment of all forms of psoriasis, a chronic skin disorder. In a separate transaction, the Company has made a total equity investment in Astralis of \$20 million in convertible preferred shares, and 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. The Company has the right to elect one member of the Board of Directors of Astralis, and Michael Ashton, the Company's Chief Executive Officer, was appointed to the Astralis Board in January 2002. For further details of the Astralis transactions see "Item 4: Information on the Company Business Operations Collaborative Arrangements Other Collaborative Arrangements"

**Item 8: Financial Information**

**CONSOLIDATED STATEMENTS AND OTHER FINANCIAL INFORMATION**

See "Item 18: Financial Statements".

**LEGAL PROCEEDINGS**

Save as disclosed below, the Company and its subsidiaries are not involved in any legal or arbitration proceedings which are expected to have, or have had in the past twelve months preceeding the date of this document, a significant impact on the Company. Previously disclosed legal proceedings in the Annual Report on Form 20-F for the year ended December 31, 2001, including the class action filed against DepoTech, have been dismissed or resolved with no significant impact on the Company.

On May 8, 2001, a summons in a civil case was filed in respect of a claim by Andrx Corporation, a generic drug manufacturer against SkyePharma Inc. in the U.S. District Court, Southern District of Florida. The lawsuit alleges violations of anti-trust law and common law of the United States and the State of Florida. The complainant seeks injunctive relief and unspecified monetary damages from Elan Corporation PLC (who was the original defendant in this case) and SkyePharma arising from an alleged agreement entered into by Elan and SkyePharma to prevent competition for a controlled release version of the product Naprelan made with the active drug Naproxen. This action was settled as to SkyePharma, Inc. with prejudice on June 7, 2002, without the payment of any damages.

On April 12, 2002, a Class Action Complaint was filed by the Action Alliance of Senior Citizens of Greater Philadelphia, a non-profit Pennsylvania corporation, individually and on behalf of all others similarly situated, against Elan Corporation PLC and SkyePharma Inc. The action was filed in the U.S. District Court for the Eastern District of Pennsylvania. On May 15, 2002, a second Class Action Complaint was filed in the same court by Jeanine Weber, and on June 12, 2002, a third Class Action Complaint was filed in the same court by Charles Frederick. On October 14, 2002, a Consolidated Class Action Complaint (the "Consolidated Complaint") was filed, covering all three cases, and on the same date the plaintiffs filed a motion requesting class certification. The Consolidated Complaint is brought under the Sherman Anti-trust Act (the "Act") and various state statutes, and alleges a contract in restraint of trade as well as an attempt to monopolise the market for Naprelan in violation of those laws. The Consolidated Complaint seeks injunctive relief and damages, multiple damages, and restitution in unspecified amounts. On November 22, 2002, the case was stayed by agreement of the parties pending final resolution of certain patent litigation between Elan and Andrx that relates to Elan's patents covering Naprelan. The case remains stayed at the present time. The Company believes that the claims asserted in the Consolidated Complaint are without merit and will vigorously defend the action.

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In late December 2002, SkyePharma, Inc. was served with a subpoena by the U.S. Federal Trade Commission ("FTC"), requesting documents relating to the same agreement between Elan and SkyePharma at issue in the Andrx lawsuit and the Pennsylvania class action litigation described above. SkyePharma, Inc. has cooperated with the FTC's request and produced documents in response to the subpoena.

Contingent liabilities and guarantees are summarized in Note 20 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F.

**DIVIDEND POLICY**

The Company has not paid dividends in the last 10 years on its ordinary shares and does not intend to pay dividends in the foreseeable future. The Company currently intends to retain all of its earnings to finance its operations and future growth. Moreover, under current U.K. law, the Company's accumulated realized profits must exceed its accumulated realized losses (on a nonconsolidated basis) before dividends can be paid.

**SIGNIFICANT CHANGES**

There have been no significant changes since the date of the Consolidated Financial Statements included in this Form 20-F.

**Item 9: The Offer and Listing**

**STOCK PRICE HISTORY**

The principal trading market for the ordinary shares is the London Stock Exchange (the "LSE").

The table below sets forth, for the periods indicated, the highest and lowest middle-market quotations for the Company's ordinary shares as derived from the Daily Official List of the LSE and the highest and lowest sales prices of the Company ADSs on The Nasdaq National Market. The mid-closing price for the ordinary shares on the LSE and the last sale price for the ADSs on The Nasdaq National Market on June 24, 2003 was 66.50 pence per ordinary share and \$11.33 per ADS.

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See "Exchange Rate Information" with respect to the exchange rates applicable to the periods set forth below.

	SkyePharma Ordinary Shares		SkyePharma ADSs	
	High	Low	High	Low
	(Pence per Company Ordinary Share)		(\$ per Company ADS)	
<b>Year ended December 31, 1998</b>	103.50	44.5	13.56	7.13
<b>Year ended December 31, 1999</b>	88.00	45.3	15.13	6.38
<b>Year ended December 31, 2000</b>	190.00	49.8	29.38	7.38
<b>Year ended December 31, 2001</b>	108.00	49.0	15.50	7.01
<b>Year ended December 31, 2002</b>	80.25	39.0	11.90	6.25
<b>Year ended December 31, 2001</b>				
First Quarter	108.0	63.5	15.50	9.06
Second Quarter	97.5	78.0	13.85	10.25
Third Quarter	90.0	50.0	12.70	7.78
Fourth Quarter	69.0	49.0	9.60	7.01
<b>Year ended December, 2002</b>				
First Quarter	74.00	52.50	10.85	7.45
Second Quarter	80.25	62.75	11.90	9.03
Third Quarter	66.00	45.00	9.75	6.95
Fourth Quarter	52.00	39.00	8.94	6.25
<b>Year ended December 31, 2003</b>				
First Quarter	50.00	41.50	8.44	6.60
Second Quarter (through June 24, 2003)	73.00	45.75	12.99	7.30
<b>Monthly Data</b>				
December 2002	45.75	39.00	7.21	6.25
January 2003	50.00	43.25	8.44	7.19
February 2003	46.25	41.50	7.55	6.60
March 2003	49.00	42.00	7.59	6.70
April 2003	49.50	45.75	8.18	7.30
May 2003	56.25	49.75	9.40	8.15
June 2003 (through June 24, 2003)	73.00	59.25	12.99	9.89

**STOCK EXCHANGES ON WHICH THE COMPANY'S SHARES ARE LISTED**

The ordinary shares were admitted to the Official List of the LSE on May 3, 1996 and are quoted under the symbol "SKP". Prior to that time, the ordinary shares traded on the LSE's Alternative Investment Market, from January 9, 1996 to May 2, 1996, and on the LSE's Unlisted Securities Market, from October 26, 1987 to January 8, 1996.

The LSE classifies equity securities based on 12 levels of normal market size, ranging from 200,000 to 500 shares. These levels of normal market size reflect the turnover by value in each of the Company's shares over the past 12 months. The ordinary shares have a normal market size of 10,000 shares. The normal market size classification for each equity security is subject to quarterly review in the light of trading volumes in the previous quarter and to adjustment, as appropriate. U.K. market makers are normally required to make a two-way market in sizes of not less than the normal market size and to report all transactions to the LSE within three minutes. In respect of securities with a normal market size greater than 2,000, transactions of not more than three times normal market size are published immediately as to size and price, but transactions in excess of three times normal market size are not published until after 60 minutes.

The Company's ADSs are quoted on The Nasdaq National Market under the symbol "SKYE". ADSs are issued by the Bank of New York as depositary under the Deposit Agreement dated as of July 8, 1998. Each ADS represents ten ordinary shares.

#### **Item 10: Additional Information**

##### **MEMORANDUM AND ARTICLES OF ASSOCIATION**

The following summarizes certain provisions of SkyePharma PLC's Memorandum and Articles of Association and applicable English law. The summary is qualified in its entirety by reference to the UK Companies Act and SkyePharma's Memorandum and Articles of Association. Investors can obtain copies of the Memorandum and Articles of Association by contacting the Company Secretary at the registered office of the Company. On May 30, 2002 the Company adopted new Articles of Association.

##### **Objects and Purposes**

The Company was incorporated in England and Wales on March 10, 1910 under the Companies Act 1908 as a Company limited by shares and was re-registered in 1982 as a public limited company under the Companies Act 1948 to 1980. The Company is registered under company number 107582. The Company was re-registered as SkyePharma PLC on January 8, 1996.

The objects of the Company are set out in full in clause 4 of its memorandum of association which provides, among other things, that the Company's objects are to carry on in any part of the world any business which, in the opinion of the directors, may seem conveniently carried on in connection with or ancillary to any of several diverse businesses, including applying for, purchasing or otherwise acquiring and holding, using, developing, selling, licensing or otherwise disposing of or dealing with patents, copyrights, designs, trade marks, secret processes, know-how and inventions and any interest therein.

##### **Directors**

The business and affairs of the Company shall be managed by the directors.

A director may not vote or count towards the quorum on any resolution concerning any proposal in which he (or any connected person) to his knowledge has a material interest (other than by virtue of his interest in securities of the Company), which includes the voting of compensation awards to themselves. This prohibition does not apply to any of the following matters:

- (i) a contract or arrangement for giving to the director security or as guarantee or indemnity in respect of
  - a) money lent by him or obligations undertaken by him or by any other person at the request of or for the benefit of the Company or any of its subsidiaries; or
  - b) a debt or obligation of the Company or any of its subsidiaries for which he himself has assumed responsibility in whole or part under a guarantee or indemnity or by the giving of security.
- (ii) where the Company or any of its subsidiary undertakings is offering securities in which offer the director is, or may be, entitled to participate as a holder of securities or in the underwriting or sub underwriting of which the director is to participate;
- (iii) relating to another company in which he and any persons connected to him do not to his knowledge hold an interest in shares representing 1 per cent or more of any class of the equity share capital or of the voting rights in that company;



(iv) relating to a pension, superannuation or similar scheme or retirement, death or disability benefits scheme or employees' share scheme which has been approved by the inland revenue or is conditional upon that approval or does not award him any privilege or benefit not awarded to the employees to whom the scheme relates; or

(v) concerning insurance which the Company proposes to maintain or purchase for the benefit of persons including directors.

A director may not vote or be counted in the quorum on any resolution which concerns his or her own appointment with the Company or any other company in which the Company is interested.

The UK Companies Act requires a director of a company who is in any way interested in a contract or proposed contract with the Company to declare the nature of his interest at a meeting of the directors of the Company.

The directors may exercise all the powers of the Company to borrow money. The borrowing powers contained in the articles of association may only be varied by amending the articles of association.

A director must retire at the conclusion of the first annual general meeting after he reaches the age of 70 and thereafter annually, and being eligible, may stand for re-election.

A director is not required to hold an interest in the shares of the Company.

At each annual general meeting of the Company one-third of the directors for the time being (rounded down if necessary) are required to resign from office.

### **Classes of Shares**

The authorized share capital of the Company is £111,400,000 divided into 1,090,000,000 ordinary shares of 10p each, 12,000,000 "A" Deferred Shares of 10p each (which have been converted into ordinary shares) and 12,000,000 "B" Deferred Shares of 10p each.

### ***Provisions set out applying to the Ordinary Shares of 10p each***

(a)  
Dividends

Under English law, dividends are payable on the Company's ordinary shares only out of profits available for distribution, as determined in accordance with accounting principles generally accepted in the UK and by the Companies Act 1985. The Company in general meeting may declare dividends by ordinary resolution, but such dividend may not exceed the amount recommended by the directors. The directors may pay interim dividends if it appears they are justified by the Company's financial position.

Dividends unclaimed for 12 years after they become due for payment shall, unless the directors resolve otherwise, be forfeited and revert to the Company.

(b)  
Voting Rights

Every member who is present in person or represented at any general meeting of the Company and who is entitled to vote has one vote on a show of hands. On a poll every member who is present or represented has one vote for every share held.

Holders of ordinary shares may appoint a proxy, including a beneficial owner of those shares, to attend, speak and vote on their behalf at any shareholder's meeting.

If any sum remains unpaid in relation to a member's shareholding, that member is not entitled to vote that share unless the board otherwise determines.

- (c) Rights to share in the Company's profits

The profits of the Company available for dividend and resolved to be distributed shall be applied in the payment of dividends (if any are declared) to members in accordance with their respective rights and priorities.

- (d) Rights to share in any surplus in the event of liquidation

On a winding up of the Company, the balance of the assets available for distribution, after deduction of any provision made under the Companies Act 1985 and subject to any special rights attaching to any class of share, shall be applied in repaying to the members of the Company the amounts paid up on the shares held by them. Any surplus assets will belong to the holders of any ordinary shares then in issue according to the numbers of shares held by them.

- (e) Redemption and sinking provisions

The Company may by special resolution create and sanction the issue of shares which are, or at the option of the Company or the holder are to be liable, to be redeemed, subject to and in accordance with the provisions of the Companies Act 1985. The special resolution sanctioning the issue shall also make such alterations to the articles of the Company as are necessary to specify the terms on which and the manner in which the shares are to be redeemed. The Company has no redeemable shares in issue and there are no provisions relating to sinking funds in the articles of the Company. The Company has not established a sinking fund.

- (f) Liability to further capital calls by the Company.

The directors may make calls upon the members in respect of any monies unpaid on their shares. Each member shall pay to the Company at the time and place specified the amount called on his shares. A call may be revoked or postponed as the directors determine.

- (g) Substantial shareholders

There are no provisions contained in the articles of the Company which discriminate against any existing or prospective holder of securities as a result of such shareholder owning a substantial number of shares.

***Provisions set out applying to the 'A' Deferred Shares***

The "A" Deferred Shares did not confer any right to participate in any profits of the Company or to receive notice of or attend any general meeting of the Company. Each "A" Deferred Share has been redesignated as an ordinary share following the sale of a Geomatrix version of Paroxetine/Paxil in accordance with the Company's existing license agreement with SmithKline Beecham, PLC which occurred in April, 2002.

***Provisions set out applying to the 'B' Deferred Shares***

The "B" Deferred Shares do not confer any right to participate in any profits of the Company or to receive notice of or attend any general meeting of the Company. Each "B" Deferred Share will be redesignated as an ordinary share on the first occasion that total reported sales of Geomatrix versions of Paroxetine/ Paxil exceed \$1 billion in any calendar year ending prior to January 1, 2006 or, if that does not happen, then if such sales exceed \$337 million in the period January 1, 2006 to May 3, 2006.

The right of redesignation attaching to the "B" Deferred Shares will lapse if this event has not taken place by May 3, 2006.

### **Variation of rights**

Whenever the capital of the Company is divided into different classes of shares the special rights attached to any class of shares may be modified either with the consent in writing of the holders of three quarters of the issued shares of the class or with the sanction of an extraordinary resolution passed at a separate general meeting of the holders.

### **Shareholders' Meetings and Notices**

The Company is required to hold a general meeting each year as its annual general meeting in addition to other meetings (called extraordinary general meetings) as the directors think fit. The type of meeting will be specified in the notice calling it. Not more than 15 months may elapse between the date of one annual general meeting and the next.

In the case of an annual general meeting or the meeting for the passing of a special resolution (requiring the consent of a 75% majority) 21 clear days' notice is required. In other cases 14 clear days' notice is required. The notice must specify the place, the date, and the hour of the meeting, and the general nature of the business to be transacted.

### **Limitations on foreign shareholders**

There are no limitations imposed by English law or the Company's Memorandum or Articles of Association on the right of non-residents or foreign persons to hold or vote the Company's ordinary shares other than the limitations that would generally apply to all of the Company's shareholders.

### **Change of Control**

There are no provisions in the Articles of Association that would have an effect of delaying, deferring or preventing a change in control of the Company and that would operate only with respect to a merger, acquisition or corporate restructuring involving the Company or any of its subsidiaries.

### **Disclosure of Interests in Shares**

The UK Companies Act gives the Company the power to require persons whom it believes to have, or to have acquired in the previous three years, an interest in its voting shares to disclose certain information with respect to those interests. Failure to supply the information required may lead to disenfranchisement of the relevant shares and a prohibition on their transfer and receipt of dividends and other payments in respect of those shares. In this context the term "interest" is widely defined and will generally include an interest of any kind whatsoever in voting shares, including an interest of a holder of SkyePharma ADSs. Disclosure of ownership is covered by the London Stock Exchange Regulations and the Companies Act. Shareholders holding beneficial interests in excess of 3% are required to disclose this interest.

### **MATERIAL CONTRACTS**

At 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. On July 20, 2000, 6 million ordinary shares were issued to Dr. Gonella at a price of 94.25 pence. Also on July 20, 2000, 12 million 'A' and 12 million 'B' non-equity Deferred Shares were issued. The contingencies determining the conversion of the Deferred Shares into ordinary shares are set out in Note 22 of the Notes to SkyePharma's Consolidated Financial Statements included in Item 18 of this Form 20-F. Following the April 2002 U.S. launch of Paxil CR by GlaxoSmithKline and the first commercial sale of Paxil, Dr. Gonella's 12 million 'A' Deferred Shares have been converted into 12 million ordinary shares. In the event that the remaining conditions are not satisfied prior to May 3, 2006, the 'B' Deferred Shares will not be converted and

will be cancelled. The vendor will not be entitled to any other compensation nor additional compensation. On issue, the ordinary and Deferred Shares were recorded in share capital and share premium. At December 31, 1999 prior to the issue of shares, in the Directors' opinion, 30 million ordinary shares were likely to be issued under the terms of the Settlement Agreement and a figure of £33 million was recorded within shares and warrants to be issued, based upon a closing share price of 110 pence on March 31, 2000, the date of the Settlement Agreement.

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, an injectable product, 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. This amount comprises total milestone payments of \$10 million for DepoMorphine through FDA approval, 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. In addition, the amount comprises total milestone payments of \$50 million for Propofol IDD-D. The Propofol IDD-D milestone payments are payable when the product successfully achieves certain regulatory milestones, including FDA approval, except that, in the event the FDA-approved labeling fails to meet the parties' target labeling, only \$10 million becomes payable upon FDA approval, with the remaining \$40 million being due upon the achievement of certain sales targets. 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. In respect of the first product launched under the agreement, the Company will pay Endo a fixed contribution in relation to marketing activities undertaken by Endo in respect of the first and second year of commercialization. Endo will be responsible for funding and conducting any post-marketing studies and for selling and marketing expenses. The agreement expires with respect to each product upon the later of the expiry of all relevant patents and the 15<sup>th</sup> anniversary of the date of first commercialization. The agreement may be terminated in various cases, including by Endo in the event the Company experiences delays in obtaining regulatory approval for the products or fails to achieve the target labeling and, without cause, upon sixty days' notice provided that, in such an event, Endo shall pay an undisclosed termination fee to the Company.

On March 13, 2000, the Company entered into an agreement with Bioglan for the manufacture, marketing and distribution of Solaraze in Europe for an up-front licensing fee and royalty payments. In December 2000, the Company entered into a further agreement with Bioglan for the license of marketing rights to the United States, Canada and Mexico for Solaraze, for which Bioglan paid a \$14 million fee and agreed to pay further significant milestone payments upon the commercialization of Solaraze. On May 13, 2000 the Company announced that it had agreed to transfer all rights to market Solaraze in Europe to Shire for total consideration of up to £15 million. Of this amount, £2.1 million is contingent on various conditions, including Solaraze's launch in certain European countries. In addition, SkyePharma will receive royalties on all European sales from Shire. In addition, the Company agreed to pay the administrators an amount of £0.7 million. For more details on the history of these agreements, see "Item 4: Information on the Company Business Operations Drug Delivery Platforms Topical Approved Topical Products Solaraze."

For a description of transactions with related parties, see "Item 7: Major Shareholders and Related Party Transactions".

## EXCHANGE CONTROLS

There are currently no limitations, either under the laws of the United Kingdom or in the Articles of Association of the Company, on the rights of non-residents to hold, or to vote on Ordinary Shares. Additionally, there are currently no United Kingdom foreign exchange control restrictions on the conduct of the Company's operations or affecting the remittance of dividends on unrestricted shareholders' equity.

## TAXATION

The following is a summary of the material U.S. federal income and the United Kingdom tax consequences of owning and disposing of ordinary shares or ADSs of the Company by a U.S. Holder as defined below and a Non-U.S. Holder that holds the ordinary shares or ADSs as capital assets.

This summary is not exhaustive of all possible tax considerations and does not take into account the specific circumstances of any particular investors (such as tax-exempt organizations, life insurance companies, dealers in securities and currencies, traders in securities that elect to use a mark-to-market method of accounting, investors liable for alternative minimum tax, investors that actually or constructively own 10% or more of the voting stock of the Company, investors that hold ordinary shares or ADSs as part of a straddle or a hedging or conversion transaction,

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holders who acquired the stock units or ADS as compensation, or investors whose functional currency is not the U.S. dollar) that may be subject to special rules. In addition to these classes of holders, for United Kingdom tax purposes, special rules may apply also to holders that are banks, regulated investment companies or other financial institutions.

This summary is based on the tax laws of the United States (including the Internal Revenue Code of 1986, as amended, its legislative history, existing and proposed regulations, published rulings and court decisions) and on the tax laws of the United Kingdom all as in effect on the date hereof, as well as on the Convention Between the Government of the United States of America and the Government of the United Kingdom of Great Britain and Northern Ireland for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income and Capital Gains entered into force April 25, 1980 (the "Old Treaty") and entered into force on March 31, 2003 (the "New Treaty"), as well as the Convention between the Government of the United States and the Government of the United Kingdom of Great Britain and Northern Ireland for the Avoidance of Double Taxation and Prevention of Fiscal Evasion with respect to Taxes on Estates of Deceased Persons and on Gifts as in effect on the date hereof (the "Estate Tax Treaty"). These laws are subject to change (or changes in interpretation), possibly with retroactive effect.

The New Treaty is effective in respect of taxes withheld at source for amounts paid or credited on or after May 1, 2003. Other provisions of the New Treaty, however, will take effect on January 1, 2004. The rules of the Old Treaty will remain applicable until these effective dates. A U.S. Holder who is eligible for the benefits of the Old Treaty and New Treaty, however, may, in certain circumstances, elect to have the Old Treaty apply in its entirety for a period of twelve months after the applicable effective dates of the New Treaty. Holders of ordinary shares or ADSs are advised to consult their own tax advisers with respect to the overall tax implications of the New Treaty, including the implications of making the election.

In addition, this summary is based in part upon the representations of the Depositary and the assumption that each obligation in the Deposit Agreement and any related agreement will be performed in accordance with their respective terms.

For purposes of this discussion, a "U.S. Holder" is any beneficial owner of ordinary shares or ADSs that is for United States federal income tax purposes:

- (1) a citizen or resident of the United States;
- (2) a United States domestic corporation;

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- (3) an estate the income of which is subject to United States federal income tax without regard to its source; or
- (4) a trust if a court within the United States is able to exercise primary supervision over the administration of the trust and one or more United States persons have the authority to control all substantial decisions of the trust.

The discussion does not address any aspects of United States taxation other than federal income taxation. In addition, the following summary of certain U.K. tax considerations does not address the tax consequences of owning and disposing the Company's ordinary shares or ADSs to a U.S. Holder:

- (1) that is resident (or, in the case of an individual, ordinarily resident) in the United Kingdom for U.K. tax purposes,
- (2) whose holding of ordinary shares or ADSs is effectively connected with a permanent establishment in the United Kingdom through which such U.S. Holder carries on business activities or, in the case of an individual who performs independent personal services, with a fixed base situated therein,
- (3) who is not otherwise eligible for benefits under the Treaty with respect to income and gain from the ordinary shares or ADSs.

***Prospective investors are urged to consult their own tax advisors regarding the United States federal, state and local and the United Kingdom and other tax consequences of acquiring, owning and disposing of ordinary shares and ADSs. In particular, a U.S. Holder should confirm with its advisor whether it is eligible for the benefits of the Old Treaty or New Treaty and should discuss the consequences of failing to be so eligible.***

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In general, and taking into account the earlier assumptions, for United States federal income and United Kingdom income tax purposes, holders of ADRs evidencing ADSs will be treated as the beneficial owners of the ordinary shares represented by those ADSs. Exchange of ordinary shares for ADRs, and ADRs for ordinary shares, generally will not be subject to United States federal income tax or to United Kingdom income tax.

### Taxation of Dividends

#### *United Kingdom Taxation*

The taxation of dividends paid in respect of the ordinary shares depends upon the law and practice in force at the time dividends are paid. The following summary is based upon current law and practice, which may change by the time that any dividends become payable.

For dividends paid on or after April 6, 1999, under the Old Treaty an Eligible U.S. Holder is entitled to receive from the U.K. a tax credit ("Tax Credit Amount") in respect of any dividend received equal to one-ninth of the amount of the cash dividend. The payment is reduced by an amount equal to 15% of the sum of the dividend payment and the tax credit amount ("the 15% U.K. withholding tax"). The 15% U.K. withholding tax will not, however, exceed such amount and reduces the Tax Credit Amount to \$0.

Under the New Treaty, an eligible U.S. holder will not be entitled to a tax credit nor be subject to a withholding tax by the United Kingdom.

For the purposes of this document, the term "Eligible U.S. Holder" means a U.S. Holder that is a beneficial owner of an ordinary share or an ADS and the cash dividend paid with respect thereto and that

(1) is an individual or a corporation resident in the United States for purposes of the Treaty (and, in the case of a corporation, is not also resident in the United Kingdom for U.K. tax purposes);

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(2) is not a corporation which, alone or together with one or more associated corporations, controls, directly or indirectly, 10% or more of the voting stock of the Company;

(3) holds the ordinary share or ADS in a manner which is not effectively connected with a permanent establishment in the United Kingdom through which such U.S. Holder carries on business or with a fixed base in the United Kingdom from which such holder performs independent personal services;

(4) under certain circumstances, is not an investment or holding company, 25% or more of the capital of which is owned, directly or indirectly by persons that are not individuals resident in, and are not nationals of, the United States;

(5) under certain circumstances, is not exempt from federal income tax on dividend income in the United States; and

(6) is eligible for benefits under the Treaty with respect to income and gain from the ordinary shares or ADS's.

