Gentium S.p.A.
Form F-1/A
January 26, 2006

As filed with the Securities and Exchange Commission on January 26, 2006
Registration No. 333-130796

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

Amendment No. 1
to
FORM F-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

GENTIUM S.p.A.
(Exact Name of Registrant as Specified in its Charter)
NOT APPLICABLE
(Translation of Registrant's Name into English)

Republic of Italy	**2834**	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

Piazza XX Settembre 2
22079 Villa Guardia (Como), Italy
+39 031 385111
(Address, including zip code, and telephone number,
including area code, of Registrant's principal executive offices)
CT Corporation System
111 Eighth Avenue, 13th Floor
New York, New York 10011
(212) 894-8940
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:
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250 Park Avenue
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Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes effective.
If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box: S

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earliest effective registration statement for the same offering. o

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered (1)	Proposed maximum offer price per share	Proposed maximum aggregate offering price	Amount of registration fee
Ordinary shares, par value €1.00 per share (2)	3,101,591(3)	$ 0(4)	$ 0(4)	$ 0(4)
Ordinary shares, par value €1.00 per share (2)	43,016(5)	$ 8.78(6)	$ 377,681(6)	$ 41
Total ordinary shares, par value € per share (2)	3,144,607(7)	--	--	$ 41

(1) Pursuant to Rule 416, this registration statement shall be deemed to cover an indeterminate number of additional ordinary shares if the number of outstanding ordinary shares of the Company is increased by a stock split, stock dividend and/or similar transaction.

(2) American Depositary Shares evidenced by American Depositary Receipts issuable upon deposit of the ordinary shares registered hereby are being registered under a separate registration statement. Each American Depositary Share represents one ordinary share.

(3) Includes 1,100,466 ordinary shares that may be issued pursuant to the exercise of warrants.

(4) The registration fee for these ordinary shares was paid in connection with the initial filing of this registration statement.

(5) Consists of 43,016 ordinary shares that may be issued pursuant to the exercise of warrants.

(6) Pursuant to Rule 457(c), the proposed maximum offering price per share and the proposed maximum aggregate offering price have been calculated on the basis of $8.78, the average of the high and low prices of the American Depositary Shares on the American Stock Exchange on January 23, 2006.

(7) Includes 1,143,482 ordinary shares that may be issued pursuant to the exercise of warrants.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall after that become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

THE INFORMATION IN THIS PRELIMINARY PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THESE SECURITIES MAY NOT BE SOLD UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PRELIMINARY PROSPECTUS IS NOT AN OFFER TO SELL NOR DOES IT SEEK AN OFFER TO BUY THESE SECURITIES IN ANY JURISDICTION WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION DATED JANUARY 26, 2006

PRELIMINARY PROSPECTUS

Gentium S.p.A.

3,144,607 American Depositary Shares
Representing 3,144,607 Ordinary Shares

The selling security holders identified in this prospectus are offering up to 3,144,607 American Depositary Shares ("ADSs"), each representing one ordinary share of our company, Gentium S.p.A. The ADSs will be evidenced by American Depositary Receipts ("ADRs"). Our ADSs are listed on the American Stock Exchange under the symbol "GNT."

We will not receive any proceeds from the sale of ADSs by the selling security holders. We are not offering any ADSs for sale under this prospectus. See "Selling Security Holders" beginning on page 114 for a list of the selling security holders. See "Plan of Distribution" beginning on page 121 for a description of how the ADSs can be sold.

Our business and an investment in our ADSs involve significant risks. These risks are described under the caption "Risk Factors" beginning on page 8 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

[_____], 2006

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information that is different. The selling security holders are offering to sell and seeking offers to buy the ADSs only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the ADSs.

We have not taken any action to permit a public offering of the ADSs outside the United States or to permit the possession or distribution of this prospectus outside the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about and observe any restrictions relating to this offering of the ADSs and the distribution of the prospectus outside of the United States. See "Plan of Distribution."

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by, and should be read in conjunction with, the more detailed information and financial statements and notes thereto appearing elsewhere in this prospectus. Before you decide to invest in the ADSs, you should read the entire prospectus carefully, including the risk factors and financial statements and related notes included in this prospectus. Except where we state otherwise, the information we present in this prospectus assumes no exercise of our outstanding options or warrants.