An Eligible U.S. Holder may claim the Treaty Payment to which he is entitled from the Inland Revenue. However, under Rev. Proc. 2000-13 an Eligible U.S. Holder may elect to be treated as receiving the Tax Credit Amount due under the Treaty without affirmatively making a claim to the Inland Revenue. Please see a complete discussion of these rules below in the discussion of U.S. taxation.

While a claim for payment is no longer necessary, if a claim for payment is made, it must be made within 6 years of the U.K. year of assessment (generally, the 12 month period ending April 5 in each year) in which the related dividend was paid. The first such claim by an Eligible U.S. Holder for payment under these procedures is made by sending the appropriate U.K. forms in duplicate to the Philadelphia Service Center, Foreign Certification Unit, P.O. Box 16347, DP535B, Philadelphia, PA 19114. If the Eligible U.S. Holder qualifies as a U.S. resident, the Internal Revenue Service will certify the form to that effect and forward it to the U.K. Inland Revenue. Forms may be obtained by writing to the U.S. Internal Revenue Service, Assistant Commissioner International, 950 L'Enfant Plaza South, S.W., Washington, D.C. 20024, Attention: Taxpayers Service Division. Because a refund claim is not considered made until the U.K. tax authorities receive the appropriate form from the Internal Revenue Service, forms should be sent to the Internal Revenue Service well before the end of the applicable limitation period. Any claim under these procedures after the first claim should be filed directly with the U.K. Financial Intermediaries and Claims Office, Fitzroy House, P.O. Box 46, Nottingham NG2 1BD, England.

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U.S. Holders who are not resident or ordinarily resident for tax purposes in the United Kingdom and have no other source of U.K. income are not required to file a U.K. income tax return.

### *United States Taxation*

Under the United States federal income tax laws, and subject to the passive foreign investment company rules discussed below, the gross amount of any dividend paid to a U.S. Holder by the Company out of its current or accumulated earnings and profits (as determined for United States federal income tax purposes) is subject to United States federal income taxation. Dividends paid to a non-corporate U.S. holder in taxable years beginning after December 31, 2002 and before January 1, 2009 that constitute qualified dividend income will be taxable to the holder at a maximum tax rate of 15% provided that the ordinary shares or ADSs are held for more than 60 days during the 120 day period beginning 60 days before the ex-dividend date and the holder meets other holding period requirements. Dividends paid by the Company with respect to its ordinary shares or ADSs generally will be qualified dividend income.

U.S. Holders that are eligible for the benefits of the Old Treaty and have properly filed Internal Revenue Form 8833 may include any United Kingdom tax deemed withheld from the dividend payment in this gross amount even though they do not in fact receive it. Subject to certain

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limitations, the United Kingdom tax deemed withheld in accordance with the Old Treaty and paid over to the United Kingdom will be creditable against the U.S. Holder's United States federal income tax liability. In addition, special rules apply in determining the foreign tax credit limitation with respect to dividends that are subject to the maximum 15% rate. Under the New Treaty, a U.S. Holder will not be entitled to a United Kingdom tax refund, but also not be subject to United Kingdom withholding tax. In that case, the U.S. Holder therefore will include in income for United States federal income tax purposes only the amount of the dividend actually received, and the receipt of a dividend will not entitle the U.S. Holder to a foreign tax credit.

The dividend is taxable to the U.S. Holder when the holder, in the case of ordinary shares, or the Depositary, in the case of ADSs, receives the dividend, actually or constructively. The dividend will not be eligible for the dividends received deduction generally allowed to United States corporations in respect of dividends received from other United States corporations. The amount of the dividend distribution includible in income of a U.S. Holder will be the U.S. dollar value of the British pounds sterling payments made, determined at the spot British pound sterling/ U.S. dollar rate on the date such dividend distribution is includible in the income of the U.S. Holder, regardless of whether the payment is in fact converted into U.S. dollars. Generally, any gain or loss resulting from currency exchange fluctuations during the period from the date the dividend payment is includible in income to the date such payment is converted into U.S. dollars will be treated as ordinary income or loss and will not be eligible for the special tax rate applicable to qualified dividend income. Such gain or loss will generally be from sources within the United States for foreign tax credit limitation purposes. Distributions in excess of current and accumulated earnings and profits, as determined for United States federal income tax purposes, will be treated as a return of capital to the extent of the U.S. Holder's basis in the ordinary shares or ADSs and thereafter as capital gain.

Dividends will be income from sources outside the United States, but generally will be "passive income" or, in the case of certain holders, "financial services income" which is treated separately from other types of income for foreign tax credit limitation purposes.

### **Taxation of Capital Gains**

#### *United Kingdom Taxation*

U.S. Holders who are not resident or (in the case of individuals only) ordinarily resident for tax purposes in the United Kingdom will not be liable for U.K. tax on capital gains realized on the disposal of their ADSs or ordinary shares unless such ADSs or ordinary shares are used, held or acquired for the purposes of a trade, profession or vocation carried on in the United Kingdom through a branch or agency.

#### *United States Taxation*

Under the United States federal income tax laws, and subject to the passive foreign investment company rules discussed below, upon a sale or other disposition of ordinary shares or ADSs, a U.S. Holder will recognize gain or loss for United States federal income tax purposes in an amount equal to the difference between the U.S. dollar value of the amount realized and the U.S. Holder's tax basis (determined in U.S. dollars) in such ordinary shares or ADSs. Generally, such gain or loss, will be long-term capital gain or loss if the U.S. Holder's holding period for such ordinary shares or ADSs exceeds one year, and will be from sources within the United States for foreign tax credit limitation purposes. Long-term capital gain of a non-corporate U.S. Holder that is recognized on or after May 6, 2003 and before January 1, 2009 is taxed at a

maximum rate of 15%.

### Passive Foreign Investment Company Rules

The Company believes that its ordinary shares and ADSs should not be treated as the stock of a passive foreign investment company, PFIC, for United States federal income tax purposes.

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However, this conclusion is a factual determination made annually and thus may be subject to change.

In general, we will be a PFIC with respect to a U.S. Holder if, for any taxable year in which the U.S. Holder holds the Company's ordinary shares or ADSs:

- (1) 75% or more of the gross income of the Company for the taxable year is passive income; or
- (2) 50% or more of the value (determined on the basis of quarterly averages) of the Company's assets is attributable to assets that produce or are held for the production of passive income.

Passive income generally includes dividends, interest, royalties, rents (other than certain rents and royalties derived in the active conduct of a trade or business) annuities and gains from assets that produce passive income of this nature. If a foreign corporation owns at least 25% by value of the stock of another corporation, the foreign corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation, and as receiving directly its proportionate share of the other corporation's income.

If the Company is treated as a PFIC, a U.S. Holder that did not make a qualified electing fund ("QEF") or mark-to-market election, each as described below, will be subject to special rules with respect to (a) any gain realized on the sale or other disposition of ordinary shares or ADSs and (b) any excess distribution by the Company to the U.S. Holder (generally, any distributions to the U.S. Holder in respect of the ordinary shares or ADSs during a single taxable year that are greater than 125% of the average annual distributions received by the U.S. Holder in respect of the ordinary shares or ADSs during the three preceding taxable years or, if shorter, the U.S. Holder's holding period for the ordinary shares or ADSs). Under these rules:

- (1) the gain or excess distribution would be allocated ratably over the U.S. Holder's holding period for the ordinary shares or ADSs;
- (2) the amount allocated to the taxable year in which the gain or excess distribution was realized would be taxable as ordinary income;
- (3) the amount allocated to each prior year, with certain exceptions, would be subject to tax at the highest tax rate in effect for that year; and
- (4) the interest charge generally applicable to underpayments of tax would be imposed in respect of the tax attributable to each such year.

A U.S. Holder that makes a QEF election will be currently taxable on its pro rata share of the Company's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year of the Company, regardless of whether or not distributions were actually received. The U.S. Holder's basis in the ordinary shares or ADSs will be increased to reflect taxed but undistributed income. Distributions of income that had previously been taxed will result in a corresponding reduction of basis in the ordinary shares or ADSs and will not be taxed again as a distribution to the U.S. Holder.

Special rules apply with respect to the calculation of the amount of the foreign tax credit with respect to excess distributions by a PFIC or, in certain cases, QEF inclusions.

A U.S. Holder will not be subject to the PFIC tax rules described above if the U.S. Holder makes a mark-to-market election with respect to its ordinary shares or ADSs. Instead, in general, an electing U.S. Holder will include in each year, as ordinary income, the excess, if any, of the fair market value of the ordinary shares or ADSs at the end of the taxable year over their adjusted basis. These amounts of ordinary income will not be eligible for the favorable tax rates applicable to qualified dividend income or long term capital gains and will be permitted an ordinary



loss in respect of the excess, if any, of the adjusted basis of the ordinary shares of ADSs over their fair market value at the end of the taxable year (but only to the extent of the net amount of previously

included income as a result of the mark-to-market election). The electing U.S. Holder's basis in the ordinary shares or ADSs will be adjusted to reflect any such income or loss amounts.

In addition, notwithstanding any election by a U.S. Holder with regard to the ordinary shares or ADSs, dividends received by the U.S. Holder from the Company will not constitute qualified dividend income to the U.S. Holder, if the Company is a PFIC either in the taxable year of the distribution or the preceding taxable year. Dividends received that do not constitute qualified dividend income are not eligible for taxation at the 15% maximum rate applicable to qualified dividend income. Instead, the gross amount of any such dividend paid by the Company out of its accumulated earnings and profits (as determined for United States federal income tax purposes) is includible in the U.S. Holder's gross income and will be subject to tax at rates applicable to ordinary income.

A U.S. Holder who owns ordinary shares or ADSs during any year that the Company is a PFIC must file Internal Revenue Service Form 8621.

### **Additional United Kingdom Tax Considerations**

#### ***Gift and Inheritance Taxes***

An individual who is domiciled in the United States and who is not a national of the United Kingdom for the purposes of the Estate Tax Treaty will normally not be subject to U.K. inheritance tax in respect of the ordinary shares or ADSs on the individual's death or on a gift of the ordinary shares or ADSs during the individual's lifetime, provided that any applicable U.S. federal gift or estate tax liability is paid, unless the ordinary shares or ADSs are part of the business property of a permanent establishment of an enterprise of the individual in the United Kingdom or pertain to a fixed base in the United Kingdom of the individual used for the performance of independent personal services.

Where the ADSs or ordinary shares have been placed in trust by a settlor who, at time of settlement, was a U.S. Holder, the ADSs or ordinary shares will normally not be subject to U.K. inheritance tax unless the settlor, at the time of settlement, was not domiciled in the United States and was a U.K. national. In the exceptional case where the ADSs or ordinary shares are subject both to U.K. inheritance tax and to U.S. federal gift or estate tax, the Estate Tax Treaty generally provides for the tax paid in the United Kingdom to be credited against tax paid in the United States or for tax paid in the United States to be credited against tax payable in the United Kingdom based on priority rules set out in that Treaty.

#### ***Stamp Duty and Stamp Duty Reserve Tax***

A transfer for value of the ordinary shares will generally be subject to U.K. ad valorem stamp duty, normally at the rate of 0.5% of the amount or value of the consideration given for the transfer, rounded up to the nearest £5. Stamp duty is normally a payable by the Purchaser.

An agreement to transfer ordinary shares for money or money's worth will normally give rise to a charge to stamp duty reserve tax ("SDRT") at the rate of 0.5% of the amount or value of the consideration unless an instrument of transfer of the ordinary shares has been executed in pursuance of the agreement and duly stamped. SDRT is a liability of the purchaser.

Stamp duty is charged at the higher rate of 1.5%, rounded up to the nearest £5, or SDRT at the rate of 1.5%, of the amount or value of the consideration, or in some circumstances the value of the ordinary shares, on a transfer or issue of the ordinary shares (a) to, or to a nominee for, a person whose business is or includes the provision of clearance services or (b) to, or to a nominee for, a person whose business is or includes issuing depositary receipts. An election is available whereby clearance services may, under certain conditions, elect for the 0.5% rate of SDRT to apply to a transfer of shares into, and to transactions within, the service.

In accordance with the terms of the Deposit Agreement, any tax or duty payable by the Depositary or the Custodian of the Depositary on the deposit of ordinary shares will be charged by the Depositary to the holder of the ADS.

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No U.K. stamp duty will be payable on the acquisition or transfer of an ADS evidenced by an ADR or beneficial ownership of an ADR, provided that any instrument of transfer or written agreement to transfer remains at all times outside the United Kingdom. An agreement for the transfer of an ADR or beneficial ownership of an ADR will not give rise to a liability to SDRT.

Any transfer for value of the underlying ordinary shares represented by ADSs evidenced by ADRs, may give rise to a liability to U.K. stamp duty or SDRT at the rate of 0.5% as indicated above. However, on a transfer from the Custodian of the Depository to a holder of an ADS upon cancellation of the ADS a fixed U.K. stamp duty of £5 per instrument of transfer only will be payable.

### DOCUMENTS ON DISPLAY

It is possible to read and copy documents referred to in this annual report on Form 20-F that have been filed with the SEC at the SEC's public reference room located at 450 Fifth Street, NW, Washington D.C. 20549. Please call the SEC at 1(800) SEC 0330 for further information on the public reference rooms and their copy charges. The Company's Securities and Exchange Commission filings made after November 4, 2002 are also available over the Internet at the Securities and Exchange Commission's website at <http://www.sec.gov>.

### Item 11: Quantitative and Qualitative Disclosures About Market Risk

The Company holds financial instruments to finance its operations and to manage the currency, interest rate and liquidity risks that arise from those operations. A discussion of the Company's treasury policies employed to manage these risks is set out below. In the numerical disclosures that follow, short-term debtors and creditors that arise directly as a result of the Company's operations are excluded from all disclosures with the exception of the table below on currency exposures.

#### LIQUIDITY RISK

The Company's policy is to maintain continuity of funding through a mixture of long-term debt and bank loans, raised to cover specific projects, and through the issue of shares to collaborative partners, where necessary, to obtain development contracts. Short-term flexibility is provided through the use of overdrafts. The maturity profile of the Company's debt at December 31, 2002 is set out below.

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#### Maturity of financial liabilities

	December 31, 2001 Total	December 31, 2002 Total	December 31, 2002 Fixed rate financial liabilities	December 31, 2002 Floating rate financial liabilities	December 31, 2002 Non-interest bearing financial liabilities
(in £ thousands)					
Within one year	7,257	2,927	1,175	1,752	
Between one and two years	1,893	5,256	4,455	801	
Between two and three years	4,206	59,633	29,454	30,179	
Between three and four years	59,570	11,573	83	180	11,310
Between four and five years	22,853	381		180	201
Beyond five years	5,786	5,695		2,426	3,269
	<b>£101,565</b>	<b>£85,465</b>	<b>£35,167</b>	<b>£35,518</b>	<b>£14,780</b>

#### Foreign Currency Risk

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All of the Company's operations are based overseas in Continental Europe, the United States and Canada giving rise to exposures to changes in foreign exchange rates, notably the Swiss Franc, Euro, U.S. Dollar and Canadian Dollar. Beginning in June 1996, and where natural hedges have not been sufficient or possible, the Company has selectively entered into forward currency contracts to fix certain of the non-sterling funding requirements of its principal subsidiaries. The contracts generally have maturities not exceeding twelve months. Gains or losses on these contracts are not recorded until the maturity of the contracts at which time they are recorded as an adjustment to administrative expenses, consistent with the underlying non-sterling expenses that are required to be funded. During 2000, £59.4 million of funding was raised in sterling, and as a result, since then, the Group has actively used forward currency contracts and currency options. No gain or loss was recognized on such contracts during 2001 or 2002.

At December 31, 2001, the Company had currency options to sell £2.8 million U.S. dollars. At December 31, 2001 the Company had accrual forward options to purchase £0.2 million Swiss francs each week for 31 weeks ending June 19, 2002 and £0.2 million Euro each week for 26 weeks ending May 22, 2002. At December 31, 2001 the Company had forward currency contracts to purchase £2.7 million Swiss francs. There were no other forward foreign currency contracts open at December 31, 2001. The unrecognized losses from such contracts at December 31, 2001 were £31,000.

At December 31, 2002, the Company had European style accrual forward options to purchase £154,000 of Swiss francs each week for the 26 weeks ending in July 2002 and £71,000 of Euro each week for the 14 weeks ending in April 2002. At December 31, 2002, the Company had agreements in place for American style accrual forward options, commencing in January 2003, to purchase £113,000 US dollars for the 44 weeks ending in November 2003 and £44,000 of Swedish Krona each week for the 45 weeks ending in November 2003. Both of these structures lapsed in January and February 2003 respectively. At December 31, 2002, the Company had forward currency contracts to purchase £4.5 million of Swiss francs, £1.1 million of Euro and £0.5 million of Swedish Krona. The unrecognized gain from such contracts at December 31, 2002 were £48,000.

The analysis below shows the net monetary assets and liabilities of Group companies that are not denominated in their functional currency and therefore give rise to exchange gains and losses in the income statements in both 2002 and 2001.

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### *Currency exposures*

**December 31, 2002**

#### **Functional currency of Operating Company**

##### Net foreign currency monetary assets/(liabilities)

	Sterling	\$US	Euro	Swiss Francs	Other	Total
	(in £ thousands)					
Sterling		2,232	617		1	2,850
\$US	(15,956)		(9)		(34)	(15,999)
Euro	(2,025)	96		2,225		296
Swiss francs	(928)	3,142	(528)		(582)	1,104
\$Canadian	1,904	400	(130)	550		2,724
Swedish Krona	(1,343)					(1,343)
	(18,348)	5,870	(50)	2,775	(615)	(10,368)

**December 31, 2001**

#### **Functional currency of Operating Company**

##### Net foreign currency monetary assets/(liabilities)

	Sterling	\$US	Euro	Swiss Francs	Other	Total
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Net foreign currency monetary assets/(liabilities)

(in £ thousands)					
Sterling		11,527		(49)	11,478
\$US	(5,231)				(5,231)
Euro	(2,260)	102		25	(2,133)
Swiss francs	3,568	4,087	406	10	(8,071)
\$Canadian		477			477
	(3,923)	16,193	406	25	12,662

**Interest Rate Risk**

The Company borrows at fixed and floating rates of interest as deemed appropriate for its circumstances. Where necessary the Company uses interest rate swaps to achieve the desired interest rate profile. During 2001, £30.0 million of the £59.4 million convertible bond liability was the subject of a cancelable interest rate swap agreement by which the Company swapped a fixed obligation to pay 6.0% to floating and paid 5.6% until December 19, 2001. The interest rate swap agreement was cancelled on December 19, 2001. The Company's management have assessed remaining interest rate exposures and deemed them not to be material. From February 27, 2002, £30 million of the £59.4 million convertible bond liability was the subject of a new cancelable interest rate swap agreement by which the Company swapped the fixed obligation to pay 6.0% to floating from and paid 5.6%. On December 19, 2002, this swap was cancelled and replaced by a subsequent swap agreement whereby £30.0 million of the £59.4 million convertible bond liability was the subject of a cancelable interest rate swap agreement by which the Company swapped the fixed obligation to pay 6.0% to floating 5.75%. The interest rate and currency profile of the Company's financial assets and liabilities is set out below.

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*Interest rate and currency profile of financial assets*

**December 31, 2002**

**Currency**

	Floating rate financial assets	Fixed rate financial assets	Non interest bearing financial assets	Total financial assets
(in £ thousands)				
Sterling	18,680	1,961	36	20,677
\$US	4,292		16,663	20,955
Swiss francs	1,870			1,870
\$Canadian	2,026		2,228	4,254
Euro	617			617
Swedish Krona	523			523
	28,008	1,961	18,927	48,896

**December 31, 2001**

**Currency**

Floating rate financial assets	Fixed rate financial assets	Non interest bearing financial	Total financial assets
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	assets			
	(in £ thousands)			
Sterling	5,690		62	5,752
\$US	14,977		11,467	26,444
Swiss francs	549		93	642
\$Canadian	48	5,389	2,228	7,665
Euro	48			48
	21,312	5,389	13,850	40,551

Total financial assets comprise fixed asset investments of £18.9 million (2001: £13.7 million), current asset investments of £2.0 million (2001: £nil) and cash and short-term bank deposits of £28.1 million (2001: £26.9 million).

Included within the sterling denominated financial assets shown above for 2002 is £5.0 million, placed on deposit for 18 months in November 2002, at a capped rate. For the period until February 15, 2003, the Company received 4.85% on each day that the 3-month sterling LIBOR rate was less than 4.25%. On February 17, 2003, the deposit was cancelled by the coupon payer and replaced with a deposit of £5.0 million, placed on deposit for 18 months at a capped rate. The Company receives 4.5% on each day that 3-month sterling LIBOR is less than predetermined levels for each 3-month period ranging from 4.00% to 4.5%.

Also included within the sterling denominated financial assets shown above for 2002 is £2.0 million placed on deposit July 1, 2002 for 24 months. The Company receives 6.0% on each day that 3-month sterling LIBOR is less than predetermined levels for each 3-month period ranging from 4.75% to 5.50%.

All other of the Company's financial assets, in both 2002 and 2001, either bear interest at floating rates based upon the floating bank rate in the country in which the funds are held. Floating rate financial assets bear interest at rates based upon the floating bank rate in the country in which the funds are held. The weighted average interest rate on fixed rate financial assets is 5% (2001: 2%). The weighted average time for which the rate is fixed is 54 months (2001: 4 months). Non-interest bearing financial assets consist of balances held in short-term current accounts.

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*Interest rate and currency profile of financial liabilities*

December 31, 2002

Currency

	Fixed rate financial liabilities	Weighted average interest rate on fixed financial liabilities	Weighted average time for which rate is fixed	Floating rate financial liabilities	Non interest bearing financial liabilities	Weighted average time to maturity	Total financial liabilities
	£'000	%	(months)	£'000	£'000	(months)	£'000
<b>Currency</b>							
Sterling	29,400	6.00	29.5	30,000	11,310	40.0	70,710
Swiss francs	4,560	3.64	13.5	4,897		417.0	9,457
Euro	863	6.25	11.0		201		1,064
\$US	25	5.25	40.0	621	3,269	144.0	3,915
Swedish Krona	319	7.25	27.8				319
	35,167	5.71	27.0	35,518	14,780	68.1	85,465

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Fixed rate financial liabilities	Weighted average interest rate on fixed financial liabilities	Weighted average time for which rate is fixed	Floating rate financial liabilities	Non interest bearing financial liabilities	Weighted average time to maturity	Total financial liabilities
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December 31, 2001

Currency

Fixed rate financial liabilities	Weighted average interest rate on fixed financial liabilities	Weighted average time for which rate is fixed	Floating rate financial liabilities	Non interest bearing financial liabilities	Weighted average time to maturity	Total financial liabilities
£'000	%	(months)	£'000	£'000	(months)	£'000
<b>Currency</b>						
Sterling	59,400	6.00		22,623	52.0	82,023
Swiss francs	4,302	3.63	5,548			9,850
French Francs	1,599	6.25	745	65	419.0	2,409
\$US			3,898	3,385	156.0	7,283
	65,301	5.85	10,191	26,073	66.4	101,565

Financial liabilities comprise total borrowings of £10.0 million (2001: £14.4 million), convertible bonds of £59.4 million (2001: £59.4 million), non-equity Deferred 'A' and 'B' Shares of £11.3 million (2001: £22.6 million), other creditors of £4.6 million (2001: £5.1 million) and provisions of £0.2 million (2001: £0.1 million).

Total financial liabilities does not agree to the total of the balance sheet captions due to the presence of £1,023,000 (2001: £1,438,000) of unamortized issue costs within the value shown on the balance sheet for convertible bonds. Certain financial instruments, such as currency options, are excluded from the analysis above where they do not alter the interest basis or currency of financial liabilities.

All other floating rate financial liabilities, in both 2002 and 2001, are interest bearing financial liabilities that bear interest at interest rates based on LIBOR, prime and other bank based lending rates in the country in which the liability arises, which are fixed for periods of up to 12 months.

**Credit Risk**

The Company is exposed to credit-related losses in the event of non-performance by third parties to financial instruments. The Company does not expect any third parties to fail to meet their

obligations given the policy of selecting only parties with high credit ratings and minimizing its exposure to any one institution.

**Fair Values**

The comparison of fair and book values of all the Company's financial instruments as at December 31, 2002 is set out below. Market values have been used to determine the fair values of all swaps and foreign currency contracts. The fair value of the non-equity Deferred 'B' Shares has been calculated by reference to the ordinary share price at December 31, 2002, based upon the Director's opinion that 12 million ordinary shares will be issued in settlement of the deferred consideration payable on the acquisition of Jago. See "Item 7: Major Shareholders and Related Party Transactions - Certain Arrangements in Respect of the Jago Acquisition" for details of the contingencies governing the issuance of these shares. The fair values of all other items have been calculated by discounting future cash flows at interest rates prevailing at December 31, 2002.

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December 31, 2002

	<u>Book Values</u>	<u>Fair values</u>
	(in £ thousands)	
<b>Financial instruments held or issued to finance the Group's operations</b>		
Fixed asset investments	18,874	17,287
Current asset investments	1,961	1,961
Cash at bank and in hand	7,394	7,394
Short-term bank deposits	20,667	20,667
Short-term borrowings and current portion of long-term borrowings	(2,927)	(2,927)
Long-term convertible debt	(59,400)	(53,863)
Other long-term debt	(11,828)	(11,707)
Non-equity Deferred 'B' Shares	(11,310)	(4,980)
	<u>(36,569)</u>	<u>(26,168)</u>
<b>Derivative financial instruments held to manage the Group's currency profile</b>		
Interest rate swaps		452
Euro currency options		(85)
US\$ currency options		(13)
Forward currency contracts		146
		<u>500</u>

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December 31, 2001

	<u>Book Values</u>	<u>Fair values</u>
	(in £ thousands)	
<b>Financial instruments held or issued to finance the Group's operations</b>		
Fixed asset investments	13,659	13,903
Cash at bank and in hand	4,534	4,534
Short-term bank deposits	22,358	22,358
Short-term borrowings and current portion of long-term borrowings	(7,257)	(7,257)
Long-term convertible debt	(59,400)	(50,194)
Other long-term debt	(12,288)	(12,055)
Non-equity Deferred 'A' and 'B' Shares	(22,620)	(14,700)
	<u>(61,014)</u>	<u>(43,411)</u>
<b>Derivative financial instruments held to manage the Group's currency profile</b>		
Euro currency options		38
US\$ currency options	(20)	(23)
Forward currency contracts		(46)
	<u>(20)</u>	<u>(31)</u>

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The excess of fair values over book values for currency options and forward currency contracts shown in the table above represents the unrecognized hedging gain on these instruments as at December 31, 2002. The actual gains or losses arising on these options will be dependent on future exchange rates and will be recognized in the profit and loss account, in 2002, as the operational transactions to which they are linked occur. The table below shows the extent to which the Company has off-balance sheet (unrecognized) and on-balance sheet (deferred) gains and losses in respect of hedges at the beginning and end of the year ended December 31, 2002.

At December 31, 2002, the Company had European style accrual forward options to purchase £154,000 of Swiss francs each week for the 26 weeks ending in July 2002 and £71,000 of Euro each week for the 14 weeks ending in April 2002.

At December 31, 2002, the Company had agreements in place for American style accrual forward options, commencing in January 2003, to purchase £113,000 of US dollars for the 44 weeks ending in November 2003 and £44,000 of Swedish Krona each week for the 45 weeks ending in November 2003. Both of these structures lapsed in January and February 2003 respectively.

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At December 31, 2002, the Company had forward currency contracts to purchase £4.5 million of Swiss francs, £1.1 million of Euro and £0.5 million of Swedish Krona. The unrecognized losses from such contracts at December 31, 2002 were £48,000.

	Unrecognized			Deferred		
	Gains	Losses	Net Total	Gains	Losses	Net Total
	(in £ thousands)					
Gains/(losses) on hedges at January 1, 2002		(31)	(31)		(20)	(20)
Changes in value from January 1, 2002 to settlement		262	262			
<b>Gains/(losses) arising in 2001 recognized in 2002</b>		231	231		(20)	(20)
Gains/(losses) on not recognized in 2002 arising before January 1, 2002 at January 1, 2002 arising in 2002	598	(98)	500			
<b>Gains/(losses) on hedges at December 31, 2002</b>	598	(98)	500			

Unrecognized gains at December 31, 2002 include £0.5 million in relation to the cancelable interest rate swap agreement. This was based upon the agreement continuing for the life of the convertible bonds and as such the gain would have been spread in the profit and loss account until 2005.

### Item 12: Description of Securities other than Equity Securities

Not applicable

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**Item 13: Defaults, Dividend Arrearages and Delinquencies**

None

**Item 14: Material Modifications to the Rights of Security Holders and Use of Proceeds**

None

**Item 15: Controls and Procedures**

As of a date within 90 days of the filing date of this annual report (the "Evaluation Date"), an evaluation was performed under the supervision and with the participation of the Company's management, including the Chief Executive Officer and the Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures (as defined in Exchange Act Rules 13a-14(c) and 15d-14(c)). Based on that evaluation, the Company's management, including the Chief Executive Officer and the Chief Financial Officer, concluded that the Company's disclosure controls and procedures were effective at the level of providing reasonable assurance as of the Evaluation Date. There have been no significant changes in the Company's internal controls or in other factors that could significantly affect internal controls subsequent to the Evaluation Date, including any corrective actions with regard to significant deficiencies and material weaknesses. In designing and evaluating the Company's disclosure controls and procedures, the Company's management, including the Chief Executive Officer and the Chief Financial Officer, recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and the Company's management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the company have been detected.

**Item 16A: Audit Committee Financial Expert**

Not applicable until the Annual Report on Form 20-F for the fiscal year ended December 31, 2003.

**Item 16B: Code of Ethics**

Not applicable until the Annual Report on Form 20-F for the fiscal year ended December 31, 2003.

**Item 16C: Principal Accountant Fees and Services**

Not applicable until the Annual Report on Form 20-F for the fiscal year ended December 31, 2003.

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**PART III**

**Item 17: Financial Statements**

The Company is furnishing financial statements pursuant to the instructions of Item 18 of Form 20-F. See "Item 18: Financial Statements".

**Item 18: Financial Statements**

The following financial statements, together with the report thereon, by PricewaterhouseCoopers LLP, are filed as part of this Form 20-F:

## Edgar Filing: SKYEPHARMA PLC - Form 20-F

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### Item 19: Exhibits

- 1.1 Memorandum and Articles of Association of SkyePharma PLC
  - 1.1.1 Memorandum of Association of SkyePharma PLC\*\*
  - 1.1.2 Articles of Association of SkyePharma PLC, as amended on May 30, 2002\*\*\*
- 4.1 Solaraze Agreements with Bioglan
  - 4.1.1 Licensing and manufacturing agreement for Europe dated March 13, 2000 between JagoTech AG and Bioglan Pharma PLC\*\*+
  - 4.1.2 Addendum agreement for the U.S. dated December 28, 2000 between JagoTech AG and Bioglan Pharma PLC\*\*+
- 4.2 Directors and Officers Service Contracts
  - 4.2.1 Contract of employment between the Company and Donald Nicholson dated February 28, 1996\*\*
  - 4.2.2 Proforma letter of appointment in respect of the appointment of Non-executive Directors\*\*
- 4.3 Share Purchase Plans
  - 4.3.1 The SkyePharma PLC Deferred Share Bonus Plan\*\*\*
- 4.4 Amendments to the 1996 Acquisition Agreement, dated April 7, 2000 and May 11, 2000, between Dr Jacques Gonella and SkyePharma PLC\*
- 4.5 Development and Marketing Strategic Alliance Agreement among Endo Pharmaceuticals Inc., SkyePharma Inc. and SkyePharma Canada Inc. dated as of December 31, 2002 ++
- 8.1

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List of SkyePharma PLC's subsidiaries (See "Item 4: Information on the Company Business Operations Organizational Structure")

10.1

Consent of independent auditors

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\*

Incorporated by reference to the Company's Annual Report on Form 20-F for the financial year ended December 31, 1999 (Commission File No. 0-29860)

\*\*

Incorporated by reference to the Company's Annual Report on Form 20-F for the financial year ended December 31, 2000 (Commission File No. 0-29860)

\*\*\*

Incorporated by reference to the Company's Annual Report on Form 20-F for the financial year ended December 31, 2001 (Commission File No. 0-29860)

+

Confidential treatment has been granted for portions of this document. The information omitted pursuant to such confidential treatment order has been filed separately with the SEC in accordance with Rule 24b-2 under the Securities Exchange Act of 1934, as amended ("Rule 24b-2").

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Confidential portions of this exhibit have been omitted and filed separately with the SEC pursuant to a confidential treatment request in accordance with Rule 24b-2.

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### SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this Annual Report on its behalf.

Date: June 27, 2003

SKYEPHARMA PLC  
(Registrant)

By: /s/ Donald Nicholson

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Name: Donald Nicholson  
Title: Finance Director

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### CERTIFICATIONS OF CHIEF EXECUTIVE OFFICER

I, Michael Ashton, certify that:

1.

I have reviewed this annual report on Form 20-F of SkyePharma PLC;

2.

Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

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3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:
- a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):
- a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and
- 6) The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date            June 27, 2003  
                  \_\_\_\_\_

Signature       /s/ Michael Ashton  
                  \_\_\_\_\_

Title            Chief Executive Officer  
                  \_\_\_\_\_

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**CERTIFICATIONS OF FINANCE DIRECTOR**

I, Donald Nicholson, certify that:

- 1.

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I have reviewed this annual report on Form 20-F of SkyePharma PLC;

2.

Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3.

Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4.

The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:

a)

designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

b)

evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

c)

presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5.

The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

a)

all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and

b)

any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and

6)

The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date June 27, 2003

Signature /s/ Donald Nicholson

Title Finance Director

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**REPORT OF INDEPENDENT AUDITORS**

## To the Board of Directors and Shareholders of SkyePharma PLC

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of income, of cash flows, of total recognized gains and losses and of movements in shareholders' funds present fairly, in all material respects, the financial position of SkyePharma PLC and its subsidiaries at December 31, 2002 and 2001 and the results of their operations and their cash flows for the three years in the period ended December 31, 2002, in conformity with accounting principles generally accepted in the United Kingdom. These financial statements are the responsibility of the Company's management; our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States, which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for the opinion expressed above.

Accounting principles generally accepted in the United Kingdom vary in certain important respects from accounting principles generally accepted in the United States. The application of the latter would have affected the determination of consolidated net income/(loss) expressed in pounds sterling for the three years in the period ended December 31, 2002, and the determination of consolidated shareholders funds and financial position also expressed in pounds sterling at December 31, 2002 and 2001 to the extent summarized in Note 30 to the Consolidated Financial Statements.

## PricewaterhouseCoopers LLP

London  
United Kingdom

April 2, 2003

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## Consolidated Income Statements

	Notes	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>Turnover</b>	2	24,292	46,126	69,573
Cost of sales	2	(15,598)	(18,820)	(24,830)
<b>Gross profit</b>		8,694	27,306	44,743
Selling, marketing and distribution expenses		(3,844)	(4,804)	(4,769)
Administration expenses				
Amortization		(3,339)	(3,824)	(6,506)
Other administration expenses		(9,291)	(12,201)	(13,686)
		(12,630)	(16,025)	(20,192)
Research and development expenses		(13,104)	(17,918)	(29,285)
Other operating income	3	2,900	6,342	14,219
<b>Operating (loss)/profit</b>	2, 4	(17,984)	(5,099)	4,716
Associated undertaking			(578)	
<b>Total operating (loss)/profit: Group and share of associates</b>		(17,984)	(5,677)	4,716
Interest receivable	6	1,806	1,251	1,081
Interest payable	7	(3,508)	(4,951)	(4,464)
<b>(Loss)/profit on ordinary activities before taxation</b>		(19,686)	(9,377)	1,333
Taxation	8	(4)	(75)	(224)

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	Notes	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>Retained (loss)/profit</b>		(19,690)	(9,452)	1,109
<b>Earnings per Ordinary Share</b>	9			
Basic		(3.9)p	(1.8)p	0.2p
Diluted		(3.9)p	(1.8)p	0.2p

There was no material difference between the (loss)/profit on ordinary activities before taxation and historic cost (loss)/profit before taxation for these periods. All results represent continuing activities.

See Notes to the Financial Statements.

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Consolidated Balance Sheets

	Notes	December 31, 2001 £'000	December 31, 2002 £'000
<b>Fixed assets</b>			
Intangible assets	10	98,228	100,015
Tangible assets	11	44,952	45,504
Investments	12	14,211	19,902
		<u>157,391</u>	<u>165,421</u>
<b>Current assets</b>			
Stock	13	2,278	1,256
Debtors	14	14,022	35,207
Investments	15		1,961
Cash and short-term bank deposits		26,892	28,061
		<u>43,192</u>	<u>66,485</u>
<b>Creditors: amounts falling due within one year</b>			
Deferred income		(11,690)	(15,069)
Other creditors		(23,498)	(19,402)
	16	<u>(35,188)</u>	<u>(34,471)</u>
<b>Net current assets</b>		<u>8,004</u>	<u>32,014</u>
<b>Total assets less current liabilities</b>		<u>165,395</u>	<u>197,435</u>
<b>Creditors: amounts falling due after more than one year</b>			
Convertible bonds due June 2005		(57,962)	(58,377)
Deferred income			(2,960)
Other creditors		(12,220)	(11,627)
	17	<u>(70,182)</u>	<u>(72,964)</u>

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	Notes	December 31, 2001 £'000	December 31, 2002 £'000
<b>Provisions for liabilities and charges</b>	18	(68)	(201)
Net assets		95,145	124,270
<b>Capital and reserves</b>			
Share capital	22	58,402	62,546
Share premium	24	287,357	316,419
Shares and warrants to be issued	23	10,617	
Other reserves	24	10,720	9,311
Profit and loss account	24	(271,951)	(264,006)
<b>Shareholders' funds</b>			
Attributable to equity interests		72,525	112,960
Attributable to non-equity interests		22,620	11,310
		95,145	124,270

For details of contingent liabilities and commitments, see Notes 20 and 21 to the Financial Statements.  
See Notes to the Financial Statements.

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Consolidated Cash Flow Statements

	Notes	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>Net cash (outflow)/inflow from operating activities</b>	(b)	(9,312)	5,909	1,552
<b>Returns on investments and servicing of finance</b>				
Interest received		1,297	2,741	943
Interest paid		(2,941)	(4,370)	(3,913)
Interest element of finance lease payments		(232)	(170)	(130)
		(1,876)	(1,799)	(3,100)
<b>Taxation</b>		(8)	(75)	(224)
<b>Capital expenditure and financial investment</b>				
Purchase of intangible fixed assets		(7,180)	(310)	(3,035)
Purchase of tangible fixed assets		(8,470)	(7,673)	(3,238)
Purchase of fixed asset investments			(8,273)	(6,285)
		(15,650)	(16,256)	(12,558)
<b>Acquisitions</b>				
Purchase of drug delivery business of Bioglan AB	(d)			(3,595)
Purchase of RTP Phama Inc.			(4,118)	
Net cash acquired with RTP Pharma Inc.			5,436	



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Notes	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
		1,318	(3,595)
<b>Cash outflow before use of liquid resources and financing</b>	(26,846)	(10,903)	(17,925)
<b>Management of liquid resources</b>			
Net (increase)/decrease in amounts held on short-term bank deposit	(21,641)	14,668	(3,872)
<b>Financing</b>			
Issue of Ordinary Share capital	2,088	468	26,168
Issue of convertible bonds	59,400		
Expenses of convertible bond issue	(2,022)		
Issue of warrants			311
Debt due within one year:			
Increase in borrowings	1,187		
Repayment of loans	(2,846)	(4,502)	(2,992)
Debt due beyond one year:			
Repayment of loans	(1,226)	(85)	(929)
Capital element of finance lease payments	(891)	(772)	(937)
	55,690	(4,891)	21,621
<b>Increase/(decrease) in cash</b>	7,203	(1,126)	(176)

See Notes to the Financial Statements.

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**Notes to the Consolidated Cash Flow Statement**

**(a) Reconciliation of movements in net debt**

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Increase/(decrease) in cash in the year	7,203	(1,126)	(176)
Cash outflow from decrease in debt and lease financing	3,776	5,454	4,858
Cash outflow/(inflow) from increase/(decrease) in liquid resources	21,641	(14,668)	3,872
Issue of convertible debt	(57,378)		
Change in net debt resulting from cash flows	(24,758)	(10,340)	8,554
Issue of loan note	(2,307)		
Finance leases acquired with subsidiary			(361)
New finance leases		(95)	(91)
Conversion of debentures	103		
Amortization of issue costs on convertible bond	(167)	(416)	(415)
Chiron promissory note			(621)
Translation difference	(907)	(21)	(1,505)

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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Movement in net debt in the year	(28,036)	(10,872)	5,561
Net debt at beginning of the year	(8,254)	(36,290)	(47,162)
Net debt at end of the year	(36,290)	(47,162)	(41,601)

Net debt is defined as cash and liquid resources less borrowings.

**(b) Reconciliation of operating (loss)/profit to net cash (outflow)/inflow from operating activities**

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Operating (loss)/profit	(17,984)	(5,099)	4,716
Depreciation	3,945	4,778	6,101
Amortization	3,339	3,824	6,506
(Increase)/decrease in stock and work in progress	(426)	(642)	1,022
Decrease/(increase) in debtors	3,247	(7,478)	(21,585)
Increase in deferred income		11,690	6,339
(Decrease)/increase in other creditors	(1,283)	1,688	(313)
(Decrease)/increase in provisions	(150)	(2,051)	133
Other		(801)	(1,367)
Net cash (outflow)/inflow from operating activities	(9,312)	5,909	1,552

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**(c) Analysis of net debt**

	At January 1, 2000 £'000	Cash flow £'000	Acquisitions (excl cash & overdrafts) £'000	Non-cash changes £'000	Exchange movement £'000	At December 31, 2000 £'000
Cash at bank and in hand	3,465	7,014			290	10,769
Overdrafts	(2,809)	189			(228)	(2,848)
Short-term bank deposits	10,209	21,641			259	32,109
	10,865	28,844			321	40,030
Debt due within one year	(4,424)	1,659		(3,055)	(411)	(6,231)
Debt due after one year	(11,305)	1,226		852	(768)	(9,995)
Convertible bonds		(57,378)		(168)		(57,546)
Finance leases	(3,390)	891			(49)	(2,548)
	(19,119)	(53,602)		(2,371)	(1,228)	(76,320)
	(8,254)	(24,758)		(2,371)	(907)	(36,290)

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	At January 1, 2001 £'000	Cash flow £'000	Acquisitions (excl cash & overdrafts) £'000	Non-cash changes £'000	Exchange movement £'000	At December 31, 2001 £'000
Cash at bank and in hand	10,769	(1,502)			184	9,451
Overdrafts	(2,848)	376		828	26	(1,618)
Short-term bank deposits	32,109	(14,668)				17,441
	40,030	(15,794)		828	210	25,274
Debt due within one year	(6,231)	4,502		(2,936)	(127)	(4,792)
Debt due after one year	(9,995)	85		2,108	(159)	(7,961)
Convertible bonds	(57,546)			(416)		(57,962)
Finance leases	(2,548)	772			55	(1,721)
	(76,320)	5,359		(1,244)	(231)	(72,436)
	(36,290)	(10,435)		(416)	(21)	(47,162)

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	At January 1, 2002 £'000	Cash flow £'000	Acquisitions (excl cash & overdrafts) £'000	Non-cash changes £'000	Exchange movement £'000	At December 31, 2002 £'000
Cash at bank and in hand	9,451	(1,828)			(229)	7,394
Bank overdraft	(1,618)	1,652			(34)	
Short-term bank deposits	17,441	3,872			(646)	20,667
	25,274	3,696			(909)	28,061
Debt due within one year	(4,792)	2,992			(42)	(1,842)
Debt due after one year	(7,961)	929		(621)	(470)	(8,123)
Convertible bonds	(57,962)			(415)		(58,377)
Finance leases	(1,721)	937	(361)	(91)	(84)	(1,320)
	(72,436)	4,858	(361)	(1,127)	(596)	(69,662)
	(47,162)	8,554	(361)	(1,127)	(1,505)	(41,601)

Cash at bank and in hand and short-term bank deposits are aggregated on the balance sheet. Debt includes a bank loan, secured mortgage, the Chiron promissory note and convertible bonds. Non-cash changes in 2002 relate to the amortization of the issue costs on the convertible bonds, the issue of the Chiron promissory note and the inception of new finance leases.

(d) Purchase of subsidiary undertakings and businesses

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Net assets/(liabilities) acquired		5,935	(375)
Goodwill		29,901	3,970
Net consideration		35,836	3,595

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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Satisfied by:			
Shares issued/allocated		29,536	
Shares to be issued/allocated		5,780	
Cash		3,528	3,500
Expenses relating to the transaction		590	95
Demand notes		(3,598)	
		35,836	3,595
Cash consideration		(3,528)	(3,500)
Expenses relating to transaction		(590)	(95)
Net cash acquired with subsidiary		5,436	
Net cash inflow/(outflow) on purchase of subsidiaries and businesses		1,318	(3,595)

See Note 27; Acquisitions

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Statement of Total Recognized Gains and Losses

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>(Loss)/profit attributable to shareholders</b>	(19,690)	(9,452)	1,109
Net currency translation effect	758	28	903
Lapse of warrants		271	1,096
<b>Total recognized gains and losses for the year</b>	(18,932)	(9,153)	3,108

As described in Note 22a; Share Capital, the 'B' Warrants relating to the acquisition of Krypton lapsed on December 31, 2002. The fair value of the warrants of £1,096,000 has been transferred from non-distributable reserves to retained profits. In 2001 the class 'C' Warrants relating to the debenture issue lapsed. The fair value of the warrants at issue of £271,000 has been transferred from non-distributable reserves to retained profits. The lapse of warrants represents a transfer of value from the warrant holders to existing shareholders. In accordance with FRS4; Capital Instruments, this is shown as a recognized gain, although total shareholders' funds remain unchanged.

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Reconciliation of Movement in Shareholders' Funds

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Shareholders' funds at the beginning of the year	72,057	68,952	95,145

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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Total recognized gains and losses for the year	(18,932)	(9,153)	3,108
Goodwill adjustments on deferred consideration	3,618	148	4,837
Equity shares issued/allocated, net of expenses	20,572	29,599	43,816
Exercise of share options, net of expenses	2,009	459	700
Non-equity shares issued, net of expenses	22,620		
Non equity shares converted to equity shares			(11,310)
(Decrease)/increase in shares and warrants to be issued	(29,528)	5,780	(5,780)
Revaluation of shares and warrants to be issued	(3,618)	(148)	(4,837)
Issue of warrants	154		311
Exercise of warrants		(56)	(624)
Lapse of warrants		(436)	(1,096)
<b>Net movement in the year</b>	<b>(3,105)</b>	<b>26,193</b>	<b>29,125</b>
Shareholders' funds at the end of the year	68,952	95,145	124,270

F-9

1 Accounting Policies

**Accounting convention and presentation**

The financial statements have been prepared under the historical cost convention and in accordance with applicable UK accounting standards. The principal accounting policies, which have been applied consistently, except for the implementation of FRS 19; Deferred Tax, are set out below. The results for the year all relate to continuing operations. The financial statements have been prepared on a going concern basis.

**New accounting policies and requirements**

The Group has implemented FRS 19; Deferred Tax. The FRS requires deferred tax to be accounted for on a full provision basis, rather than the partial provision basis adopted in 2001 and earlier years. The adoption of FRS 19 has had no material impact on the financial statements. Once the Group has achieved sustained profitability, the Directors will consider the appropriateness of recognising a deferred tax asset in respect of losses carried forward.

**Consolidation**

The consolidated financial information includes the financial statements for the Company, its subsidiary undertakings and the Group's share of the net assets and results of associated undertakings. Intra- group sales and profits are eliminated fully on consolidation. The results of subsidiaries sold or acquired are included in the consolidated profit and loss account up to the date of their sale or from their date of acquisition respectively. The share of results of associated undertakings sold or acquired are included in the profit and loss account up to the date of their sale or from the date of their acquisition respectively.

Where the Group has contractual agreements with other participants to engage in joint activities that do not create an entity carrying on a trade or business of its own, they are accounted for as a joint arrangement. The Group includes its share of the assets, liabilities and cash flows in such joint arrangements measured in accordance with the terms of each arrangement, which is usually pro-rata to the Group's interest in the joint arrangement.

**Revenue recognition**

Turnover comprises contract development and licensing, royalty and manufacturing and distribution income. Contract development and licensing income represents amounts invoiced to customers for services rendered under development and licensing agreements including milestone payments and technology access fees. Contract revenue is recognised when earned and non-refundable and to the extent that there are no future obligations pursuant to the revenue, in accordance with the contract terms. Refundable contract revenue is treated as deferred until

such time as it is no longer refundable. Royalty income represents income earned as a percentage of product sales. Advance royalties received are treated as deferred income until earned, when they are recognised as income. Manufacturing and distribution revenues principally comprise contract manufacturing fees invoiced to third parties and income from product sales.

### **Research and development costs**

Research costs are charged as an expense in the period in which they are incurred. Development costs are also recognised as an expense in the period in which they are incurred, unless all of the criteria are met for asset recognition. The major asset recognition criteria include: the ability to define clearly the product or process, demonstration of its technical feasibility and that a commercial market for it exists. Development costs recognised as an asset do not exceed the probable net amount to be recovered in marketing the product or process and they are amortized over the estimated economic life.

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### **Foreign currency transactions**

Foreign currency transactions by Group companies are recorded in local currency at the exchange rate ruling on the date of transaction. Assets and liabilities expressed in foreign currencies are translated into sterling at the exchange rates ruling at the balance sheet date. Exchange differences which relate to the retranslation of net assets of overseas companies are taken directly to reserves. All other foreign exchange differences are taken to the profit and loss account in the year in which they arise. The Group uses the average exchange rates prevailing during the year to translate the results of overseas subsidiaries into sterling and year-end rates to translate the net assets of those undertakings.

### **Pension costs**

The costs of the Group's defined contribution pension arrangements are charged to the profit and loss account in the year to which they relate. The costs of the Group's defined benefits scheme are charged on a systematic basis allowing for the expected pension cost over the service lives of employees, based on actuarial advice.

### **Employee Share Plans**

Incentives in the form of shares are provided to employees under share option and share award schemes. In respect of award schemes the Group provides finance to an employee share ownership trust to purchase company shares on the open market to meet the Group's obligation to provide shares when employees exercise their award. The difference between the purchase price of the shares and the exercise price of the award is charged, or credited, to the profit and loss account over the periods of service in respect of which the award was granted.

The costs of running the employee share ownership trust are charged to the profit and loss account as they accrue.

Shares held by the employee share ownership trust are accounted for as fixed asset investments at cost less accrual for costs charged.

### **Intangible fixed assets**

Intangible fixed assets comprise goodwill, intellectual property and capitalised development costs. Goodwill, being the difference between the fair value of the purchase consideration and the Group's share of the fair value of the net assets acquired, is capitalised and amortized over a period of 20 years or less in line with the Directors' view of its useful economic life. Prior to the introduction of FRS 10, the policy adopted was to write off goodwill to reserves. As permitted by FRS 10 goodwill written off to reserves in previous years has not been reinstated on the balance sheet and adjustments to such goodwill have been taken directly to reserves. Goodwill previously written off to reserves is charged to the profit and loss account in the event of disposal of the related business.

Intellectual property comprises acquired patents, trademarks, know-how and other similarly identified rights. These are recorded at their fair value at acquisition date and are amortized in equal instalments over their estimated useful economic lives, from the date when the transfer of technology is complete. The period over which the Group expects to derive economic benefits does not exceed 20 years. Costs associated with internally developed intellectual property are generally treated as research and development costs. Development costs are recognised under the criteria stated above.

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**Tangible fixed assets**

Tangible fixed assets are included in the balance sheet at cost less accumulated depreciation. Depreciation is provided on tangible fixed assets at rates calculated to write off the cost, less estimated residual value, of each asset over its expected useful life. The rates and bases are as follows:

Freehold land	not depreciated
Freehold buildings	2% 5% straight line
Short leasehold property	period of lease
Plant, equipment and fixtures	10% 33% straight line
Motor vehicles	20% straight line
Finance leases	period of lease

**Fixed asset investments**

Investments that are held for continuing use in the business are classified as fixed asset investments and recorded in the balance sheet at cost or Directors' valuation, less provision for permanent diminution in value.

**Impairment of fixed assets**

The carrying values of fixed assets are reviewed for impairment when there is an indication that the assets may be impaired. First year impairment reviews are conducted for acquired goodwill and intangible assets. Impairment is determined by reference to the higher of net realisable value and value in use, which is measured by reference to discounted future cash flows. Any provision for impairment is charged to the profit and loss account in the year concerned.

**Stock and work-in-progress**

Stock and work-in-progress are valued at the lower of cost and net realisable value and calculated using the first-in, first-out basis.

**Current asset investments**

Investments held other than for continuing use in the business are classified as current asset investments and recorded in the balance sheet at the lower of cost and net realisable value.

**Liquid resources**

Liquid resources comprise short-term bank and commercial deposits with a maturity of less than one year.

**Leased and hired assets**

Leasing agreements which transfer to the Group substantially all of the risks and rewards of ownership of an asset are treated as finance leases, as if the asset had been purchased outright. The assets are included in tangible fixed assets and the capital element of amounts owed to the finance company at the balance sheet date is included in creditors as amounts falling due either within or after more than one year. Repayments are treated as consisting of both capital and interest with the interest element being charged to the profit and loss account in proportion to the outstanding obligations. Payments under operating leases and short-term hire contracts are charged to the profit and loss account as they fall due.

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**Convertible debt**

On issue, convertible debt is stated at the amount of net proceeds after deducting issue costs. On conversion the amount recognised in shareholders' funds in respect of the shares issued is equal to the carrying value at the date of conversion. Interest payable on convertible debt is calculated to unwind the issue costs and any discount on issue at a constant rate over the term of the debt.

**Deferred consideration**

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Provisions for deferred consideration comprise the fair value of contingent consideration arising from acquisitions. The eventual outcome is subject to the Group's future performance and certain contractual terms. Provisions are reviewed annually by the Directors, and changes to the estimated fair value of the contingent consideration are recorded as an adjustment to goodwill or the underlying asset value. Where the effect of the time value of money is material, provisions are reflected at their present value, and the interest element arising on discounting the liability is recorded as interest payable in the profit and loss account as it unwinds.

### Deferred taxation

Deferred taxation is provided on timing differences which at the balance sheet date result in an obligation to pay more tax or a right to pay less tax at a future date, at rates expected to apply when they crystallise based on current tax rates and law. Deferred tax assets are recognised to the extent that it is regarded as more likely than not that they will be recovered. Deferred tax assets and liabilities are not discounted.

### Financial instruments

The Group uses derivative financial instruments to hedge its exposure to fluctuations in interest and foreign exchange rates. Specifically, the Group uses interest rate swaps, forward currency contracts and currency options. Receipts and payments on interest rate swaps are recognised on an accruals basis, over the life of the swap, as an adjustment to interest payable. Gains and losses on forward currency contracts and currency options are not recognised until the period that the foreign currency exposure is recognised. Option premia are deferred in the balance sheet and recognised upon the maturity of the option agreement.

## 2 Segmental Analysis

SkyePharma's strategy is to be a provider of integrated drug delivery services to the pharmaceutical industry, providing a full complement of drug delivery products and services ranging from formulation and development through to commercial manufacturing. As such SkyePharma's operations represent a single business segment, pharmaceuticals, served by a range of drug delivery technologies and services.

The tables below present an analysis of turnover, loss/profit before interest, total assets, total long-lived assets and net assets by geographical area together with an analysis of cost of sales, capital expenditure and depreciation. A breakdown of turnover and cost of sales is also presented based upon the various drug delivery products and services provided.

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As there is only one business segment the totals shown in the following tables represent the total for the segment and the consolidated financial statements.

#### (a) Turnover

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>By class of business:</b>			
<b>Pharmaceuticals</b>			
<b>Contract development and licensing</b>			
Milestone payments	11,997	28,379	47,736
Research and development costs recharged	4,808	9,857	7,705
	16,805	38,236	55,441
Royalties receivable	4,011	1,468	6,751
Manufacturing and distribution	3,476	6,422	7,381
	<b>24,292</b>	<b>46,126</b>	<b>69,573</b>
<b>By location of customer:</b>			
North America	4,284	5,482	34,047
U.K.	13,178	21,411	21,000



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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Europe	6,095	16,511	10,333
Rest of the world	735	2,722	4,193
	<u>24,292</u>	<u>46,126</u>	<u>69,573</u>
By location of operation:			
Europe	22,646	30,268	34,449
North America	1,646	15,858	35,124
	<u>24,292</u>	<u>46,126</u>	<u>69,573</u>

(b) Cost of sales

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
By class of business:			
Pharmaceuticals			
Contract development and licensing	(6,986)	(7,917)	(12,649)
Royalties payable	(1,539)	(572)	(1,374)
Manufacturing and distribution	(7,073)	(10,331)	(10,807)
	<u>(15,598)</u>	<u>(18,820)</u>	<u>(24,830)</u>

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(c) (Loss)/Profit on ordinary activities before taxation

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
By class of business:			
Pharmaceuticals	(19,686)	(9,377)	1,333
By location of operation:			
U.K.	(5,291)	(6,840)	(7,695)
Europe	973	6,985	7,652
North America	(13,666)	(5,244)	4,759
Operating (loss)/profit	(17,984)	(5,099)	4,716
Associated undertaking		(578)	
Net interest payable	(1,702)	(3,700)	(3,383)
(Loss)/profit on ordinary activities before taxation	<u>(19,686)</u>	<u>(9,377)</u>	<u>1,333</u>

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Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<hr/>	<hr/>	<hr/>
<hr/>	<hr/>	<hr/>

(d) Total assets and net assets

	Total assets		Net assets	
	December 31, 2001 £'000	December 31, 2002 £'000	December 31, 2001 £'000	December 31, 2002 £'000
By class of business:				
Pharmaceuticals	200,583	231,906	95,145	124,270
By location of operation:				
U.K.	65,639	74,068	136,410	151,673
Europe	62,032	73,149	(74,268)	(69,489)
North America	72,912	84,689	33,003	42,086
Total and consolidated	200,583	231,906	95,145	124,270

(e) Capital expenditure

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
By class of business:			
Pharmaceuticals	8,736	7,646	4,352

(f) Depreciation & amortization

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
By class of business:			
Pharmaceuticals	7,281	9,105	12,607

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(g) Long lived assets

	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
By location of operation:		
U.K.	38,645	36,875

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	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Europe	49,820	58,012
North America	68,926	70,534
	157,391	165,421

**3 Other operating income**

Paul Capital Royalty Acquisition Fund have provided a total of \$30 million between 2000 and 2002 in return for the sale of a portion of future royalty and revenue streams from DepoMorphine, Xatral OD, Solaraze and DepoCyt. The monies will be used to fund the clinical development and regulatory submission of DepoMorphine. Income of £9.7 million (2001: £6.3 million) was recognized as other operating income under this agreement on a cost to complete basis. No royalty payments have been made to Paul Capital under this agreement during the year.

In March 2002 the Group announced another transaction under which Paul Capital will pay SkyePharma a further \$30 million during 2002 and 2003 in return for a portion of the potential future royalty and revenue streams from nine products from the Group's drug pipeline. The monies will be used principally to fund the clinical development of Propofol IDD-D and HFA-formoterol. Income of £4.5 million (2001: £nil) was recognized as other operating income under this agreement on a cost to complete basis. Royalty payments of £0.7 million (\$1 million) have been made to Paul Capital under this agreement during the year, and are included within royalties payable.

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**4 Operating Loss/Profit**

Operating loss/profit is stated after charging:

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Auditors remuneration			
audit of SkyePharma PLC	64	93	194
audit of subsidiary undertakings-overseas	117	101	160
Fees to auditors for other work			
auditors' U.K. firm	222	499	1,045
auditors' overseas firms	312	240	214
Depreciation of tangible fixed assets			
owned assets	3,501	4,343	5,616
assets held under finance leases	441	435	485
Amortization of intangible fixed assets			
amortization of goodwill	2,099	2,844	3,799
amortization of intellectual property	1,082	1,282	2,483
Research and development expenses			
current year expenditure	13,104	17,918	29,285
amortization of deferred expenditure	158	201	224
Operating lease rentals			
hire of plant and machinery	373	266	434
other	2,593	3,659	3,336

It is the Group's policy to employ the auditors on assignments additional to their statutory audit duties where their expertise and experience with the Group are important, principally tax advice and due diligence reporting on acquisitions, or where they are awarded assignments on a competitive basis. During the year the auditors earned the following non-audit fees from the Group:

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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Due diligence and other audit-related work	159	215	311
Tax advice	231	297	681
Accounting advice and regulatory returns	144	227	267
<b>Total non-audit fees</b>	<b>534</b>	<b>739</b>	<b>1,259</b>

**5 Employees**

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Employment costs:			
Wages and salaries	13,506	15,502	20,614
Social security costs	2,011	2,451	3,091
Pension costs	532	822	1,525
	<b>16,049</b>	<b>18,775</b>	<b>25,230</b>

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The average number of persons employed by the Group during the year was as follows:

	Year to December 31, 2000 Number	Year to December 31, 2001 Number	Year to December 31, 2002 Number
Pharmaceuticals	373	411	492

**Directors' Remuneration**

The tables below set out details of the Directors' emoluments for the years ended December 31, 2000, 2001 and 2002.

Year ended December 31, 2000	Fees and Salary £'000	Benefits £'000	Bonuses £'000	Total £'000
<b>Executive Directors</b>				
I R Gowrie-Smith	376	20	60	456
M Ashton	323	59	52	434
D Nicholson	161	10	26	197
	<b>860</b>	<b>89</b>	<b>138</b>	<b>1,087</b>
<b>Non-Executive Directors</b>				
Sir M G Beavis	25			25
R S Harris	25			25
Dr A N Karabelas (from November 30, 2000)	2			2
Dr K R Mansford	25			25

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Year ended December 31, 2000	Fees and Salary £'000	Benefits £'000	Bonuses £'000	Total £'000
W Zeller	37			37
Dr J Gonella	25			25
T Howson (from September 28, 2000)	6			6
Dr T Rinderknecht (to November 3, 2000)	33			33
N W Wray (to November 30, 2000)	21			21
	199			199
	1,059	89	138	1,286
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Year ended December 31, 2001

	Fees and Salary £'000	Benefits £'000	Bonuses £'000	Total £'000
<b>Executive Directors</b>				
I R Gowrie-Smith	406	20	134	560
M Ashton	350	58	115	523
D Nicholson	180	10	70	260
	936	88	319	1,343
<b>Non-Executive Directors</b>				
Sir M G Beavis	30			30
R S Harris	28			28
Dr A N Karabelas	28			28
Dr K R Mansford	28			28
W Zeller	37			37
Dr J Gonella (to June 6, 2001)	11			11
T Howson (to November 26, 2001)	71			71
	233			233
	1,169	88	319	1,576

Year ended December 31, 2002

	Fees and Salary £'000	Benefits £'000	Bonuses £'000	Total £'000
<b>Executive Directors</b>				
I R Gowrie-Smith	426	29	144	599
M Ashton	367	55	179	601
D Nicholson	189	10	92	291
	982	94	415	1,491

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	Fees and Salary £'000	Benefits £'000	Bonuses £'000	Total £'000
<b>Non-Executive Directors</b>				
Sir M G Beavis	53			53
R S Harris	51			51
Dr A N Karabelas	35			35
Dr K R Mansford	50			50
W Zeller	61			61
Dr D R Ebsworth (from April 11, 2002)	21			21
T Yamamoto (from October 30, 2002)	4			4
	275			275
	1,257	94	415	1,766

The emoluments of W Zeller include remuneration in respect of his capacity as a non-executive director of subsidiary companies amounting to an aggregate of 30,000 Swiss Francs. Benefits relate to car allowances and medical insurance and for M Ashton include a living allowance and, in 2001, school fees.

Bonus for Executive Directors includes cash payment and shares purchased under the Deferred Share Bonus Plan but excludes the value of Matching Shares, which will be provided by

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the Company at the end of the holding period (3 years), subject to the satisfaction of certain conditions.

Fees for Non-executive Directors include the cash amount of fees and the one-off additional payment of fees in shares.

**Pensions**

Contributions made to defined contribution pension schemes on behalf of the Executive Directors are set out below:

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
I R Gowrie-Smith	47	51	53
M Ashton	40	44	46
D Nicholson	20	23	24
	107	118	123

Total Directors' emoluments, excluding pension contributions, amounted to £1,765,768 (2001: £1,575,775).

No Director waived emoluments in the years ended December 31, 2002 or 2001.

**Directors' Interests**

The following tables set out the interests of Directors (including the interests of their immediate families and persons connected with the Directors) as at December 31, 2000, December 31, 2001 and December 31, 2002. All interests are beneficial unless otherwise stated below. Interests in Ordinary Shares include shares acquired by the Executive Directors, other than Matching Shares, under the Deferred Share Bonus

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Plan and Share Purchase Plan.

**Number of ordinary shares**

	<b>December 31, 2000</b>	<b>December 31, 2001</b>	<b>December 31, 2002</b>
I R Gowrie-Smith	25,122,972	25,122,972	25,184,156
M Ashton	110,000	110,000	179,194
D Nicholson	137,000	137,000	171,381
Sir M G Beavis	172,000	172,000	210,297
R S Harris	46,500	101,500	131,083
Dr A N Karabelas (from November 30, 2000)			6,667
Dr K R Mansford	16,000	16,000	52,990
W Zeller	55,000	55,000	91,162
Dr D R Ebsworth (from April 11, 2002)			8,000
T Yamamoto (from October 30, 2002)			
Dr J Gonella (to June 6, 2001)	96,472,890		
T Howson (from September 28, 2000 to November 26, 2001)			
	<b>122,132,362</b>	<b>25,714,472</b>	<b>26,034,930</b>

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In addition to the interests shown above at December 31, 2002, Mr I R Gowrie-Smith had a beneficial interest in 20,000 convertible bonds and Dr A N Karabelas had a beneficial interest in 2,000 American Depository Receipts, all issued by the Company.

**Number of "B" warrants**

	<b>December 31, 2000</b>	<b>December 31, 2001</b>	<b>December 31, 2002</b>
I R Gowrie-Smith	19,797,143	19,797,143	
Sir M G Beavis	84,000	84,000	
	<b>19,881,143</b>	<b>19,881,143</b>	

**Ordinary Options over shares of 10 pence each**

<b>Directors</b>	<b>January 1, 2002</b>	<b>Granted</b>	<b>December 31, 2002</b>	<b>Exercise price</b>	<b>Date from which options can be exercised</b>	<b>Expiry date</b>	<b>Performance condition (see note)</b>
I R Gowrie-Smith	1,234,568		1,234,568	81.0p	12-06-99	12-06-06	1
	575,539		575,539	69.5p	04-19-02	04-19-09	1
	1,008,313		1,008,313	80.6p	06-12-04	06-12-11	2
		1,178,022	1,178,022	72.3p	04-12-05	04-12-12	2
M Ashton	639,077		639,077	93.0p	03-31-01	03-31-08	1
	871,451		871,451	69.5p	04-19-02	04-19-09	1
	868,486		868,486	80.6p	06-12-04	06-12-11	2
		1,014,661	1,014,661	72.3p	04-12-05	04-12-12	2
D Nicholson	533,333		533,333	75.0p	04-29-99	04-29-06	1
	86,022		86,022	93.0p	03-31-01	03-31-08	1

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Directors	January 1, 2002	Granted	December 31, 2002	Exercise price	Date from which options can be exercised	Expiry date	Performance condition (see note)
	172,662		172,662	69.5p	04-19-02	04-19-09	1
	446,650		446,650	80.6p	06-12-04	06-12-11	2
		521,826	521,826	72.3p	04-12-05	04-12-12	2

**Super Options over shares of 10 pence each**

Directors	January 1, 2002	Granted	December 31, 2002	Exercise price	Date from which options can be exercised	Expiry date	Performance condition (see note)
I R Gowrie-Smith	2,385,009		2,385,009	56.67p	05-25-04	05-25-09	3
M Ashton	2,044,293		2,044,293	56.67p	05-25-04	05-25-09	3
D Nicholson	1,022,147		1,022,147	56.67p	05-25-04	05-25-09	3

**Performance condition 1** Options granted may be exercised only if, over a period of three consecutive years, the shareholder return of the Company exceeds the growth in the FTSE All Share Index over the same period.

**Performance condition 2** Options granted vest after three years on a scale between 0% and 100% depending on the Company's performance relative to the performance of a comparator group of companies.

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**Performance condition 3** Options granted may be exercised only if, over a period of five consecutive years, the shareholder return of the Company lies within top quartile growth of the FTSE 250 Share Index over the same period.

No options were exercised by any Director during the year.

All options held by and granted to the Directors are subject to the performance conditions and terms of the SkyePharma Executive Share Option Scheme, the European and North American Scheme and the SkyePharma PLC 1999 Share Option scheme as described above.

As at December 31, 2002, none of the Directors had any interests in shares of any other Group company. The market value of Ordinary Shares at December 31, 2002 was 41.5 pence. The market value of Ordinary Shares during 2002 ranged from the lowest closing mid-price of 39 pence to the highest closing mid-price of 80.25 pence. The holdings of the Directors have not changed since December 31, 2002 except for the following:

**SkyePharma PLC Share Purchase Plan**

As a result of transactions on January 31, 2003, February 28, 2003 and March 31, 2003 by the SkyePharma PLC Share Purchase Plan (an Inland Revenue approved all employee share purchase plan), Michael Ashton and Donald Nicholson, Directors of the Company, as trustees of the Plan became the non-beneficial owners of an additional 13,961 Ordinary Shares of the Company. Of these shares the Directors of the Company have the following beneficial interests in Partnership Shares (Ordinary Shares of the Company) as a result of their personal participation in the Plan: Ian Gowrie- Smith: 527; Michael Ashton: 800 and Donald Nicholson: 800. In accordance with the rules of the Plan these Directors have been awarded Matching Shares (Ordinary Shares in the Company) on the basis of one Matching Share for each Partnership Share. The beneficial ownership of these Matching Shares will pass to the Directors in three years' time subject to continued employment and the retention of the underlying Partnership Shares: Ian Gowrie- Smith: 527; Michael Ashton: 800 and Donald Nicholson: 800. Partnership Shares were purchased at a price of 46, 45 and 50 pence per share. Matching Shares were awarded at a price of 46, 45 and 50 pence per share.

**SkyePharma PLC Deferred Share Bonus Plan**

On January 30, 2003, under the SkyePharma PLC Deferred Share Bonus Plan the Executive Directors and other senior executives have invested 50% of their net bonus relating to the year 2002 into shares in the Company, the "Executive Shares". The total net number of Executive Shares allocated on January 30, 2003 to all Plan Members was 553,773 at a price per share of 44.83 pence (Matching Shares 1,024,069 at 44.83 pence).



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In respect of the following Executive Directors the number of Executive Shares and conditional Matching Shares awarded are as follows:

Directors	Executive Shares	Conditional Matching Shares
I R Gowrie-Smith	96,173	160,289
M Ashton	119,653	199,421
D Nicholson	61,535	102,559

The register of Directors' interests, which is open to inspection, contains full particulars of Directors' shareholdings and options to acquire shares in the Company.

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### 6 Interest Receivable

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Interest	1,806	1,215	1,081
Share of interest receivable of associate		36	
	1,806	1,251	1,081

### 7 Interest Payable

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Interest payable on bank loans, overdrafts and other loans:			
Repayable within five years, not by instalments	268	91	88
Repayable within five years, by instalments	715	470	112
Repayable wholly or partly in more than five years	241	360	373
Finance leases	232	170	130
Interest on convertible bonds	2,052	3,860	3,761
	3,508	4,951	4,464

### 8 Taxation

(Loss)/profit on ordinary activities before taxation, as shown in the consolidated income statements, is analyzed over its component parts as follows:

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
U.K.	4,069	1,269	146
Overseas	(23,755)	(10,646)	1,187

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	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
	(19,686)	(9,377)	1,333

Current taxation charge based on profit for the year:

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Overseas taxation	(19)	(75)	(224)
(Under provision)/over provision in previous years	15		
	(4)	(75)	(224)

Overseas taxation relates principally to withholding tax paid on remittance of milestones to the U.S. and royalties to Switzerland which are not recoverable.

There was no deferred tax component in the tax charge for the years presented.

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The Group has estimated total tax losses available to be set off against future taxable profits of £178.9 million (December 31, 2001: £163.9 million, December 31, 2000: £165.5 million). These losses arise primarily in the U.K., Switzerland and the U.S.A. Of the £178.9 million of losses carried forward, £0.3 million expire in 2003, £52.0 million expire between 2004 and 2006, £120.8 million expire from 2007 onwards and £5.8 million of losses may be carried forward indefinitely.

The above charges reconcile with the applicable U.K. statutory corporation tax rate as follows:

	Year to December 31, 2000 %	Year to December 31, 2001 %	Year to December 31, 2002 %
Statutory U.K. Corporation tax rate	30.0	30.0	30.0
Tax rate differences	12.0	19.0	18.2
Permanent differences	15.0	16.9	19.1
Tax losses not recognized as deferred tax assets	(21.9)	(35.0)	(23.6)
Other items not recognized as deferred tax assets	(35.2)	(31.7)	(26.9)
Prior year items	0.1		
Effective tax rate	(0.0)	(0.8)	16.8

## 9 Earnings per Ordinary Share

	Year to December 31, 2000	Year to December 31, 2001	Year to December 31, 2002
Basic and diluted attributable (loss)/profit (£'000)	(19,690)	(9,452)	1,109

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	Year to December 31, 2000	Year to December 31, 2001	Year to December 31, 2002
Basic weighted average number of shares in issue ('000)	508,228	526,250	577,018
Dilutive potential Ordinary Shares ('000)			20,077
Diluted weighted average number of shares in issue ('000)	508,228	526,250	597,095
<b>Earnings per Ordinary Share:</b>			
Basic	(3.9)p	(1.8)p	0.2p
Diluted	(3.9)p	(1.8)p	0.2p

For diluted earnings per Ordinary Share, the weighted average number of Ordinary Shares in issue is adjusted to assume conversion of all dilutive potential Ordinary Shares. In 2000 and 2001 there was no difference between basic and diluted earnings per Ordinary Share since all potential Ordinary Shares were anti-dilutive. Shares held by the SkyePharma PLC General Employee Benefit Trust are excluded from the weighted average number of shares.

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10 Intangible Fixed Assets

	Goodwill £'000	Intellectual property £'000	Development costs £'000	Total £'000
<b>Cost</b>				
At January 1, 2001	46,026	29,771	1,692	77,489
Exchange adjustments		292	24	316
Additions	29,901	433		30,334
Lapse of warrants	(165)			(165)
At December 31, 2001	75,762	30,496	1,716	107,974
Exchange adjustments		663	62	725
Additions	285	3,401		3,686
Acquisitions	3,970			3,970
At December 31, 2002	80,017	34,560	1,778	116,355
<b>Amortization</b>				
At January 1, 2001	3,310	1,679	414	5,403
Exchange adjustments		13	3	16
Charge for the year	2,341	1,282	201	3,824
Transfer on acquisition of subsidiary interest	503			503
At December 31, 2001	6,154	2,974	618	9,746
Exchange adjustments		82	6	88
Charge for the year	3,799	2,483	224	6,506
At December 31, 2002	9,953	5,539	848	16,340
Net book value at December 31, 2001	69,608	27,522	1,098	98,228

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	Goodwill £'000	Intellectual property £'000	Development costs £'000	Total £'000
Net book value at December 31, 2002	70,064	29,021	930	100,015

In May 2002, SkyePharma acquired the entire drug delivery business of Bioglan AB for £3.6 million in cash 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 technologies that had remained with Bioglan after the January 2001 development and commercialization licensing agreement with Bioglan. See note 27; Acquisitions.

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**11 Tangible Fixed Assets**

	Land and buildings £'000	Laboratory equipment and machines £'000	Assets in the course of construction £'000	Office and other equipment £'000	Motor vehicles £'000	Total £'000
<b>Cost</b>						
At January 1, 2001	24,620	20,587	3,609	3,643	321	52,780
Exchange adjustments	(258)	13	(31)	17	1	(258)
Additions	2,518	4,130	277	643	78	7,646
Acquisitions	384	1,516		118		2,018
Transfer	1,047	2,162	(2,393)	(816)		
Disposals		(8)		(69)	(43)	(120)
At December 31, 2001	28,311	28,400	1,462	3,536	357	62,066
Exchange adjustments	1,205	1,019	86	8	22	2,340
Additions	579	2,586	732	334	121	4,352
Acquisitions		656				656
Transfer	17	314	(333)	2		
Disposals		(122)		(517)	(141)	(780)
At December 31, 2002	30,112	32,853	1,947	3,363	359	68,634
<b>Depreciation</b>						
At January 1, 2001	4,821	5,528		1,924	219	12,492
Exchange adjustments	(83)	(4)		8		(79)
Charge for the year	1,358	2,320		1,044	56	4,778
Transfer	(886)	1,260		(374)		
Disposals		(8)		(40)	(29)	(77)
At December 31, 2001	5,210	9,096		2,562	246	17,114
Exchange adjustments	272	327		27	11	637
Charge for the year	1,774	3,807		480	40	6,101
Disposals		(83)		(508)	(131)	(722)
At December 31, 2002	7,256	13,147		2,561	166	23,130
Net book value at December 31, 2001	23,101	19,304	1,462	974	111	44,952

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	Land and buildings £'000	Laboratory equipment and machines £'000	Assets in the course of construction £'000	Office and other equipment £'000	Motor vehicles £'000	Total £'000
Net book value at December 31, 2002	22,856	19,706	1,947	802	193	45,504

Land and buildings, at net book value, is as follows:

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Freehold property	17,365	19,084	19,499
Long leaseholds		384	331
Short leaseholds	2,434	3,633	3,026
	19,799	23,101	22,856

Included in freehold property is an amount of £4,903,000 (December 31, 2001: £4,537,000) in respect of land which is not depreciated.

Laboratory equipment and machines include cost of £4,240,000 (December 31, 2001: £3,569,000) and accumulated depreciation of £1,856,000 (December 31, 2001: £1,255,000) in respect of assets held under finance leases and hire purchase contracts.

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12 Fixed Asset Investments

	Interest in associate £'000	Unlisted investments £'000	Own shares £'000	Total £'000
<b>Cost</b>				
At January 1, 2001				
Additions		11,431	790	12,221
Acquisition of RTP Pharma Inc.	25,232	2,228		27,460
Net assets	1,914			
Goodwill	23,318			
Share of losses retained	(39)			(39)
Transfer on acquisition of subsidiary interest	(25,193)			(25,193)
Charge for the year			(238)	(238)
At December 31, 2001		13,659	552	14,211
Additions		5,215	1,070	6,285
Charge for the year			(594)	(594)
At December 31, 2002		18,874	1,028	19,902
<b>Amortization</b>				
At January 1, 2001				
Charge for the year	503			503
Transfer on acquisition of subsidiary interest	(503)			(503)

At December 31, 2001 and 2002

	Interest in associate £'000	Unlisted investments £'000	Own shares £'000	Total £'000
Net book value at December 31, 2001	13,659	552	14,211	
Net book value at December 31, 2002	18,874	1,028	19,902	

#### **Astralis Limited**

Astralis Ltd is an emerging biotechnology company based in the U.S., and engaged primarily in the research and development of novel treatments for immune system disorders and skin diseases. The company is currently developing two products. Its primary product, Psoraxine, is an innovative vaccine under development for the treatment of psoriasis. The company's second product is for the treatment of leishmaniasis.

During the year SkyePharma acquired a further 750,000 series A convertible preferred shares of Astralis Limited for £5.2 million (\$7.5 million). As at December 31, 2002 the total SkyePharma holding was 200,000 common shares, 20,000 warrants and 1,750,000 series A convertible preferred shares, representing approximately 23.0% of the ordinary share capital assuming conversion. The shares, warrants and convertible preferred shares are held at cost of £12.7 million. As at December 31, 2002 Astralis had net assets of £4.9 million and a retained loss for the year of £12.2 million.

#### **Transition Therapeutics Inc.**

Transition Therapeutics Inc. is a biopharmaceutical company based in Canada and engaged primarily in the business of developing products for the treatment of multiple sclerosis, diabetes and restenosis.

As at December 31, 2002, the total SkyePharma holding of Transition was 4,930,814 shares, representing approximately 8.2% of the ordinary share capital. The shares are recorded at cost of £2.2 million.

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#### **Cade Struktur Corp.**

As at December 31, 2002, the total SkyePharma holding of Cade Struktur Corp., a Canadian company, was 869,086 shares, representing approximately 16.8% of the ordinary share capital. SkyePharma has not attributed a value to these shares and they have been recorded at zero cost. The shares were originally acquired consequent upon the acquisition of the assets of Hyal Pharmaceutical Corp.

#### **Other investments**

The Group has other investments of £4.0 million in a collaborative partner based in the US, representing approximately 14.2% of the ordinary share capital assuming conversion, recorded at Directors' valuation based on a number of considerations including comparable transactions and discounted future cash flows.

#### **Own shares**

During 2001 the Company established an employee share ownership trust, the SkyePharma PLC General Employee Benefit Trust. The purpose of the trust is to hold shares in the Company, which may subsequently be awarded to Directors and employees under the Deferred Share Bonus Plan and Share Purchase Plans. During the year, the trust purchased 2 million shares and 893,415 shares were allocated at an average price of 66 pence per share. As at December 31, 2002 the trust held 1,805,681 shares at a carrying value of £1.0 million and a market value of £0.7 million. This shortfall is not considered to represent a permanent diminution in value.

### **13 Stock**

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	December 31, 2001 £'000	December 31, 2002 £'000
Raw materials and consumables	896	919
Work in progress	1,313	263
Finished goods	69	74
	<u>2,278</u>	<u>1,256</u>

The replacement cost of stock is not materially different from original cost.

**14 Debtors**

	December 31, 2001 £'000	December 31, 2002 £'000
Trade debtors	8,662	24,627
Other debtors	1,829	2,224
Royalties receivable	168	1,700
Prepayments and accrued income	3,347	6,502
Interest receivable	16	154
	<u>14,022</u>	<u>35,207</u>

Trade debtors includes allowance for doubtful accounts amounting to £Nil (December 31, 2001: £Nil).

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**15 Current Asset Investments**

Current asset investments are represented by a convertible loan note ("the notes") carrying a 5% coupon, due at par with accrued interest in June 2007. The notes were received from GeneMedix plc in June 2002 as an initial payment under an agreement to jointly develop an extended release formulation of interferon alpha-2b using SkyePharma's DepoFoam technology. The notes are convertible at any time, at SkyePharma's option, into between approximately 8.3 million and 11.2 million GeneMedix ordinary shares. There are no restrictions or a lock-up period on conversion of the notes. GeneMedix can elect to redeem in cash some or all of the notes on conversion under certain circumstances. The notes have been recorded at the lower of cost and net realisable value assuming conversion.

**16 Creditors: Amounts Falling Due Within One Year**

	December 31, 2001 £'000	December 31, 2002 £'000
Bank overdrafts	1,618	
Bank loans	1,521	1,572
Current portion of secured mortgage (note 17)	248	270
Current portion of Chiron loan note	3,023	
Trade creditors	3,716	3,344
Corporation tax	3	3
Other taxation and social security costs	1,031	893
Royalties payable	1,455	738
Accrued legal and professional fees	1,334	1,189
Accrued convertible bond interest	1,891	1,891

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	December 31, 2001 £'000	December 31, 2002 £'000
Obligations under hire purchase and finance leases	847	1,085
Deferred income	11,690	15,069
Accruals	6,811	8,417
	<u>35,188</u>	<u>34,471</u>

At December 31, 2002 the Group had loans with the Basellandschaftliche Kantonalbank of £0.9 million (CHF2 million) and £0.7 million (CHF1.5 million). These loans are renewable annually and bear interest at 6.5% and 6.0% respectively. The loans are secured on the assets of Jago and guaranteed by SkyePharma PLC.

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**17 Creditors: Amounts Falling Due After More Than One Year**

	December 31, 2001 £'000	December 31, 2002 £'000
Secured mortgage	7,159	7,502
Chiron promissory note		621
Chiron loan note	802	
Accrued rent	3,385	3,269
Convertible bonds due June 2005	57,962	58,377
Deferred income		2,960
Obligations under finance leases	874	235
	<u>70,182</u>	<u>72,964</u>
Bank and other loans are repayable as follows:		
Between one and two years	1,050	5,158
Between two and three years	4,179	180
Between three and four years	166	180
Between four and five years	166	180
After five years	2,400	2,425
	<u>7,961</u>	<u>8,123</u>
Obligations under finance leases are repayable as follows:		
Between one and two years	843	97
Between two and three years	27	55
Between three and four years	4	83
	<u>874</u>	<u>235</u>

At December 31, 2002 the Group had a property mortgage facility with the Basellandschaftliche Kantonalbank of £7.8 million (CHF17.3 million) of which £0.3 million (CHF0.6 million) is shown within current liabilities. The mortgage is in two tranches, both secured by the assets of Jago and guaranteed by SkyePharma PLC. The first tranche of £3.3 million (CHF7.4 million) bears interest at 4.25% and is repayable by instalments over 21 years semi-annually. The second tranche of £4.5 million (CHF9.9 million) bears interest at 3.0% and is repayable in 2004.



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At December 31, 2002 the Group had a promissory note with Chiron of £0.6 million (\$1 million) which formed part of the consideration for the reacquisition of the DepoCyt marketing, distribution and sales rights. The promissory note is repayable in 2004 and bears interest at LIBOR plus 300 points. It is guaranteed by SkyePharma PLC. The Chiron loan note was settled during the year.

In June 2000, the Company issued £59.4 million 6% Convertible Bonds (the "Bonds") due 2005. The Bonds are convertible at the option of the holder into Ordinary Shares at a conversion price of 83 pence at any time up to June 19, 2005. Unless previously redeemed or converted, the Bonds will be redeemed by the Company at their principal amount on June 19, 2005.

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### 18 Provisions for Liabilities and Charges

	Deferred consideration £'000	Pension £'000	Other National Insurance £'000	Total £'000
At January 1, 2001	2,008	85	26	111
Exchange adjustments		(10)		(10)
Charged in the year			149	149
Utilized	(2,008)	(24)	(158)	(182)
At December 31, 2001		51	17	68
Exchange adjustments		22		22
Charged in the year		128		128
Utilized			(17)	(17)
At December 31, 2002		201		201

#### Deferred consideration provision

On April 17, 2001, £2.0 million (\$3.0 million) was paid to Medac GmbH as the final portion of the deferred consideration due under the terms of the acquisition agreement for the nano-particulate intellectual property acquired in 1999.

#### Pension provision

The pension provision relates to the retirement commitments under a defined benefit scheme for SkyePharma Production SAS employees (Note 26: Pension Arrangements).

#### National Insurance provision

A balance sheet provision of £Nil (December 31, 2001: £17,000) has been recognized in accordance with UITF 25; National Insurance contributions on share option gains.

### 19 Deferred Taxation

Full Potential	
At December 31, 2001 £'000	At December 31, 2002 £'000

	<b>Full Potential</b>	
Accelerated capital allowances	3,091	4,848
Other timing differences	21,085	6,866
U.K. tax benefits from losses carried forward	1,305	1,288
Overseas tax benefits from losses carried forward	34,881	29,731
Potential deferred tax asset	60,362	42,733

No deferred tax asset is recognized, given the uncertainty of the recoverability of the Group's tax losses carried forward.

## 20 Contingent Liabilities and Guarantees

At December 31, 2002 the Company had provided guarantees on various bank borrowings of its subsidiaries as set out in Note 16; Creditors: amounts falling due within one year and Note 17; Creditors: amounts falling due after more than one year.

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In December 1999 SkyePharma Production SAS entered into a leasing arrangement with Lombard North Central PLC by which certain pharmaceutical manufacturing and laboratory equipment was the subject of a four-year sale and leaseback arrangement. The Company has guaranteed the obligations of the lessee under this lease to an amount of £3.0 million (€4.6 million).

In common with most business enterprises, Group companies are subject to a number of claims from third parties, the outcome of which cannot at present be determined but which are not considered to be material in the context of these Financial Statements. Provision has been made in these accounts for any liabilities which are expected to materialize from such claims.

## 21 Commitments

	<b>December 31, 2001 £'000</b>	<b>December 31, 2002 £'000</b>
<b>Capital commitments</b>		
Contracted for but not provided in the accounts	340	197
	<b>December 31, 2001 £'000</b>	<b>December 31, 2002 £'000</b>
<b>Commitments under operating leases to pay rentals for the next year</b>		
Operating leases on land and buildings which expire:		
In one year or less	187	50
In two to five years	1,304	707
In five years or more	2,532	1,816
	4,023	2,573
	<b>December 31, 2001 £'000</b>	<b>December 31, 2002 £'000</b>
Other operating leases which expire:		
In one year or less	42	18
In two to five years	47	53
In five years or more	2	

	December 31, 2001 £'000	December 31, 2002 £'000
	91	71

## 22 Share Capital

### Equity share capital

	December 31, 2001 Number of shares	December 31, 2002 Number of shares	December 31, 2001 £'000	December 31, 2002 £'000
<b>Authorized</b>				
Ordinary Shares of 10p each	1,114,000,000	1,114,000,000	111,400	111,400

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	Ordinary Shares of 10p each Number	Nominal value £'000
<b>Issued, allotted and fully paid</b>		
At January 1, 2000	494,086,980	49,409
Exercise of "B" Warrants	196,356	20
Exercise of share options	3,226,173	322
Conversion of debentures	219,204	22
Shares issued to acquire DepoTech	12,132,600	1,213
Shares issued to Dr Gonella	6,000,000	600
Shares issued to Medac	1,461,455	146
At December 31, 2000	517,322,768	51,732
Exercise of "B" Warrants	22,008	2
Exercise of share options	736,644	74
Exercise of DepoTech Warrants	41,820	4
Shares issued to acquire RTP Pharma Inc.	41,900,099	4,190
At December 31, 2001	560,023,339	56,002
Exercise of "B" Warrants	2,051,607	205
Exercise of share options	1,323,853	133
Shares allocated in respect of RTP Pharma Inc.	8,059,268	806
Issue of shares to Kowa Company Limited	30,000,000	3,000
Conversion of Deferred "A" Shares	12,000,000	1,200
At December 31, 2002	613,458,067	61,346

SkyePharma achieved control of RTP Pharma Inc. in December 2001 when agreement was reached to acquire the majority of the outstanding voting shares in RTP. In March 2002 SkyePharma announced the acquisition of the outstanding voting shares in RTP in return for the issue of SkyePharma Ordinary Shares. The total consideration of £39.4 million including acquisition costs comprised 49,959,367 Ordinary Shares and £4.1 million cash.

The cash consideration received on the issue of Ordinary Shares during the year amounted to £26,168,000 (2001: £468,000). Of this, 30 million Ordinary Shares were allotted to Kowa Company Limited for a total consideration of £25.3 million.

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Following the U.S. launch and first commercial sale of Paxil CR by GlaxoSmithKline in April 2002, the 12 million Deferred "A" Shares were converted into 12 million Ordinary Shares.

### Non-equity share capital

	December 31, 2001 Number of shares	December 31, 2002 Number of shares	December 31, 2001 £'000	December 31, 2002 £'000
<b>Authorized and issued</b>				
Deferred "A" Shares of 10p each	12,000,000		1,200	
Deferred "B" Shares of 10p each	12,000,000	12,000,000	1,200	1,200
	<b>24,000,000</b>	<b>12,000,000</b>	<b>2,400</b>	<b>1,200</b>

The Deferred "A" and "B" Shares were issued to Dr Gonella, the vendor of Jago, on July 20, 2000 under the Settlement Agreement that established the full and final settlement of the deferred consideration payable on the acquisition of Jago. The holders of Deferred "A" and "B" Shares have no rights to participate in the profits of the Company, no voting rights and on a winding up or

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other return of capital only receive the nominal value of their shares if the holders of Ordinary Shares in the capital of the Company have received the sum of £1 million per Ordinary Share and, as such, are classified as non-equity shares.

Under the terms of the Settlement Agreement, following the U.S. launch and first commercial sale of Paxil CR by GlaxoSmithKline in April 2002, the 12 million Deferred "A" Shares were automatically converted into 12 million Ordinary Shares.

The 12 million Deferred "B" Shares automatically convert to 12 million Ordinary Shares on the Company's receipt of a royalty statement under the current Licence Agreement stating that reported sales of Paroxetine/Paxil in combination with the Geomatrix technology have exceeded \$1,000 million during any calendar period prior to January 1, 2006 or exceeded \$337 million between January 1, 2006 and May 3, 2006. In the event that this condition is not satisfied prior to May 3, 2006, the Deferred "B" Shares will not be converted and will be cancelled. The vendor will not be entitled to any other compensation nor additional compensation.

The Deferred "A" and "B" Shares were issued on July 20, 2000 when the price of an Ordinary Share was 94.25 pence. The difference between the nominal value of the Deferred "B" Shares and their fair value, taken to be 94.25 pence, at issue has been recorded as non-equity share premium. See Note 24; Reserves.

### Warrants

The Company has the following warrants outstanding:

#### (a) "B" Warrants

	Number
At January 1, 2001	56,745,495
Warrants exercised	(220,080)
At December 31, 2001	56,525,415
Warrants exercised	(20,516,073)
Warrants lapsed	(36,009,342)
At December 31, 2002	

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The "B" Warrants, which were issued in January 1996 on the basis of one warrant for every ten existing Ordinary Shares subscribed pursuant to the placing, rights issue and capitalization of loan notes and in consideration for the outstanding warrants of Krypton, entitle the holders to subscribe for Ordinary Shares at any time during the period beginning six months after the date of issue and ending on December 31, 2002 at an effective price of 40 pence per Ordinary Share (based on ten warrants). Consequent upon the consolidation of existing Ordinary Shares in May 1996 the terms under which the "B" Warrants may be exercised were amended so that a holder was required to exercise ten "B" Warrants to acquire one Ordinary Share.

All outstanding "B" Warrants lapsed on December 31, 2002 and so the market value of "B" Warrants as at December 31, 2002 was nil pence (December 31, 2001: 3.25 pence). The market value of "B" Warrants during the period from January 1, 2002 to December 31, 2002 ranged from the lowest mid-price of nil pence to the highest mid-price of 4.75 pence per "B" Warrant.

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### *(b) "D" and "E" Warrants*

The "D" and "E" Warrants were issued in March 2002 as part of the consideration for the agreement with Paul Capital to fund new product development. The "D" and "E" Warrants entitle the holders to subscribe for a total of 5 million Ordinary Shares at any time during the period to December 31, 2008 at an exercise price of 73.75 pence per Ordinary Share. A value of £0.3 million has been attributed to the "D" and "E" Warrants which has been recorded within Other Reserves.

### *(c) Other Warrants*

Warrants were issued in December 1999 as part of the acquisition of DepoTech and entitle the holders to subscribe for 291,777 Ordinary Shares at any time during the period beginning December 31, 1999 and ending on February 25, 2005 at an exercise price of \$1.453 (90.25 pence) per Ordinary Share.

### *Share options*

The Company encourages employee participation in its shares through ownership and continues to operate various Share Option Schemes and the Unapproved Share Option Scheme. Under the terms of these Schemes the Board may offer options to purchase Ordinary Shares in the Company to employees, including Directors, at a price not less than the higher of the nominal value and the market value of the shares.

Options granted to U.K. and European employees are only exercisable between the third and tenth anniversary of the date of grant, and are subject to the Company's Code of Conduct for dealing in Shares, and the Model Code. Options granted to U.S. employees prior to 2001 vest at 25% per annum from the date of grant and there were no performance criteria. U.K. and European options may only be exercised if the growth in the Company's share price over a consecutive three-year period exceeds the growth over the same period in the FT-SE All Share Index for options granted prior to 2001. This condition was satisfied for the first time in March 2000. Employees with options that are within their exercise period are now able to exercise those options within any one-year period from the date the performance condition is satisfied. Super Options are exercisable after five years and are subject to higher performance conditions in accordance with those recommended by the Association of British Insurers.

Following changes to the option plans approved at the Annual General Meeting June 2001, options granted since that date to Directors and senior employees are subject to performance conditions linked to the total shareholder return of a comparator group of companies, and are not subject to retesting. Options granted to other US employees continue to vest at 25% per annum with no performance criteria, and other European employees who are not Directors or senior employees can exercise their options after three years and are not subject to performance conditions.

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The following table summarizes the activity in share options for the years to December 31, 2001 and December 31, 2002:

Share Options	Option Price
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At January 1, 2001	26,316,828	44.8p	93.0p
Granted	9,962,366	55.1p	80.6p
Exercised	(736,644)	44.8p	75.0p
Cancelled or expired	(818,435)	44.8p	91.3p
At December 31, 2001	34,724,115	44.8p	93.0p
Granted	11,234,887	57.1p	78.6p
Exercised	(1,323,853)	44.8p	69.5p
Cancelled or expired	(4,178,216)	44.8p	93.0p
At December 31, 2002	40,456,933	44.8p	93.0p

The market value of Ordinary Shares as at December 31, 2002 was 41.5 pence (December 31, 2001: 61.25 pence). The market value of Ordinary Shares during 2002 ranged from the lowest closing mid-price of 39.0 pence to the highest closing mid-price of 80.25 pence per share.

At December 31, 2002 the following Ordinary Shares were under option to employees or former employees of the Group:

Option Price for each Ordinary Share of 10p	Number of Options over Ordinary Shares of 10p	Expiry Date
75.0p	1,427,676	04-29-06
92.0p	417,255	05-28-06
81.0p	1,234,568	12-06-06
66.5p	646,281	04-07-07
51.0p	124,073	01-28-08
93.0p	796,362	03-31-08
44.8p	1,464,612	10-05-08
69.5p	3,232,813	04-19-09
56.7p	8,421,310	05-25-09
56.9p	238,066	09-07-09
91.3p	1,036,268	06-06-10
81.7p	1,853,441	11-03-10
80.6p	6,602,439	06-12-11
55.6p	1,318,008	10-31-11
55.1p	552,514	12-24-11
72.3p	9,147,254	04-12-12
78.6p	515,653	05-24-12
51.7p	1,428,340	09-25-12
	40,456,933	

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23 Shares and Warrants to be issued

	£'000
At January 1, 2001	4,985
Goodwill adjustments on deferred consideration	(148)
Shares allocated in respect of RTP Pharma Inc.	5,780
At December 31, 2001	10,617
Goodwill adjustments on deferred consideration	(4,837)
Shares issued in respect of RTP Pharma Inc.	(5,780)

£'000

At December 31, 2002

**(a) Krypton**

The deferred consideration on the acquisition of Krypton was revised in April 1996, such that a maximum of 37.5 million Ordinary Shares would be issued contingent on a change in control of the Company at a share price of not less than 80 pence compounded at an annual rate of 10%, or satisfaction of the following conditions and hurdles:

- (i) 2.5 million Ordinary Shares on each Krypton product obtaining ANDA approval before December 31, 2003 subject to a maximum of 7.5 million Ordinary Shares;
- (ii) an additional 10 million Ordinary Shares in the event that the aggregate annual sales of the Krypton products exceeds \$50 million and the Company is profitable in respect of these products before December 31, 2003;
- (iii) an additional 10 million Ordinary Shares in the event that the aggregate annual sales of the Krypton products and annual revenues of the Company exceeds \$200 million and the Company is profitable in respect of these products before December 31, 2003;
- (iv) an additional 10 million Ordinary Shares in the event that the aggregate annual sales of the Krypton products and annual revenues of the Company exceeds \$275 million and the Company is profitable in respect of these products before December 31, 2003.

In the event that two of hurdles (ii), (iii) and (iv) are satisfied in relation to any single year's sales, only the first such hurdle will be considered as having been satisfied.

Certain of the hurdles relating to the Krypton acquisition were not formulated to take account of the detailed arrangements currently envisaged by the Company. Should the annual revenues of the Company approach the amounts specified in hurdles (iii) and (iv), SkyePharma may need to renegotiate elements of the Krypton acquisition agreement.

As no Krypton products are marketed and no licensing partners have been identified for the products the Directors have taken the view that the above hurdles can no longer be reasonably expected to be met. Consequently no provision for deferred consideration has been recognized as at December 31, 2002.

**(b) RTP**

As part of the RTP acquisition deferred consideration may be due to the former RTP shareholders in consideration for the loss of certain option rights. If the SkyePharma share price, as calculated under the terms of the agreement, 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. In the opinion of the Directors, the outcome cannot be estimated with any degree of certainty. Therefore this deferred consideration has not been recognized as at December 31, 2002.

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**(c) Paul Capital Royalty Acquisition Fund**

In March 2002 the Group announced a second transaction with Paul Capital Royalty Acquisition Fund under which SkyePharma will issue Ordinary Shares up to a value of \$7.5 million if royalties and milestones received by SkyePharma in respect of those products included in the transaction are not in excess of minimum annual payments required to be made to Paul Capital. During 2002 the royalties received by SkyePharma were substantially in excess of the minimum payments required to be made to Paul Capital, consequently the company has not

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provided for any additional obligations under this provision.

### 24 Reserves

	Equity share premium £'000	Non-equity share premium £'000	Other Reserves £'000	Profit and loss account £'000
At January 1, 2000	221,091		11,058	(247,632)
Exchange adjustments				758
On issue of shares and warrants	20,121	20,220	212	
On exercise of warrants	58		(58)	
On conversion of debentures	79			
Goodwill adjustments on deferred consideration				3,618
Loss for the year				(19,690)
At December 31, 2000	241,349	20,220	11,212	(262,946)
Exchange adjustments				28
On issue of shares and warrants	25,736			
On exercise of warrants	52		(56)	
On lapse of warrants			(436)	271
Goodwill adjustments on deferred consideration				148
Loss for the year				(9,452)
At December 31, 2001	267,137	20,220	10,720	(271,951)
Exchange adjustments				903
On issue of shares and warrants	37,366	(10,110)	311	
On exercise of share options	567			
On exercise of warrants	1,239		(624)	
On lapse of warrants			(1,096)	1,096
Goodwill adjustments on deferred consideration				4,837
Profit for the year				1,109
At December 31, 2002	306,309	10,110	9,311	(264,006)

Other reserves relate to a merger reserve on acquisition and a warrant reserve on the issue of the "D" and "E" Warrants.

As at December 31, 2002 the cumulative amount of goodwill eliminated against reserves was £147,632,000 (2001: £152,469,000; 2000: £152,617,000).

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### 25 Financial Instruments

The Group holds financial instruments to finance its operations and to manage the currency risk that arises from these operations. The Group finances its operations through a combination of shareholders' funds, convertible bonds, bank loans and other borrowings. The main risks arising from the Group's financial instruments are liquidity risk, foreign currency risk, interest rate risk and credit risk.

#### Liquidity risks

The Group's policy is to maintain continuity of funding through a mixture of long-term debt and bank loans, raised to cover specific projects, and through the issue of shares to collaborative partners, where necessary, to obtain development contracts. Short-term flexibility is provided through the use of overdrafts. The maturity profile of the Group's debt is set out below at Note (c).

#### Foreign currency risk



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All of the Group's operations are based overseas in Continental Europe and North America giving rise to exposures to changes in foreign exchange rates notably the Swiss Franc, Euro, Swedish Krona, U.S. Dollar and Canadian Dollar. To minimize the impact of any fluctuations, the Group's policy has historically been to maintain natural hedges by relating the structure of borrowings to the trading cash flows that generate them. Where subsidiaries are funded centrally, this is achieved by the use of long-term loans the exchange differences on which are taken to reserves. Where it was not possible to use natural hedges, currency options, accrual forward options and forward currency contracts were used. The Group has used these financial instruments during the year to minimize the currency exposure on operational transactions. Foreign currency exchange movements did not have a material impact on the results of operations in 2002 compared with 2001.

### Interest rate risk

The Group borrows at fixed and floating rates of interest as deemed appropriate for its circumstances. Where necessary the Group uses several interest rate swaps to achieve the desired interest rate profile. During the year the Group had several cancellable, floating rate, interest rate swaps on £30 million of the 6% convertible bond liability. The interest rate profile of the Group's financial assets and liabilities is set out in Notes (a) and (b) respectively.

### Credit risk

The Group is exposed to credit related losses in the event of non-performance by third parties to financial instruments. The Group does not expect any third parties to fail to meet their obligations given the policy of selecting only parties with high credit ratings and minimizing its exposure to any one institution.

In the numerical disclosures that follow, short-term debtors and creditors that arise directly as a result of the Group's operations are excluded from all disclosures with the exception of Note (f) on currency exposures.

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### (a) Interest rate and currency profile of financial assets

December 31, 2002

	Floating rate financial assets £'000	Fixed rate financial assets £'000	Non-interest bearing financial assets £'000	Total financial £'000
<b>Currency</b>				
Sterling	18,680	1,961	36	20,677
\$US	4,292		16,663	20,955
Swiss francs	1,870			1,870
\$Canadian	2,026		2,228	4,254
Euro	617			617
Swedish Krona	523			523
	28,008	1,961	18,927	48,896

Total financial assets comprise fixed asset investments of £18.9 million (2001: £13.7 million), current asset investments of £2.0 million (2001: £nil) and cash and short-term bank deposits of £28.1 million (2001: £26.9 million).

Floating rate financial assets bear interest at rates based upon the floating bank rate in the country in which the funds are held. The weighted average interest rate on fixed rate financial assets is 5% (2001: 2%). The weighted average time for which the rate is fixed is 54 months (2001: 4 months).

December 31, 2001

Floating rate financial assets	Fixed rate financial assets	Non-interest bearing financial	Total financial £'000
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	£'000	£'000	assets £'000	
<b>Currency</b>				
Sterling	5,690		62	5,752
\$US	14,977		11,467	26,444
Swiss francs	549		93	642
\$Canadian	48	5,389	2,228	7,665
Euro	48			48
	<b>21,312</b>	<b>5,389</b>	<b>13,850</b>	<b>40,551</b>

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(b) Interest rate and currency profile of financial liabilities

December 31, 2002

Currency	Fixed rate financial liabilities £'000	Weighted average interest rate on fixed financial liabilities %	Weighted average time for which rate is fixed (months)	Floating rate financial liabilities £'000	Non- interest bearing financial liabilities (months)	Weighted average time to maturity (months)	Total financial liabilities £'000
Sterling	29,400	6.00	29.5	30,000	11,310	40.0	70,710
Swiss Francs	4,560	3.64	13.5	4,897			9,457
Euro	863	6.25	11.0		201	417.0	1,064
\$US	25	5.25	40.0	621	3,269	144.0	3,915
Swedish Krona	319	7.25	27.8				319
	<b>35,167</b>	<b>5.71</b>	<b>27.0</b>	<b>35,518</b>	<b>14,780</b>	<b>68.1</b>	<b>85,465</b>

Financial liabilities comprise total borrowings of £10.0 million (2001: £14.4 million), convertible bonds of £59.4 million (2001: £59.4 million), non-equity Deferred "A" and "B" Shares of £11.3 million (2001: £22.6 million), other creditors of £4.6 million (2001: £5.1 million) and provisions of £0.2 million (2001: £0.1 million).

Total financial liabilities does not agree to the total of the balance sheet captions due to the presence of £1,023,000 (2001: £1,438,000) of unamortized issue costs within the value shown on the balance sheet for convertible bonds.

All floating rate financial liabilities, in both 2002 and 2001, are interest bearing financial liabilities that bear interest at interest rates based on LIBOR, prime and other bank based lending rates in the country in which the liability arises, which are fixed for periods of up to 12 months.

December 31, 2001

Currency	Fixed rate financial liabilities £'000	Weighted average interest rate on fixed financial liabilities %	Weighted average time for which rate is fixed (months)	Floating rate financial liabilities £'000	Non- interest bearing financial liabilities (months)	Weighted average time to maturity (months)	Total financial liabilities £'000
Sterling	59,400	6.00	41.5		22,623	52.0	82,023
Swiss Francs	4,302	3.63	23.6	5,548			9,850
French Francs	1,599	6.25	23.0	745	65	419.0	2,409

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	Fixed rate financial liabilities £'000	Weighted average interest rate on fixed financial liabilities %	Weighted average time for which rate is fixed (months)	Floating rate financial liabilities £'000	Non- interest bearing financial liabilities (months)	Weighted average time to maturity (months)	Total financial liabilities £'000
\$US				3,898	3,385	156.0	7,283
	65,301	5.85	39.9	10,191	26,073	66.4	101,565

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(c) Maturity of financial liabilities

	December 31, 2001 £'000	December 31, 2002 £'000	December 31, 2002 Fixed rate financial liabilities £'000	December 31, 2002 Floating rate financial liabilities £'000	December 31, 2002 Non-interest bearing financial liabilities £'000
Within one year	7,257	2,927	1,175	1,752	
Between one and two years	24,513	5,256	4,455	801	
Between two and three years	4,206	59,633	29,454	30,179	
Between three and four years	59,570	11,573	83	180	11,310
Between four and five years	233	381		180	201
Beyond five years	5,786	5,695		2,426	3,269
	101,565	85,465	35,167	35,518	14,780

(d) Borrowing facilities

As at December 31, 2002 the Group had the following undrawn committed borrowing facilities available.

	December 31, 2001 £'000	December 31, 2002 £'000
Expiring within one year	369	1,646

(e) Fair values

The comparison of fair and book values of all the Group's financial instruments as at December 31, 2002 is set out below. Market value or Directors' valuation have been used to determine the fair value of fixed and current asset investments. Market values have been used to determine the fair values of all swaps and foreign currency contracts. The fair value of the non-equity Deferred "B" Shares has been calculated by reference to the Ordinary Share price at December 31, 2002, based upon the Directors' opinion that 12 million Ordinary Shares will be issued in settlement of the deferred consideration payable on the acquisition of Jago. See note 22; Share capital, for details of the contingencies that shall determine the issuance of the Ordinary Shares. The fair values of all other items have been calculated by discounting future cash flows at interest rates prevailing at December 31, 2002.

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December 31, 2002

	Book Values £'000	Fair values £'000
<b>Financial instruments held or issued to finance the Group's operations</b>		
Fixed asset investments	18,874	17,287
Current asset investments	1,961	1,961
Cash at bank and in hand	7,394	7,394
Short-term bank deposits	20,667	20,667
Short-term borrowings and current portion of long-term borrowings	(2,927)	(2,927)
Long-term convertible debt	(59,400)	(53,863)
Other long-term debt	(11,828)	(11,707)
Non-equity Deferred "B" Shares	(11,310)	(4,980)
	<u>(36,569)</u>	<u>(26,168)</u>
<b>Derivative financial instruments held to manage the Group's currency profile</b>		
Interest rate swaps		452
Euro currency options		(85)
US\$currency options		(13)
Forward currency contracts		146
		<u>500</u>

December 31, 2001

	Book Values £'000	Fair values £'000
<b>Financial instruments held or issued to finance the Group's operations</b>		
Fixed asset investments	13,659	13,903
Cash at bank and in hand	4,534	4,534
Short-term bank deposits	22,358	22,358
Short-term borrowings and current portion of long-term borrowings	(7,257)	(7,257)
Long-term convertible debt	(59,400)	(50,194)
Other long-term debt	(12,288)	(12,055)
Non-equity Deferred "A" and "B" Shares	(22,620)	(14,700)
	<u>(61,014)</u>	<u>(43,411)</u>
<b>Derivative financial instruments held to manage the Group's currency profile</b>		
Euro currency options		38
US\$currency options	(20)	(23)
Forward currency contracts		(46)
	<u>(20)</u>	<u>(31)</u>

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(f) Currency exposures

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The following analysis shows the net monetary assets and liabilities of Group companies that are not denominated in their functional currency and therefore give rise to exchange gains and losses in the income statements in both 2002 and 2001.

### December 31, 2002

#### Net foreign currency monetary assets/(liabilities)

Functional currency of Operating Company	Sterling £'000	\$US £'000	Euro £'000	Swiss francs £'000	\$ Canadian £'000	Total £'000
Sterling		2,232	617		1	2,850
\$US	(15,956)		(9)		(34)	(15,999)
Euro	(2,025)	96		2,225		296
Swiss francs	(928)	3,142	(528)		(582)	1,104
\$Canadian	1,904	400	(130)	550		2,724
Swedish Krona	(1,343)					(1,343)
	<u>(18,348)</u>	<u>5,870</u>	<u>(50)</u>	<u>2,775</u>	<u>(615)</u>	<u>(10,368)</u>

### December 31, 2001

#### Net foreign currency monetary assets/(liabilities)

Functional currency of Operating Company	Sterling £'000	\$US £'000	Euro £'000	Swiss francs £'000	\$ Canadian £'000	Total £'000
Sterling		11,527			(49)	11,478
\$US	(5,231)					(5,231)
French francs	(2,260)	102		25		(2,133)
Swiss francs	3,568	4,087	406		10	8,071
\$Canadian		477				477
	<u>(3,923)</u>	<u>16,193</u>	<u>406</u>	<u>25</u>	<u>(39)</u>	<u>12,662</u>

### (g) Hedging

As explained above, the Group's policy is to hedge interest rate exposures through the use of interest rate swaps and currency exposures through the use of currency options, accrual forward options and forward currency contracts.

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The table below shows the extent to which the Group has off-balance sheet (unrecognized) and on-balance sheet (deferred) gains and losses in respect of hedges at the beginning and end of the year:

### December 31, 2002

	Unrecognized			Deferred		
	Gains £'000	Losses £'000	Net Total £'000	Gains £'000	Losses £'000	Net Total £'000
Gains/(losses) on hedges at January 1, 2002		(31)	(31)		(20)	(20)
Changes in value from January 1, 2002 to settlement		262	262			

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	Unrecognized			Deferred		
<b>Gains/(losses) arising in 2001 recognized in 2002</b>		231	231		(20)	(20)
Gains/(losses) not recognized in 2002 arising before January 1, 2002						
Arising in 2002	598	(98)	500			
<b>Gains/(losses) on hedges at December 31, 2002</b>	598	(98)	500			

At December 31, 2002, the Company had European style accrual forward options to purchase £154,000 of Swiss francs each week for the 26 weeks ending in July 2002 and £71,000 of Euro each week for the 14 weeks ending in April 2002.

At December 31, 2002, the Company had agreements in place for American style accrual forward options, commencing in January 2003, to purchase £113,000 of US dollars for the 44 weeks ending in November 2003 and £44,000 of Swedish Krona each week for the 45 weeks ending in November 2003. Both of these structures lapsed in January and February 2003 respectively.

At December 31, 2002, the Company had forward currency contracts to purchase £4.5 million of Swiss francs, £1.1 million of Euro and £0.5 million of Swedish Krona.

The excess of fair values over book values for currency options shown in note 25 (e) represents the unrecognized hedging gain on these instruments as at December 31, 2002. The actual gains or losses arising on these currency options will be dependent on future exchange rates and will be recognized in the profit and loss account, in 2003, as the operational transactions to which they are linked occur.

Unrecognized gains at December 31, 2002 include £0.5 million in relation to the cancellable swap agreement. This is based upon the swap agreement continuing for the life of the convertible bond and as such the gain would be spread in the profit and loss account until 2005. The Royal Bank of Scotland exercised its right to cancel the swap on December 19, 2001 and was replaced with a comparable swap on February 27, 2002. Similarly, it was again cancelled and replaced on December 15, 2002.

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**December 31, 2001**

	Unrecognized			Deferred		
	Gains £'000	Losses £'000	Net Total £'000	Gains £'000	Losses £'000	Net Total £'000
Gains/(losses) on hedges at January 1, 2001	1,043	(104)	939			
Changes in value from January 1, 2001 to settlement	(923)	104	(819)			
<b>Gains/(losses) arising in 2000 recognized in 2001</b>	120		120			
Gains/(losses) not recognized in 2001 arising before January 1, 2001						
Arising in 2001		(31)	(31)		(20)	(20)

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	Unrecognized		Deferred	
<b>Gains/(losses) on hedges at December 31, 2001</b>		(31)		(20)

**26 Pension Arrangements**

The Group operates various defined contribution plans for its employees in the U.K., Switzerland, U.S., Sweden and Canada. The Group's contributions to these plans are charged to the profit and loss account in the period to which they relate, and the assets are held in separate trustee administered funds. The charge for the year amounted to £939,000 (2001: £822,000).

The Group operates an unfunded defined benefit scheme in respect of its employees in France based on the national collective agreement of the pharmaceutical industry, and a provision of £201,000 is included in Note 18; Provisions for liabilities and charges. The charge for the year was £128,000.

Under the transitional provisions of FRS17; Retirement Benefits certain disclosures for the defined benefit scheme in France are required as follows:

As at December 2002 a valuation was performed by professionally qualified actuaries on the present value of the accrued liabilities calculated under the projected unit method.

The principal assumptions made by the actuaries were:

	2001 % per annum	2002 % per annum
Inflation rate	2.0	1.75
Rate of increase in salaries	3.0	2.75
Discount rate	5.5	5.25

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**Analysis of amounts charged to the profit and loss account in respect of the defined benefit scheme**

	2002 £'000
Current service cost	24
Past service cost	
Interest on pension scheme liabilities	21
<b>Total charge to the profit and loss account</b>	<b>45</b>

**Movement in deficit during the year**

	2002 £'000
At January 1, 2002	382
Exchange adjustment	25
Total charge to the profit and loss account	45
Benefit payments made	(9)
Actuarial gain recognized in the statement of total recognized gains and losses	(61)

	<b>2002</b>
	<b>£'000</b>
At December 31, 2002	382

**Amounts recorded in the statement of total recognized gains and losses under FRS17**

	<b>2002</b>
	<b>£'000</b>
Experience gains arising on scheme liabilities (£'000)	17
Percentage of scheme liabilities (%)	4
Changes in assumption relating to the present value of scheme liabilities (£'000)	44
Percentage of scheme liabilities (%)	12
Total actuarial gain (£'000)	61
Percentage of scheme liabilities (%)	16
<b>Profit and loss reserve under FRS17</b>	

	<b>2002</b>
	<b>£'000</b>
Profit and loss reserve per balance sheet	(264,006)
Pension liability under FRS 17	(382)
Pension liability under SSAP 24	201
Profit and loss reserve under FRS 17	(264,187)

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**Net assets under FRS17**

	<b>2002</b>
	<b>£'000</b>
Net assets per balance sheet	124,270
Pension liability under FRS 17	(382)
Pension liability under SSAP 24	201
Net assets under FRS 17	124,089

**27 Acquisitions**

**(a) Drug delivery business of Bioglan AB**

On May 13, 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 include Bioglan's Biosphere injectable technology and those rights to DermaStick, Crystalip and ES- Gel topical drug delivery technologies that remained with Bioglan after the January 2001 development and commercialization licensing agreement.

The acquisition method has been adopted and goodwill of £4.0 million arose on the acquisition. By consideration of the likely commercial life of the technology acquired, the Directors have determined that a suitable period over which to amortize the goodwill is 20 years.

**Book values  
and  
fair values**



	<u>£'000</u>
<b>Fixed assets</b>	
Tangible assets	676
<b>Current assets</b>	
Debtors	44
<b>Creditors: amounts falling due within one year</b>	(1,095)
<b>Net current liabilities</b>	(1,051)
<b>Net liabilities</b>	(375)
<b>Satisfied by:</b>	
Cash	3,500
Expenses relating to the transaction	95
<b>Consideration</b>	3,595
<b>Goodwill</b>	3,970

**Results of the drug delivery business of Bioglan AB**

The drug delivery business of Bioglan AB prior to the acquisition formed part of Bioglan AB and did not report as a separate unit.

During the period May 13, 2002 to December 31, 2002 the drug delivery business of Bioglan AB contributed £0.5 million to turnover, a loss of £1.5 million to operating profit and a cash outflow of £1.3 million to net cash inflow from operating activities.

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**(b) RTP Pharma Inc.**

SkyePharma achieved control of RTP Pharma Inc. in December 2001 when agreement was reached to acquire the majority of the outstanding voting shares in RTP. In March 2002 SkyePharma announced the acquisition of the outstanding voting shares in RTP in return for the issue of SkyePharma Ordinary Shares. The total consideration of £39.4 million including acquisition costs comprised 49,959,367 Ordinary Shares and £4.1 million cash. As part of the RTP acquisition deferred consideration may be due to be the former RTP shareholders. See note 23(b); Shares and warrants to be issued.

No material adjustments have been made to the provisional fair values.

**28 Related party transactions**

At the end of December 1998, Ian Gowrie- Smith (through a family- owned trust) acquired a 50% interest in 10 East 63rd Street Inc., the company which owns 10 East 63rd Street, a property in New York. In December 2002 Mr Gowrie- Smith acquired the remaining 50% interest. SkyePharma PLC has been in occupation of that property since January 1997, subject to a tenancy agreement renewed in February 2001 at which time the annual rent was increased to \$360,000 per annum based upon an independent valuation. On April 1, 2002 the company took additional space within the property at which time the annual rent was increased to \$420,000 per annum. Until April 1, 2002 approximately one-third of the premises was subleased to Fifth Avenue Capital Inc.

**29 Principal Subsidiary Undertakings**

Company	Country of incorporation	% held	Principal activities
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SkyePharma Canada Holdings Inc. <sup>(1 and 2)</sup>	Canada	100	Holding company
SkyePharma Canada Inc. <sup>(2)</sup>	Canada	100	Research and development
SkyePharma Production SAS <sup>(1)</sup>	France	100	Manufacturing of pharmaceuticals
Krypton Limited	Gibraltar	100	Exploitation of intellectual property
SkyePharma AB <sup>(1)</sup>	Sweden	100	Research and development
Jago Holding AG	Switzerland	100	Holding company
Jago Research AG	Switzerland	100	Exploitation of intellectual property
Jagotec AG	Switzerland	100	Exploitation of intellectual property
SkyePharma AG	Switzerland	100	Research and development
SkyePharma Holding AG <sup>(1)</sup>	Switzerland	100	Holding company
SkyePharma Holding Inc. <sup>(1)</sup>	U.S.	100	Holding company
SkyePharma Inc.	U.S.	100	Development of pharmaceuticals
SkyePharma US Inc.	U.S.	100	Development of pharmaceuticals and licensing

(1) Denotes investment directly held by the Company.

(2) On January 1, 2003 SkyePharma Canada Holdings Inc. and SkyePharma Canada Inc. were amalgamated under Canadian law. The name of the amalgamated corporation is SkyePharma Canada Inc.

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30 Summary of Material Differences between U.K. and U.S. GAAP

The financial statements of the Group are prepared in accordance with U.K. GAAP (Generally Accepted Accounting Principles), which differs in certain respects from U.S. GAAP. Such differences include methods for measuring and presenting the amounts shown in the consolidated financial statements, as well as additional disclosures required by U.S. GAAP.

**I. Reconciliation of net loss/profit and shareholders' funds**

The tables below summarize the material adjustments to the loss/profit for the year and shareholders' funds which would be required if U.S. GAAP had been applied instead of U.K. GAAP.

Note 30.I	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>(Loss)/Profit under U.K. GAAP</b>	(19,690)	(9,452)	1,109
U.S. GAAP adjustments:			
Purchase accounting and goodwill			
Amortization of goodwill and other intangibles	(1a,c,e) (5,873)	(5,708)	3,399
Depreciation of tangible fixed assets	(1b) 727	488	518
Write-off of acquired in-process research and development costs	(1e)	(18,893)	(4,646)
Results of equity investments (RTP)	(1d)	(559)	
Deferred taxes	(1c)		401
Share-based compensation	(4) (734)	(215)	(181)
Revenue recognition	(5) (189)	(1,934)	(26,987)
Sale of royalty interests			
Revenue recognition	(6) (2,900)	(6,342)	(14,219)
Interest expense	(6)	(1,222)	(5,850)
Royalty payments	(6)		664
Financial instruments	(8)	(31)	531

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Note 30.I	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Loss before cumulative effect of change in accounting principles under U.S. GAAP	(28,659)	(43,868)	(45,261)
Cumulative effect of change in accounting principles (SAB 101)	(5)	(542)	
<b>Net loss under U.S. GAAP</b>	<b>(29,201)</b>	<b>(43,868)</b>	<b>(45,261)</b>
Loss per ordinary share under U.S. GAAP before cumulative effect of change in accounting principles (pence)	(5.6)p	(8.3)p	(7.8)p
Cumulative effect of change in accounting principles per ordinary share (pence)	(0.1)p		
<b>Net loss per ordinary share under U.S. GAAP (pence)</b>	<b>(13)</b>	<b>(5.7)p</b>	<b>(7.8)p</b>

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**Shareholders' funds**

Note 30.I	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
<b>Shareholders' funds under U.K. GAAP</b>	95,145	124,270
U.S. GAAP adjustments:		
Purchase accounting and goodwill		
Goodwill	(1a,c,e) 73,259	83,719
Other intangible fixed assets	(1a,c) 5,174	4,344
Tangible fixed assets	(1b) (7,192)	(7,930)
Investments	(1c,10) 796	(1,893)
Deferred taxes	(1c) (2,738)	(1,439)
Contingent consideration charged to goodwill reserve	(1f) 27,457	22,620
Measurement of purchase consideration	(1g)	
Shares relating to contingent consideration	(3)	(11,310)
Shares and warrants to be issued, deferred shares and shares issued to Dr Gonella	(2) (34,070)	(11,310)
Share-based compensation	(4) (193)	(305)
Employee Benefit Trust	(7) (552)	(1,859)
Deferred revenue	(5) 771	(23,179)
Funding liabilities	(6) (15,256)	(37,698)
Financial instruments	(8) (31)	500
<b>Shareholders' funds under U.S. GAAP</b>	<b>142,570</b>	<b>138,530</b>

Certain adjustments as of and for the year ended December 31, 2000 have been reclassified for comparative purposes.

**(1) Business combinations**

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Under both U.K. and U.S. GAAP the acquisitions of Jago Holdings AG, SkyePharma Production SAS (formerly Laboratories Novalis Production SAS), SkyePharma Inc. (formerly DepoTech Corporation), SkyePharma Canada Inc. (formerly RTP Pharma Inc.) and SkyePharma AB are accounted for as acquisitions/purchases. Both U.K. and U.S. GAAP require the purchase consideration to be allocated to the net assets acquired at their fair value at the date of acquisition, with the difference between the consideration and the fair value of the net assets acquired treated as goodwill. In the allocation of consideration, and the treatment of deferred consideration, certain differences between U.K. and U.S. GAAP arise as set out below.

### (a) Goodwill and other intangible fixed assets

Prior to the introduction of FRS10, as permissible under U.K. GAAP, no intangible assets had been recognized as a result of purchase accounting as the intangible assets were considered to be an integral part of the business acquired and were, therefore, included within goodwill and eliminated against shareholders' funds. Where the aggregate of the fair values of the net assets acquired exceeded the cost of the acquired net assets resulting in negative goodwill, such excess was credited directly to reserves. Following the introduction of FRS10 there is a requirement to capitalize such goodwill as an intangible asset and amortize it over a suitable period not normally exceeding 20 years. The Group adopted transitional provisions under FRS10 not to reinstate goodwill, previously eliminated against reserves, as an intangible asset.

U.S. GAAP requires an allocation of the purchase consideration to identifiable intangible assets, including any resulting from research and development. Goodwill and identifiable intangible fixed

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assets are reflected as assets. Prior to 2002, goodwill was amortized over its useful life, with the exception of goodwill arising on acquisitions made after June 30, 2001. Effective January 1, 2002 goodwill is no longer amortized under U.S. GAAP, but instead subject to annual impairment tests. This results in a reversal of goodwill amortization charged under U.K. GAAP. Intangible fixed assets recognized under U.S. GAAP purchase accounting requirements are amortized over their estimated revenue earning life. Negative goodwill, if any, is eliminated by reducing the value of all non-current assets acquired.

Goodwill as of December 31, 2001 and 2002 is presented net of accumulated amortization of £33,896,000 and £30,097,000 respectively.

Other intangible fixed assets as of December 31, 2001 and 2002 are presented net of accumulated amortization of £54,000 and £419,000 respectively.

### (b) Tangible fixed assets

Prior to the introduction of FRS10 under U.K. GAAP for business acquisitions, where the aggregate of the fair values of the net assets acquired exceeded the cost of the acquired net assets resulting in negative goodwill, such excess was credited directly to reserves. Negative goodwill arising on the acquisition of Jago Production SAS has been accounted for according to this policy. Under U.S. GAAP such excess is eliminated by proportionately reducing the value of the non-current assets acquired.

Tangible fixed assets as of December 31, 2001 and 2002 are presented net of accumulated depreciation of £3,530,000 and £4,163,000 respectively.

### (c) Acquisition of RTP

In 2001, the Group purchased the majority interest of RTP through a two-step acquisition effected in July and December 2001. Under U.K. GAAP, the aggregate purchase price was £39.4 million, including £35.3 million of ordinary shares, £3.5 million of cash, and £0.6 million in acquisition costs. The acquisition was recorded using the purchase method of accounting under both U.K. and U.S. GAAP. Goodwill was determined as the difference between the purchase price and the fair value of the net assets acquired. Under both U.K. and U.S. GAAP the investment in RTP was equity accounted for until control was gained on December 27, 2001 and consolidated from that date on.

The adjustments between U.K. and U.S. GAAP related to the RTP acquisition relate mainly to differences in (i) the valuation of contingent purchase price consideration, (ii) the methods of purchase price allocation and (iii) amortization of goodwill.

*Contingent consideration.* Under U.K. GAAP, contingent consideration has not been recognized as part of the acquisition cost. Under U.S. GAAP, the Company has applied EITF 97-15, "Accounting for Contingency Arrangements Based on Security Prices in a Purchase Business Combination" to estimate the contingent consideration as of the acquisition date. Under EITF 97-15 a contingency arrangement that

does not result in a guarantee of the minimum value of the total consideration should be recorded at an amount equal to the maximum number of shares that could be issued multiplied by the fair value per share at the date of the acquisition. However, the recorded amount may not exceed the target value of the consideration issued at the date of acquisition (i.e., the lowest total value at which additional consideration would not be required to be issued). The subsequent payment or issuance of additional consideration resulting from either of these security price contingencies would not change the recorded cost of the acquisition. The application of the provisions of EITF 97-15 has resulted in a £5.3 million increase in the purchase consideration.

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*Purchase price allocation.* Under U.S. GAAP an intangible asset shall be recognized as an asset apart from goodwill if it arises from contractual or other legal rights or if it is separable, that is, it is capable of being separated or divided from the acquired entity and sold, transferred, licensed, rented, or exchanged. In addition, U.S. GAAP requires amounts allocated to acquired in-process research and development that do not have an alternative use to be expensed through earnings in the period of acquisition. Under U.S. GAAP, the investment in Waratah Pharmaceuticals Inc ("Waratah") was fair valued based on prices quoted by the Canadian Venture Stock Exchange as of each acquisition date. The difference between the fair value and the equity value of the investment was allocated to goodwill. Under U.K. GAAP, the investment was fair valued when the Company gained control in December 2001. The deferred taxation impact of all these differences has been recognized in the purchase price allocation for U.S. GAAP purposes.

In January 2002 Waratah merged with Transition Therapeutics Inc. ("Transition") and Waratah shareholders were awarded 0.83333 Transition shares for every one share of Waratah held. After the merger, the Group holds approximately 8.2% of Transition ordinary shares, which are listed on the Canadian TSX Venture. Under U.K. GAAP, the Group continued to account for the investment at cost. Under U.S. GAAP, on the merger date the Group ceased to apply the equity method of accounting and carries the investment in Transition at adjusted cost.

*Goodwill.* Under U.K. GAAP goodwill is being amortized over 20 years on a straight-line basis. Under U.S. GAAP, goodwill is not amortized but is subject to regular impairment tests. In addition, under U.S. GAAP, the excess of the fair value of the net assets acquired in December 2001 over the purchase consideration (negative goodwill) resulting from difference in the purchase price allocation has been allocated as a pro rata reduction of the non-current assets acquired including in-process research and development.

**(d) Results of equity investments (RTP)**

In accordance with the equity method of accounting under U.K. and U.S. GAAP, the Group records its relative share of profits and losses reported by associated companies. Accordingly, this adjustment includes the Group's proportionate share of U.K. to U.S. GAAP adjustments related to net income of RTP between July 19 and December 27, 2001.

**(e) Acquired in-process research and development costs**

Under U.K. GAAP acquired in-process research and development is considered part of goodwill. Under U.S. GAAP acquired in-process research and development which does not have an alternative future use is separately identified and written off directly to net income in the period that the acquisition was made. The reversal of the UK GAAP amortization of the portion of goodwill allocated to acquired in-process research and development under U.S. GAAP has been included within the "Amortization of Goodwill" caption in the reconciliation of net loss.

Acquired in-process research and development of £4,646,000 in 2002 represents the fair value of Bioglan AB's efforts to develop the technologies described in note 27; Acquisitions. In May 2002 the group acquired the drug delivery business of Bioglan AB for £3.6 million in cash and the assumption of £0.4 million of net liabilities. For U.S. GAAP purposes, the Group valued acquired in-process research and development with no alternative future use at £5.1 million, which created negative goodwill of £1.1 million that was allocated among non-current assets acquired including acquired research and development. Accordingly, the fair value of tangible fixed assets acquired in the amount of £0.7 million was reduced to £nil and £4.6 million of in-process research and development was expensed in the period of acquisition. Acquired in-process research and development of £18,893,000 in 2001 represents the fair value of the RTP's efforts to internally develop its Insoluble Drug Delivery technology platform. The Group has determined the fair values

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of the acquired in-process research and development, which rely on information available at the acquisition date and assumptions as to future operations as of that date.

**(f) Contingent consideration charged to goodwill**

The Group effected the acquisition of Krypton and Jago through the exchange of warrants and shares. The issuance of certain of these warrants and shares is contingent upon the occurrence of certain future events. Under U.K. GAAP, the Group estimated the fair value of the contingent consideration to determine the acquisition cost. The resulting goodwill was eliminated against shareholders' funds.

Under U.S. GAAP the acquisition cost has been adjusted to remove the contingent consideration, which is only recognized when it is determinable beyond reasonable doubt, therefore contingent consideration charged to goodwill reserves has been reversed out of shareholders' funds under U.S. GAAP.

**(g) Measurement of purchase consideration**

The Company effected its acquisition of Krypton in 1996 through the exchange of shares and warrants and recorded the consideration at the estimated fair value of the shares and warrants.

Under U.K. GAAP, the fair value of the shares and warrants issued for the acquisition was estimated by reference to the price that the Company's shares were issued for on the same day under a rights issue and public placing. U.S. GAAP requires that the fair value of shares and warrants issued to effect a business combination be based on the market price for a reasonable period before and after the date the terms of the acquisition were agreed to and announced. The effect of this difference was to increase the value measurement of purchase consideration by £11,942,000 which was fully allocated to acquired in-process research and development and wrote off to income in 1996 with an offsetting adjustment to share premium on acquisition. As a result, the impact of this adjustment in net equity was £nil and at December 31, 2001 and 2002 it represents an increase of £11,942,000 in retained losses and an increase in share premium by the same amount.

**(2) Deferred shares and shares and warrants to be issued**

Under U.K. GAAP, contingent consideration payable in connection with the acquisition of Jago is included within shareholders' funds as "deferred shares". As of December 31, 2001, the Group had also recorded contingent consideration payable within shareholders' funds in the amount of £4.8 million in connection with the acquisition of Krypton. The amount at December 31, 2002 related to Krypton was £nil.

Under U.S. GAAP, contingent consideration is recognized only when determinable beyond reasonable doubt, therefore deferred shares and shares and warrants to be issued have been reversed out of shareholders' funds under U.S. GAAP.

In addition, under U.K. GAAP in connection with the acquisition of RTP, £5.8 million of the total consideration was payable in shares which were issued subsequent to December 31, 2001. As of December 31, 2001, these shares had been included within shareholders' funds and warrants to be issued. Under U.S. GAAP, such amounts would be recorded as a liability until the shares are issued.

**(3) Shares issued related to contingent consideration**

In April 2002, all contingencies related to the Deferred "A" Shares were removed based on the first commercial launch of Paxil CR. In connection with the removal of these contingencies, in 2002 the Group issued 12 million Ordinary Shares to Dr. Gonella, the vendor of Jago. Under U.S. GAAP,

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these shares were recorded within shareholders' funds at the market value at the date the contingencies were removed.

Under U.K. GAAP the shares were recorded at the market price at the date of issuance of deferred shares (July 20, 2000). The adjustment reverses the value of equity share capital and premium in the amount of £11.3 million. A corresponding adjustment in the amount of £9.4 million has been recorded within Goodwill and other intangible fixed assets that represents the fair value of shares issued under U.S. GAAP.

**(4) Share-based compensation**

Under U.K. GAAP, the Company does not recognize compensation expense associated with its stock option plans granted to employees.

Under U.S. GAAP the Company has adopted Financial Accounting Standard No. 123, "Accounting for Stock-Based Compensation" (FAS 123). In accordance with the provisions of FAS 123, the Company has elected to continue to apply the recognition principles of APB

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Opinion No. 25, "Accounting for Stock Issued to Employees," and related interpretations ("APB 25") in accounting for its plans. For awards under the Company's option plans where the exercise price of the option equals the market price of the shares on the date of grant and the number of options granted is known (fixed plan), no compensation expense is recognized. For awards under the Company's variable option plans, an estimate of compensation expense is made when it is probable that the relevant performance targets will be achieved. Compensation cost under these plans is measured based on the market value of the shares at the date the number of options to ultimately be awarded is known less the exercise price of the option. Periodic charges to expense are made for the difference between the market price and the exercise price when it is probable that the performance criteria will be met. A compensation expense of £181,000 (2001: £215,000, 2000: £734,000) has been recognized under APB 25 in relation to those options where it is considered probable that the performance criteria will be met.

Had the Company elected to recognize compensation expense based upon the fair value at the grant date for awards under stock option plans consistent with the methodology prescribed by FAS 123, the Company's U.S. GAAP net loss would have been increased by £3,138,000, £2,883,000 and £1,725,000 in the years ended December 31, 2002, 2001 and 2000, respectively. Earnings per share would have been reduced by 0.5p, 0.5p and 0.3p per share in the years ended December 31, 2002, 2001 and 2000, respectively. These pro forma amounts may not be representative of future disclosures since the estimated fair value of stock options is amortized to expense over the vesting period, and additional options may be granted in future years. The fair value for these options was estimated at the date of grant using the Black-Scholes option-pricing model with the following weighted average assumptions for the year ended December 31, 2002: dividend yield 0.0% (2001 and 2000: 0.0%); expected volatility 55.0% (2001: 58.0%, 2000: 55.0%); risk-free interest rate 5.1% (2001: 5.2%, 2000: 5.5%); and expected option term 7 years (2001 and 2000: 7 years). The weighted average fair value of options granted during the year ended December 31, 2002 for which the exercise price equals the market price on the grant date was 43.0p (2001: 41.0p, 2000: 49.0p). No options were granted for which the exercise price was below or exceeded the market price.

At December 31, 2002 there were 40,456,933 outstanding options with a weighted average option price of 69.4 pence (2001: 34,724,115 and 68.6 pence, 2000: 26,316,828 and 66.0 pence). During the year ended December 31, 2002 11,234,887 options were granted at a weighted average option price of 70.0 pence and 4,178,216 options were cancelled or expired at a weighed average option price of 69.5 pence. During the year ended December 31, 2001 9,962,366 options were granted at a weighted average option price of 75.1 pence and 818,435 options were cancelled or expired at a weighted average option price of 72.5 pence. During the year ended December 31,

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2000 4,059,406 options were granted at a weighted average option price of 85.0 pence and 2,303,717 options were cancelled or expired at a weighted average option price of 73.0 pence.

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

### **(5) Revenue recognition**

Under U.K. GAAP contract revenue is recognized when it is earned and non-refundable and to the extent that there are no future obligations pursuant to the revenue, in accordance with the contract terms. Refundable contract revenue is treated as deferred until such time as it is no longer refundable. Under U.S. GAAP, SAB 101 requires deferral and amortization of up-front licensing fees where there is a continuing involvement with the licensed asset through the provision of research and development services, manufacturing services or other similar activities even if the fee is non-refundable. As a result, under U.S. GAAP certain non-refundable up-front payments have been deferred over the development period of the contract term on certain agreements. The Company adopted SAB 101 as of January 1, 2000 and on this date the Company recorded a cumulative- effect-type adjustment to net income of £542,000. This adjustment represents the difference between shareholders' funds as of December 31, 1999 and the shareholders' funds that would have been reported at that date if SAB 101 had been applied retroactively for all periods that would have been affected.

Deferred revenue reflects the amount of revenue not currently eligible for recognition under U.S. GAAP as well as the reversal of £7.8 million (£4.8 million as of December 31, 2001) deferred income under U.K. GAAP related to the sale of royalty interests, which is treated as debt under U.S. GAAP.

### **(6) Sale of royalty interests**

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Under U.K. GAAP payments received from a third party in return for the sale of a portion of potential future royalty and revenue streams from a selection of products are reflected within other operating income when the risk of reimbursement has effectively been transferred to the third party. The monies are used to fund internal research and development. Royalties repaid to third parties are treated as cost of goods sold.

U.S. GAAP requires such payments to be recorded as debt where there is continuing involvement in the generation of the cash flows due to the third party. The U.S. GAAP adjustment includes the reversal of income recorded from the third party as well as recording the interest charge for the period on the outstanding funding liability balance. Repayments made to third parties in the form of royalty payments that are expensed under U.K. GAAP are reversed under U.S. GAAP since they are treated as repayment of debt.

### **(7) Employee Benefit Trust**

Under U.K. GAAP the Ordinary Shares of the Company held by the SkyePharma PLC General Employee Benefit Trust are recorded at cost and accounted for as investments. The value of shares and options granted are deducted from the cost value of shares held in the Employee Benefit Trust and charged to current period expense or over the vesting period if options vest over a period of time.

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Under U.S. GAAP the Ordinary Shares of the Company purchased by the Employee Benefit Trust are accounted for at cost as treasury shares which reduce shareholder's funds. Gains or losses arising on subsequent issuance of the shares to employees are recorded as adjustments to shareholders' funds. The reduction in cost, which is expensed under U.K. GAAP, is reversed under U.S. GAAP to maintain the treasury shares at cost. All employee compensation expense is recorded under APB 25.

### **(8) Financial Instruments**

Under U.K. GAAP, periodic gains and losses on interest and foreign currency derivatives are not recognized in the income statement until the operational transactions to which they are linked occur. For U.S. GAAP reporting purposes, on January 1, 2001 the Group adopted Financial Accounting Standard No. 133 "Accounting for Derivative Instruments and Hedging Activities" ("FAS 133") as amended by FAS 137 and FAS 138. FAS 133 establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other contracts (collectively, referred to as derivatives) and for hedging activities. FAS 133 requires that an entity recognize all derivatives as either assets or liabilities in the balance sheet and measure those instruments at fair value. Changes in fair values are recorded in earnings or other comprehensive income, depending on whether the derivative instrument is part of a hedge transaction and, if it is, the type of hedge transaction. FAS 133 prescribes requirements for designation and documentation of hedging relationships and ongoing assessments of effectiveness in order to qualify for hedge accounting.

The Group has also reviewed its contractual arrangements for the existence of embedded derivatives that should be separately accounted for under FAS 133. If embedded derivatives are identified as a result of this review, they are recorded separately from their host contracts at fair value, with changes in fair value recognized in current earnings. The Group did not identify any such embedded derivatives as of January 1, December 31, 2001 or December 31, 2002.

Accordingly, under U.S. GAAP all derivative instruments have been recorded on the balance sheet at fair value upon adoption of FAS 133. The Company did not designate any of its derivatives as qualifying hedge instruments under FAS 133. In accordance with the transition provisions of FAS 133 on January 1 2001, the Company recorded a cumulative-effect-type adjustment of £643,000 within Other Comprehensive Income in connection with certain foreign currency derivative instruments. During 2001 the Group reclassified within earnings all the transition adjustment that was recorded in Other Comprehensive Income. In addition, the difference between the previous carrying amount of certain interest rate derivatives and their fair values was reported as a cumulative-effect-type adjustment of net income of £820,000. The Group also recognized an offsetting amount on the related hedged liabilities by adjusting their carrying amounts at that date. As a result, the net cumulative-effect-type adjustment of net income is £nil. The adjustment of the carrying amount of the hedged liability was amortized to earnings over the period of the derivative.

### **(9) Deferred Taxes**

Under U.K. GAAP, deferred tax is provided on timing differences which at the balance sheet date result in an obligation to pay more tax or a right to pay less tax at a future date. Deferred tax assets are recognized to the extent that it is more likely than not that they will be recovered. Under U.S. GAAP, full provision is required for deferred tax liabilities and deferred tax assets including losses carried forward recognized subject to valuation allowances. Given the uncertainty of the recoverability of the Group's tax losses carried forward, no deferred tax asset is recognized under U.K. GAAP and a valuation allowance has been provided in full for the deferred tax assets recognized under U.S. GAAP (December 31, 2002: £42,733,000; December 31, 2001: £60,362,000; December 31, 2000: £48,294,000). The breakdown of the potential



deferred tax assets and additional tax disclosures are included in Notes 8 and 19 to the financial statements.

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#### (10) Fixed Asset Investments

Under U.K. GAAP, fixed asset investments are stated at cost or Directors' valuation, less provision for permanent diminution in value. Under U.S. GAAP certain investments previously equity accounted are carried at adjusted cost.

#### (11) Joint arrangements

Under U.K. GAAP, where the Group has certain contractual agreements with other participants to engage in joint activities that do not create an entity carrying on a trade or business of its own, they are accounted for as a joint arrangement. The Group includes its share of the assets, liabilities and cash flows in such joint arrangements measured in accordance with the terms of each arrangement, which is usually pro-rata to the Group's interest in the joint arrangement. Under U.S. GAAP, such arrangements are viewed as synthetic Joint Ventures and accounted for under the gross equity method. This difference does not have an impact on the overall net loss of the Group but under U.S. GAAP, selling and marketing costs and research and development costs would be reduced by £1,801,000 (2001: £2,896,000; 2000: £2,250,000) and £nil (2001: £nil; 2000: £2,665,000) respectively and be shown net as the Group's share of the operating loss in the Joint Venture. The difference has no impact on the Group's overall consolidated cash flow although under U.S. GAAP operating cash outflows would be £1,801,000 (2001: £6,857,000; 2000: £4,915,000) higher and cash outflows from investing activities would be £1,801,000 (2001: £6,857,000; 2000: £4,915,000) lower.

#### (12) Consolidated Cash Flow Statements

The consolidated cash flow statements prepared in accordance with FRS 1; Cash flow statements (Revised) presents substantially the same information as that required under U.S. GAAP. However, there are certain differences from U.K. GAAP with regard to the classification of items within the cash flow statement and with regard to the definition of cash and cash equivalents.

Under U.K. GAAP, cash flows are presented separately for trading activities, returns on investments and servicing of finance, taxation, capital expenditure, acquisitions and disposals, management of liquid resources and financing activities. Under U.S. GAAP, however, only three categories of cash flow activities are reported, being operating activities, investing activities and financing activities. Cash flows from taxation and returns on investments and servicing of finance would, with the exception of dividends paid, be included as operating activities under U.S. GAAP. Cash flows from capital expenditure, acquisitions and disposals would be combined as investing activities under U.S. GAAP.

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Under U.S. GAAP, cash and cash equivalents do not include overdrafts, but do include investments with remaining maturities of less than 3 months when acquired. A summarized consolidated statement of cash flows under U.S. GAAP is set out below.

	Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
Net cash used in operating activities	(11,196)	4,035	(1,772)
Net cash used in investing activities	(15,650)	(14,938)	(16,153)
Net cash provided by financing activities	55,501	(5,267)	19,969
Net (decrease)/increase in cash and cash equivalents	28,655	(16,170)	2,044
Cash and cash equivalents at beginning of year	13,674	42,878	26,892
Exchange adjustments	549	184	(875)
Cash and cash equivalents at end of year	42,878	26,892	28,061

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Year to December 31, 2000 £'000	Year to December 31, 2001 £'000	Year to December 31, 2002 £'000
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**(13) Earnings per share**

Diluted "earnings per share" (EPS) is not presented since the Group reported a net loss under U.S. GAAP and the common equivalent shares from warrants, stock options and contingent issuance of shares would have an anti-dilutive effect on earnings per share. The securities that could potentially dilute basic EPS in future are set out below:

	Year to December 31, 2000 Number	Year to December 31, 2001 Number	Year to December 31, 2002 Number
Stock outstanding in terms of basic earnings per share	508,228,000	526,250,000	577,018,000
"B" Warrants outstanding	5,674,550	5,652,542	
"C" Warrants outstanding	1,800,000		
"D" Warrants outstanding			2,500,000
"E" Warrants outstanding			2,500,000
DepoTech Warrants outstanding	291,777	291,777	291,777
Warrants assumed from SkyePharma Inc.	2,054,825		
Employee stock options outstanding	26,316,828	34,724,115	40,456,933
Convertible bonds	45,000,000	71,566,265	71,566,265
	<b>589,074,203</b>	<b>638,192,922</b>	<b>694,041,198</b>
Stock outstanding in terms of diluted EPS			
Contingent shares relating to Krypton consideration (see note 23; Shares and Warrants to be issued)	7,500,000	7,500,000	
Contingent warrants relating to Krypton consideration (see note 23; Shares and Warrants to be issued)	750,000	750,000	
Contingent shares relating to RTP deferred consideration (see note 23; Shares and Warrants to be issued)			8,100,000
Paul Capital Royalty Acquisition Fund (see note 23; Shares and Warrants to be issued)			11,225,722
Deferred Shares relating to Jago consideration (see note 22; Share Capital)	24,000,000	24,000,000	12,000,000
	<b>621,324,203</b>	<b>670,442,922</b>	<b>725,366,920</b>

Contingent shares to be issued relating to Jago, RTP and Paul Capital Royalty Acquisition Fund have been set out above. While these are potentially dilutive, they would not be used for calculating diluted EPS under U.S. GAAP as the amount is not determinable beyond reasonable doubt.

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**II. Additional disclosures**

The following disclosures are included to comply with the United States Securities and Exchange Commission's regulations for foreign registrants. As indicated, certain disclosures are presented on a U.K GAAP measurement basis.

**(1) Acquisition of the drug delivery business of Bioglan AB**

In May 2002 SkyePharma acquired the entire drug delivery business of Bioglan AB. The acquired rights include Bioglan's Biosphere injectable technology and those rights to DermaStick, Crystalip and ES-Gel topical drug delivery technologies that remained with Bioglan after

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the January 2001 development and commercialization licensing agreement.

The combination of these and the Group's existing technologies will significantly enhance SkyePharma's topical technology base. In addition, the acquired Biosphere injectable technology will complement SkyePharma's existing DepoFoam sustained release injectable technology in providing additional drug delivery options for proteins and peptides.

### (2) Acquisition of RTP

For U.S. GAAP purposes, the Group has determined the fair values of the net assets acquired as of each acquisition date based on information currently available and on current assumptions as to future operations. The Group acquired RTP through two purchases in July and December 2001 and therefore, the Group has identified the cost of each investment, the fair value of the underlying assets acquired, and the goodwill for each step acquisition. The Group has obtained independent appraisals of the fair values of the acquired intangible assets and their remaining useful economic lives. The Group has also completed the review and determination of the fair values of the other assets acquired and liabilities assumed. The following table summarizes the fair values of the assets acquired and liabilities assumed in each step acquisition:

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	July 19, 2001 £'000	December 27, 2001 £'000
Current assets	9,992	6,602
Intangible assets	2,658	7,523
Tangible assets	2,451	2,017
Investments	4,672	2,220
Acquired in-process research and development costs	20,998	19,719
Goodwill	32,927	(2,204)
<b>Total assets acquired</b>	<b>73,698</b>	<b>35,877</b>
Current liabilities	4,776	2,701
Demand notes	3,657	3,598
Deferred taxes	2,500	2,999
<b>Total liabilities assumed</b>	<b>10,933</b>	<b>9,298</b>
<b>Net assets</b>	<b>62,765</b>	<b>26,579</b>
Equity interest acquired	40.2%	59.8%
Net assets acquired	25,232	15,894
<b>Net consideration</b>		
Cash	3,529	
Acquisition expenses	590	
Shares of SkyePharma <sup>(1)</sup>	21,113	19,492
Demand notes acquired		(3,598)
<b>Total</b>	<b>25,232</b>	<b>15,894</b>

(1)

It represents 26,189,061 and 23,770,306 shares of SkyePharma for the first and second purchase, respectively. Of the total number of shares, 8,059,268 (4,313,982 and 3,745,286 for the first and the second purchase, respectively) were issued subsequent to December 31, 2001 and therefore, under U.S. GAAP the value of those shares has been recorded as a liability. For the first purchase, the shares have been valued based on the average market price of the Company's common shares over a short period before and after the terms of the acquisition were agreed to. For the second purchase, the shares have been valued given consideration to the provisions of EITF 97-15, "Accounting for Contingency Arrangements Based on Security Prices in a Purchase Business Combination". As a result, the total consideration has been recorded at an amount equal to the target value of the consideration issued at the date of acquisition (i.e., the lowest total value at which additional consideration would not be required to be issued) as this amount is lower

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than the maximum number of shares that could be issued multiplied by the fair value per share at the date of the acquisition.

The intangible assets acquired were allocated as follows:

	<b>July 19, 2001 £'000</b>	<b>December 27, 2001 £'000</b>
Patents	2,658	7,523
Equity interest acquired	40.2%	59.8%
Net assets acquired	1,069	4,499

The useful economic life of the acquired intangible assets is approximately 20 years. The £13.3 million of goodwill on the first purchase was assigned to the pharmaceutical reportable segment. The £1.3 million negative goodwill on the second purchase was allocated as a pro rata reduction of the amounts assigned to the non current assets acquired and the acquired in-process research and development costs. Goodwill is non-deductible for tax purposes.

In connection with the acquired in-process research and development (IPR&D), £18.9 million expensed in the period ended December 31, 2001 as the IPR&D projects had not reached technological feasibility nor had any alternative future use. This amount represents the valuation of the IPR&D at each acquisition date less the allocation of a portion of the negative goodwill on the

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second purchase. RTP was in the in the process of applying its Insoluble Drug Delivery ("IDD") technology to several products, including the propofol, fenofibrate and busulfan. Each of these in-process IDD formulated drugs were analysed and valued separately using the income approach. The income approach includes an analysis of the markets, projected cash flows, and technical and commercial risks associated with achieving such cash flows. The estimated cash flows were projected over periods ranging from 15 to 20 years after the acquisition dates, and were discounted at rates ranging from 20% to 25% in order to determine the present value. The discount rates were selected on a project-by-project basis and were based on the Group's weighted average cost of capital adjusted for the risks associated with the fact that RTP had yet to obtain FDA approval for its drug delivery technology, estimated growth, profitability, technical and commercial risks of the acquired IPR&D projects. Should the development of the products incorporating the acquired technology be completed successfully, the Company anticipates that the products could begin to generate cash flows over the three-year period following the acquisitions. However, development of these technologies remains a significant risk due to the remaining effort to achieve technological feasibility. The valuation of the acquired IPR&D also gave consideration to the stage of completion of the projects at the time of the acquisition and the degree to which the projects relied on prior, existing technology. With respect to the stage of completion, propofol and busulfan were in Phase II and fenofibrate was in Phase I. All other products were at similar, or earlier, stages of completion.

### Reasons for the acquisition

RTP was acquired for its IDD technology, its late stage proprietary product pipeline available for out licensing, its third party clients and client products that are different but complimentary to the Group's and the match between SkyePharma and RTP's solubilization intellectual property.

### Pro forma financial data

The following unaudited pro forma financial information for the years ended December 31, 2001 and 2000 has been prepared in accordance with U.K. GAAP, and assumes the RTP acquisition occurred as at the beginning of the respective periods, after making certain adjustments, including the amortization of intangible assets. The pro forma results have been prepared for comparative purposes only and are not necessarily indicative of the results of operations that may occur in the future or that would have occurred had the acquisition of RTP been affected on the dates indicated. The unaudited pro forma amounts do not consider synergies resulting from acquisitions and do not purport to be indicative of the results of operations which actually would have resulted had the acquisitions occurred on the date indicated, or which may result in the future.

<b>Year to December 31, 2000 £'000</b>	<b>Year to December 31, 2001 £'000</b>
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Turnover	24,950	48,499
Net loss	(32,508)	(15,810)
Basic and diluted loss per Ordinary Share	(5.9p)	(2.8p)

**(3) Concentration of credit risk, major customers and suppliers**

Financial instruments that potentially subject the Group to concentration of credit risk consist primarily of cash and cash equivalents and short-term bank deposits.

The Group places its cash and cash equivalents and short-term bank deposits through high credit quality financial institutions diversifying its holdings of short-term financial instruments across a range of money market instruments of a variety of counter parties and, by policy, limits the amount of credit exposure with any one counter party.

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The Company normally enters into several agreements to conduct its business including research and development, manufacturing and distribution and royalty contracts. The Company's customers are primarily pharmaceutical and biotechnology companies. In 2002 the Company had revenue from research and development contracts with three third parties (2001: three; 2000: one) representing 54% of total revenues (2001: 59%; 2000: 38%), where revenue derived from each party individually represented over 10% of total revenues in each year. In February 2002, the affairs of a major customer were placed into administration. The marketing rights of this customer were transferred to two third parties. Royalties receivable in 2002 relate predominantly to three customers (2001: one; 2000: one).

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. However, whilst regulatory requirements applicable to drugs tend to make the substitution of suppliers costly and time-consuming the Company is likely to be able to gain access to alternative supplies.

**(4) Recent U.S. GAAP Pronouncements**

On January 1, 2002 the Group adopted SFAS No. 142 "Goodwill and Other Intangible Assets." SFAS 142 requires that goodwill will no longer be amortized over its estimated useful life. The Group must instead identify and value its reporting units for the purpose of assessing, at least annually, potential impairment of goodwill allocated to each reporting unit. Separate intangible assets with finite lives continue to be amortized over their useful lives. During the second quarter of 2002, the Group completed the transitional goodwill impairment test prescribed in SFAS 142 with respect to existing goodwill. The transitional goodwill impairment test involved a comparison of the fair value of the Group's reporting unit, as defined under SFAS 142, with its carrying amount as of the adoption date. As a result of the transitional impairment tests performed as of January 1, 2002, there was no indicator of goodwill impairment. If the Group had accounted for goodwill under SFAS 142 for the year ended December 31, 2001, the impact on reported U.S. GAAP results would have been as follows:

	<b>£'000</b>
Net loss under U.S. GAAP	(43,868)
Add: Goodwill amortization	8,552
Adjusted net loss under U.S. GAAP	(35,316)
Adjusted basic and diluted loss per Ordinary Share under U.S. GAAP (pence)	(6.7)p

The estimated aggregate amortization expense for intangible assets with finite lives including intellectual property and development costs under U.S. GAAP for each of the succeeding five years is as follows:

<b>Years ending December 31,</b>	<b>£'000</b>
2003	2,300
2004	2,300
2005	2,300
2006	2,300
2007	2,300

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On January 1, 2002 the Group adopted SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." SFAS 144 develops one accounting model for long-lived assets, including discontinued operations to be disposed of by sale. It requires that all long-lived assets be

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measured at the lower of carrying amount or fair value less cost to sell whether reported in continuing or discontinued operations. The adoption of SFAS 144 has not had a material impact on the Group's financial position or results of operations.

In August 2001, the FASB issued SFAS No. 143, "Accounting for Obligations Associated with the Retirement of Long-Lived Assets". This standard will be effective for the Group's fiscal year beginning January 1, 2003. The standard requires that such obligations be capitalised as part of the assets' cost at the time of initial recognition, with the related liability discounted to its fair value at the date of recognition. The income statement impact of adopting this standard will be presented as a cumulative effect of a change in accounting principle. The Group does not believe the adoption of this standard will have a material impact on its financial position or results of operations.

In April 2002, the FASB issued SFAS No. 145. This standard will require gains and losses from extinguishment of debt to be classified as extraordinary items only if they meet certain criteria. Any gain or loss on extinguishment will be recorded in the most appropriate line item to which it relates within net income before extraordinary items. SFAS 145 is effective for fiscal years beginning after May 15, 2002. However, certain sections are effective for transactions occurring after May 15, 2002. The Group does not expect the adoption of this standard will have a material impact on its financial position or results of operations.

SFAS 146 "Accounting Costs Associated with Exit or Disposal Activities", which was issued at the end of June 2002, addresses issues regarding the recognition, measurement, and reporting of costs associated with exit and disposal activities, including restructuring activities. This standard will be implemented with effect from January 1, 2003. The Group does not expect the adoption of this standard will have a material impact on its financial position or results of operations.

In November 2002, the FASB issued Interpretation No. 45 (FIN 45), "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others". FIN 45 expands on the accounting guidance of other SFASs FIN 45 elaborates on the existing disclosure requirements for most guarantees, including loan guarantees such as standby letters of credit. It also clarifies that at the time a company issues a guarantee, it must recognize an initial liability for the fair value, or market value, of the obligations it assumes under that guarantee and must disclose that information in its interim and annual financial statements. FIN 45 will be implemented on a prospective basis to guarantees issued or modified after December 31, 2002. The disclosure requirements in this Interpretation are effective for financial statements of periods ending after December 15, 2002. The Group is currently evaluating the impact of this interpretation on its financial position and results of operations.

In January 2003, the FASB issued Interpretation No. 46, "Consolidation of Variable Interest Entities" (FIN 46). Under this interpretation, certain entities known as "Variable Interest Entities" (VIE) must be consolidated by the "primary beneficiary" of the entity. The primary beneficiary is generally defined as having the majority of the risks and rewards arising from the VIE. For VIE's in which a significant (but not majority) variable interest is held, certain disclosures are required. The measurement principles of this interpretation will be effective for the Group's December 31, 2003 financial statements. The Group is currently assessing the impact of this interpretation on its financial position and results of operations.

In November 2002, the Financial Accounting Standards Board issued Emerging Issues Task Force issue No. 00-21, "Revenue Arrangements with Multiple Deliverables" (EITF 00-21). EITF 00-21 addresses certain aspects of the accounting by a company for arrangements under which it will perform multiple revenue-generating activities. EITF 00-21 addresses when and how an arrangement involving multiple deliverables should be divided into separate units of accounting. EITF 00-21 provides guidance with respect to the effect of certain customer rights due to company

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nonperformance on the recognition of revenue allocated to delivered units of accounting. EITF 00-21 also addresses the impact on the measurement and/or allocation of arrangement consideration of customer cancellation provisions and consideration that varies as a result of future actions of the customer or the company. Finally, EITF 00-21 provides guidance with respect to the recognition of the cost of certain deliverables that are excluded from the revenue accounting for an arrangement. The provisions of EITF 00-21 will apply to revenue arrangements entered into in fiscal years beginning after June 15, 2003. The Group is currently evaluating the impact of EITF 00-21 on its

financial position and results of operations.

#### (5) Leases

The Group leases certain tangible assets under long-term arrangements. As of December 31, 2002 the approximate future minimum lease payments under non-cancelable leases that have initial or remaining non-cancelable lease terms in excess of one year are as follows:

	Year ending December 31,	
	Finance £'000	Operating £'000
2003	1,089	2,644
2004	100	2,651
2005	56	3,309
2006	84	2,090
2007		2,101
Thereafter		18,665
	<hr/>	<hr/>
Total minimum lease payments	1,329	31,460
Less interest payable under finance leases	(9)	
	<hr/>	<hr/>
	1,320	31,460
	<hr/>	<hr/>

At December 31, 2002 total future minimum rentals under non-cancelable sub leases were £652,000 (December 31, 2001: £1,143,000).

#### (6) Commitments

The Group conducts R&D activities under a number of collaboration arrangements with pharmaceutical companies to develop products utilizing its technologies. These activities are conducted under varying fixed price or cost plus arrangements which are designed to permit the Group to recover its development costs. The Group does not have any actual or contingent obligations to deliver successful results under any of these arrangements, and amounts earned under these contracts are not refundable, even if the research effort is unsuccessful. Except as described below, the Group does not consider any individual contract to be significant.

##### *Oral*

The Company is currently receiving significant royalty revenues under two collaborative arrangements for its Geomatrix technology: Xatral OD and Paxil CR. Under the terms of these agreements, each of the development partners bore all of the costs of research and development according an agreed budget and are obligated to pay the Company continuing royalties of between 1.5% and 5% of net sales. In return, the Company granted the development partners exclusive licenses to use the Geomatrix technology in these products throughout the world. The license agreement for Xatral OD was signed in May 1999 with Sanofi-Synthelabo. The license agreement for Paxil CR was signed in March 1996 with SmithKline Beecham plc (now part of GlaxoSmithKline).

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The only collaborative arrangement involving Geomatrix technology in which the Company is responsible for conducting clinical trials is the development and licensing agreement for a once-daily version of Requip (ropinirole) with GlaxoSmithKline, which was entered into in September 1999 with SmithKline Beecham (now part of GlaxoSmithKline). Under the terms of the agreement with GlaxoSmithKline the Company is responsible for all development activities for Requip oral controlled release tablets up to regulatory filing, in collaboration with GlaxoSmithKline. As part of the agreement, GlaxoSmithKline made an equity investment of £4.9 million in the Company and will pay milestone payments at intervals up to product approval, including an up-front payment. In December 2001 and June 2003, the Company and GlaxoSmithKline amended the 1999 license for Requip to take account of additional activities that had been undertaken by SkyePharma. Under the terms of the amendments, the timeline of certain milestone payments was renegotiated together with additional development revenues to reimburse SkyePharma for the additional activities. On commercialization of once-daily Requip, the Company will receive royalties on future product sales. GlaxoSmithKline will take responsibility for preparing and pursuing all necessary regulatory approvals. The once-daily version commenced Phase III clinical trials in June 2003.

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The Company has a development and license agreement for Dilacor XR, signed in 1998 with Rorer, a member of the Rhône Poulenc Rorer Group (now part of Aventis Pharma). In 1997, Rorer granted to Watson Laboratories, Inc. (with the consent of the Company) exclusive rights to market, advertise, promote, sell and distribute Dilacor XR. The grant of rights to Watson Laboratories does not affect any entitlements of the Company or any of the material terms of the collaborative arrangement. The Company no longer receives royalties under this agreement.

### *Injectable*

In March 1994, SkyePharma Inc., formerly known as DepoTech, entered into a collaboration agreement with Chiron. The objective of the collaboration was to develop and commercialize DepoCyt for use in the treatment of neoplastic meningitis from lymphomas and solid tumors, and to explore the use of the Company's DepoFoam for certain other Chiron compounds. The Chiron agreement, as amended, granted Chiron rights to market and sell DepoCyt in the United States. Chiron funded, and was obligated to fund, 50% of the clinical development expenses in the United States. Canadian registration expenses and the cost of clinical trials required in Europe were funded by Chiron until June 1997, when the Chiron agreement was amended in connection with the agreement with Pharmacia Corporation described below. Under the Chiron agreement SkyePharma Inc. manufactured DepoCyt, Chiron marketed, sold, and distributed DepoCyt in the United States, and the parties shared all profits equally. The Company also funded 50% of the sales and marketing expenses incurred for DepoCyt. Chiron also had a right of first refusal to obtain a license to alternate DepoFoam formulations of cytarabine under terms and conditions to be negotiated. Following an evaluation of the markets and certain other factors, SkyePharma Inc. and Chiron mutually agreed not to further develop certain additional generic cancer compounds named in the Chiron agreement.

In June 1997, SkyePharma Inc. and Chiron amended their agreement, and SkyePharma Inc. repurchased rights to DepoCyt in Canada and Europe from Chiron for aggregate cash payments of up to \$13.7 million, of which \$2.0 million was expensed and paid to Chiron in December 1997. The remaining \$11.7 million originally was payable upon the earlier of six months following U.S. or European regulatory notification that the application to market or sell DepoCyt is approvable or approved. In March 1999, SkyePharma Inc. and Chiron further amended the agreement with Chiron, such that SkyePharma Inc. issued a note payable for \$9.7 million on receipt of FDA approval of DepoCyt on April 1, 1999. During 2000, SkyePharma and Chiron amended the March 1999 agreement whereby SkyePharma Inc. would have issued a note payable for \$3.5 million to Chiron upon the filing of an application for DepoCyt for pediatric indications in the

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United States. Under the amendment dated October 4, 2000, this note became payable on the earlier of the filing of an application for DepoCyt for pediatric indications in the United States or the date on which Phase IV clinical trials, required by the FDA as a condition of product approval, commenced. The \$3.5 million note was issued in December 2000. The notes were secured on the rights to DepoCyt and bore a floating rate of interest based on LIBOR. The remaining Chiron loan notes were repaid during 2002.

In July 1997, SkyePharma Inc. entered into a marketing and distribution agreement with Pharmacia Corporation. Under the agreement, Pharmacia Corporation acquired rights to market and sell DepoCyt in countries outside the United States. Pharmacia Corporation was generally responsible for submitting regulatory filings, and for labeling, packaging, distributing, marketing and selling DepoCyt in this territory. SkyePharma Inc. agreed to manufacture DepoCyt and receive a share of the net sales of this product from Pharmacia Corporation, if any. SkyePharma Inc. received a cash payment of \$2.0 million when the agreement was signed. The agreement also provided for reimbursement by Pharmacia Corporation of certain clinical trial expenses and regulatory fees incurred by SkyePharma Inc. In February 2000, the Company and Pharmacia Corporation renegotiated certain aspects of this agreement relating to milestone payments and reimbursement of clinical trials expenses. In addition, the Company recovered the rights to DepoCyt for Japan and Canada. In June 2000, Pharmacia Corporation notified the Company that it was terminating the 1997 Marketing and Distribution Agreement. Subsequently, Pharmacia Corporation assigned the European marketing application to the Company and the Company continued to pursue the European marketing approval. In April 2001, the Company received notification that the CPMP had recommended the granting of marketing authorization for DepoCyte, for the treatment of neoplastic meningitis from lymphomas. The CPMP's recommendation was forwarded to the European Commission for ratification. In June 2001, the Company licensed the marketing and distribution rights for DepoCyte in Europe and the Philippines to Elan. In August 2001, the European Commission approved DepoCyte for marketing through the European Union.

In June 2000, the Company licensed the marketing and distribution rights for DepoCyt in Canada to Paladin Inc. and in June 2001, the Company licensed the marketing and distribution 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.

In November 2002, the Company re-acquired 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, Enzon Pharmaceuticals, Inc. licensed the North American rights to DepoCyt and 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 reduce should a defined sales target be exceeded. The



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Company is also entitled to milestone payments based on the achievement of certain sales levels and the approval of additional indications. At December 31, 2002, the Company had a promissory note with Chiron of \$1 million which formed part of the consideration for the reacquisition of the DepoCyt marketing, distribution and sales rights. The promissory note is repayable in 2004 and bears interest at LIBOR plus 3%.

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

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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. In respect of the first product launched under the agreement, the Company will pay Endo a fixed contribution in relation to marketing activities undertaken by Endo in respect of the first and second year of commercialization. Endo will be responsible for funding and conducting any post-marketing studies and for selling and marketing expenses. The agreement expires with respect to each product upon the later of the expiry of all relevant patents and the 15<sup>th</sup> anniversary of the date of first commercialization. The agreement may be terminated in various cases, including by Endo in the event the Company experiences delays in obtaining regulatory approval for the products or fails to achieve the target labeling and, without cause, upon sixty days' notice, provided that, in such an event, Endo shall pay an undisclosed termination fee to the Company.

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. 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.

### *Inhalation*

In November 1998, the Company and Novartis agreed to jointly develop a new formulation of Novartis' Foradil asthma drug using the Company's multi-dose dry powder inhaler. The Company is responsible for development of the drug in its finished form, to include supplying both the powder and the device as a product to Novartis. 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 December 2001, the Company signed exclusive agreements with AstraZeneca PLC to develop the next generation of AstraZeneca's Pulmicort metered dose inhaler. 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 approval. The Company received a signing fee of \$2 million and progress related payments could total up to \$10 million once marketing approval is granted. 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

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stable and suitable for use in an HFA-MDI. Phase II clinical studies on the AstraZeneca formulation have been completed and Phase III clinical studies commenced in June 2003.

### **Topical**

As set out above under the caption "Item 4: Information on the Company Business Operations Drug Delivery Platforms Topical Approved Topical Products Solaraze", the Company entered into two agreements with Bioglan: for the manufacture, marketing and distribution of Solaraze in Europe and for the license of marketing rights to the United States, Canada and Mexico. As set out under the aforementioned caption, during 2001, SkyePharma agreed the transfer of rights to market Solaraze in the United States, Canada and Mexico from Bioglan to Quintiles. On May 13, 2002, following negotiations with the Administrators of Bioglan, SkyePharma announced an agreement to transfer all rights to market Solaraze in Europe to Shire for a total consideration up to £15 million, plus royalties on European sales. Of this total consideration, £2.1 million is contingent on conditions including Solaraze's launch in certain European countries.

On February 9, 2000, the Company granted Sakai an exclusive license its patented rights and know-how under the ES-Gel system in relation to acyclovir to enable Sakai to develop, register and sell acyclovir in Japan for the treatment of Herpes Simplex and Herpes Zoster infections. The project has recently completed the feasibility stage and it is anticipated that it will enter clinical trials in 2003. In the case that the Company utilizes the results derived from the Sakai development programme outside Japan, the Company must pay a royalty on net sales to Sakai.

In June 2000, SkyePharma entered into a research and development collaboration with Kings College London for the investigation of the use of HA as a carrier or vector for active substances in drug delivery applications, principally for administration by the topical route. The projects being pursued under this agreement are all at the pre-clinical stage of development.

### **Solubilization**

In December 2002, the Company entered into a development and commercialization agreement under which Endo received an exclusive license to the U.S. and Canadian marketing and distribution rights for two of the Company's patented development products, DepoMorphine, an injectable product, and Propofol IDD-D, 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 \$50 million for Propofol IDD-D, payable when the product successfully achieves certain regulatory milestones, including FDA approval, except that, in the event the FDA-approved labeling fails to meet the parties' target labeling, only \$10 million becomes payable upon FDA approval, with the remaining \$40 million being due upon the achievement of certain sales targets. 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. In respect of the first product launched under the agreement, the Company will pay Endo a fixed contribution in relation to marketing activities undertaken by Endo in respect of the first and second year of commercialization. Endo will be responsible for funding and conducting any post-marketing studies and for selling and marketing expenses. The agreement expires with respect to each product upon the later of the expiry of all relevant patents and the 15<sup>th</sup> anniversary of the date of first

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commercialization. The agreement may be terminated in various cases, including by Endo in the event the Company experiences delays in obtaining regulatory approval for the products or fails to achieve the target labeling and, without cause, upon sixty days' notice, provided that, in such an event, Endo shall pay an undisclosed termination fee to the Company.

SkyePharma Canada and Jagotec AG have signed an exclusive agreement with Baxter Healthcare Corporation to collaborate on the use of the IDD and nano-particulate technology for the formulation of injectable medications. Details of this collaboration are set out above under the caption "Item 4: Information on the Company Business Operations Drug Delivery Platforms Solubilization Solubilization Products in Development New Product Feasibility Programs".

### **Other Collaborative Arrangements**

In December 2000, SkyePharma entered into an agreement with Paul Capital. Under the agreement, Paul Capital has provided a total of \$30 million between 2000 and 2002, in return for the sale of a portion of potential future royalty and revenue streams from DepoMorphine, Xatral OD, Solaraze and DepoCyt. The monies will be used to fund the clinical development of DepoMorphine. Between January 2003 and

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December 2014, Paul Capital will receive 15% of the annual royalties and revenues from the stated products up to an agreed ceiling. Once the predetermined ceiling is reached, the percentage participation will fall to 3% for the remainder of the period until December 31, 2014.

In March 2002, SkyePharma entered into a second 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. The nine products referred to are Propofol IDD-D and HFA-formoterol, the lipid-lowering drug fenofibrate, an anti-cancer agent busulfan, an intravenous formulation of the antibiotic oxytetracycline, oral budesonide to treat inflammatory bowel disease, HFA-budesonide and Foradil, for the treatment of asthma, and the anti-depressant Paxil CR. Between January 2002 and December 2015, Paul Capital could receive between 4% and 20% of the annual royalties and revenues from the total of nine products. The 20% rate applies first. The percentage then falls, when an agreed return is achieved, to 12.5% until a second ceiling is reached, before falling to 4% for the remainder of the period until December 31, 2015. During 2002 and 2003, the 20% rate will be reduced based on the percentage of the total \$30 million already funded. In addition, should the share of royalties received by Paul Capital not meet minimum returns, SkyePharma may issue SkyePharma ordinary shares up to a value of \$7.5 million. The number of ordinary shares to be issued is capped based upon a minimum price of 55 pence per share. Also under the terms of these agreements, Paul Capital has been issued warrants carrying rights to subscribe for 5 million SkyePharma Ordinary Shares at an exercise price of 73.75 pence, representing a 25% premium to the average trading price for the five trading days immediately prior to the closing date.

In December 2001, the Company entered into several agreements concerning the development of Astralis' novel injectable vaccine therapy, for the treatment of all forms of psoriasis, a chronic skin disorder. A first generation of Psoraxine, developed by Astralis, has completed clinical studies in Venezuela with encouraging results. Under the terms of a technology access agreement, the Company received from Astralis a \$5 million license fee, for access to DepoFoam and other relevant drug delivery technologies. In addition, through a service agreement, the company will provide all development, manufacturing, pre-clinical and clinical development services to Astralis for second generation Psoraxine, up to the completion of Phase II clinical studies. In the event that Phase II studies are successfully completed, Astralis will offer SkyePharma the option to acquire the worldwide licensing and distribution rights to Psoraxine. If SkyePharma does not exercise the

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option, Astralis will seek a marketing partner to fund Phase III clinical studies and to provide a sales and marketing infrastructure. Astralis filed an IND application to start Phase Ib clinical studies with the FDA in March 2003. The FDA has informed Astralis that, before clinical trials may proceed, Astralis will have to provide the FDA with additional information and address certain issues regarding the design of the pre-clinical studies. No assurance can be given that the FDA will release the hold placed on the study or whether or when Astralis may commence clinical trials.

In a separate transaction, the Company has made a total equity investment in Astralis of \$20 million in convertible preferred shares, and now owns 25.4% of Astralis assuming the Company was to convert its convertible preferred shares of Astralis into Astralis common stock. The Company made an initial investment of \$10 million on signing the agreement. The additional instalments of \$2.5 million were paid on January 31, 2002, April 30, 2002, July 31, 2002 and January 31, 2003.

On May 14, 2002, SkyePharma announced its intention to enter a wide ranging strategic collaboration with Kowa Company Ltd., a leading Japanese company with substantial pharmaceutical interests, which proposed, under a Subscription Agreement signed on May 13, 2002, to make a strategic investment in SkyePharma. Kowa and SkyePharma also signed a separate non-binding Letter of Intent to evaluate Kowa's acquisition of a 50% interest in SkyePharma's manufacturing facility in Lyon. Kowa and the Company are still evaluating the proposal. On June 25, 2002, the Company announced that in accordance with the terms of an agreement dated May 13, 2002, and following shareholder approval at an Extraordinary General Meeting of the Company held on June 7, 2002, thirty million ordinary shares of 10p each in SkyePharma PLC had been allotted to Kowa Company Limited, for a total consideration of £25,320,000. This represented a holding of 5.01% after the investment. As part of its investment, Kowa had the right to appoint a non-executive director to the board of SkyePharma and on October 30, 2002, the Company confirmed the appointment of Mr. Torao Yamamoto as a Non-executive Director of SkyePharma.

Kowa and SkyePharma have an active relationship involving the formulation and scaled-up manufacture for formulations of a new lipid-lowering agent NK-104 to support late-stage clinical development of the drug. The two parties now intend to strengthen their commercial relationship through manufacturing formulations of NK-104. Kowa and SkyePharma have also identified areas of synergy to exploit further their respective product and development pipelines. Kowa's sales and marketing experience should create opportunities to expand the market for SkyePharma's products into both Europe and Japan. In addition, SkyePharma's broad portfolio of drug delivery technology has the potential to create improved drugs from Kowa's marketed products and development pipeline. SkyePharma and Kowa are already cooperating on an undisclosed project using SkyePharma's enhanced solubilization technology.

In January 2003, the Company and Enzon Pharmaceuticals, Inc. agreed a strategic alliance based on a broad technology access agreement. The two companies will draw on their combined drug delivery technology and expertise to jointly develop up to three products for future

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commercialization. These products will be based on the Company's proprietary platforms in the areas of oral, injectable and topical drug delivery, supported by technology to enhance drug solubility and Enzon's proprietary PEG modification technology, for which Enzon received a US\$3.5 million technology access fee. The Company will receive a milestone payment for each product based on its own proprietary technology that enters Phase II clinical development. Research and development costs related to the technology alliance will be shared equally, as will future revenues generated from the commercialization of any jointly-developed products. PEG technology involves the attachment of polyethylene glycol to therapeutic proteins or small molecules, for the purpose of enhancing therapeutic value. Polyethylene glycol is a relatively non-reactive and non-toxic polymer that is frequently used in food and pharmaceutical products. The attachment of polyethylene glycol to a molecule increases its molecular weight, and for some

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proteins and small molecules can impart better solubility and stability, reduce immune responses, improve therapeutic and/or safety profiles and simplify or improve dosing regimens.

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