THE COMPANY

Our Business Focus

We are a biopharmaceutical company focused on the research, discovery and development of drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. In 1986, our founding company received approval to sell in Italy a drug called "defibrotide" to treat deep vein thrombosis, and, in 1993, it received approval to manufacture and sell defibrotide to both treat and prevent all vascular disease with risk of thrombosis. For the nine months ended September 30, 2005, we derived approximately €1.348 million of revenues, or approximately 67.6% of our product sales of €1.995 million, from sales of defibrotide for these uses in Italy to Sirton, a subsidiary of our largest shareholder, FinSirton, which currently owns 39% of our stock. Our primary focus is on the development of defibrotide for other uses in the United States and Europe. We have not received approval by the U.S. Food and Drug Administration, or FDA, or any European regulators to sell defibrotide for these other uses. We do not expect revenues from any of our product candidates until at least 2007 and, as a result, we will require additional funding in order to obtain FDA and European regulatory approvals for our product candidates and for working capital. See "Risk Factors".

We are building upon our extensive experience with defibrotide, which our predecessors discovered over 18 years ago, to develop it for a variety of additional uses, including to treat and prevent hepatic Veno-Occlusive Disease, or VOD, a condition in which some of the veins in the liver are blocked as a result of toxic cancer treatments such as chemotherapy. A severe form of VOD with multiple-organ failure is a potentially devastating complication with a survival rate after 100 days of only approximately 20%, according to our review of more than 200 published medical articles. Results from a Phase II clinical trial conducted at Harvard University's Dana-Farber Cancer Institute of VOD with multiple-organ failure that concluded in December 2005 showed that the survival rate after 100 days was approximately 39% after treatment with defibrotide, although those results were based on the treatment of only 142 patients and may not show the safety or effectiveness of the product candidate. We believe that there is no drug approved by the FDA or European regulators to treat or prevent VOD.

Our Advanced Product Candidates

The stages of development and status of our most advanced product candidates are summarized below. For additional information on our most advanced and additional product candidates and the clinical trials, see "Business - Advanced Product Candidates" and "- Additional Product Candidates."

Product Candidate	Intended Use	Stage of Development/Status
Defibrotide	Treat VOD with multiple-organ failure	Phase III in the United States/Orphan drug designation in the United States and Europe; fast track designation in the United States
Defibrotide	Prevent VOD	

		Phase II/III in Europe/Orphan drug designation in Europe
Defibrotide	Treat multiple myeloma	Phase I/II in Italy

Our Development and Commercialization Strategy

Our goal is to research, discover, develop and manufacture drugs derived from DNA extracted from natural sources to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. The primary elements of our strategy are:

· **Obtain regulatory approvals for our advanced product candidates.** Although clinical trials are being conducted for these uses of defibrotide, the regulatory process is difficult and expensive. We do not expect revenues from defibrotide to treat VOD with multiple-organ failure until at least 2007 and do not expect revenues from defibrotide to prevent VOD or defibrotide to treat multiple myeloma until at least 2009.

· **Discover and develop additional product candidates.** We intend to continue to discover and develop, either internally or through collaborative arrangements, additional products candidates including:

· Defibrotide for additional uses such as to increase the number of stem cells available for transplant and to prevent deep vein thrombosis in markets outside of Italy;

· Other drugs, such as oligotide, to protect against damage to blood vessel wall cells from certain cancer treatments; and

· Gen 301, which we believe may prevent and treat oral ulcers that develop during and after cancer treatments.

· **Enter into collaborative and strategic agreements to assist us in the development and marketing of our products and product candidates.** To date, we have entered into a limited number of license and sales agreements. These agreements include:

· Our license for the right to market defibrotide to treat VOD in North America, Central America and South America, upon regulatory approval, to Sigma-Tau Pharmaceuticals, Inc., which markets drug treatments for rare conditions and diseases. Sigma-Tau Pharmaceuticals, Inc. is an United States subsidiary of Sigma Tau Finanziaria S.p.A., an international family of pharmaceutical companies;

· Our license for the right to distribute our formulation of mesalazine to treat inflammatory bowel disease in Italy to Crinos, a subsidiary of Stada, a large European pharmaceutical company. Crinos also markets defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement with us; and

· Our sale of the rights to develop and sell our formulation of mesalazine to treat inflammatory bowel disease in Canada, upon Health Canada approval, and in the United States, upon FDA approval, to Axcan Pharma, Inc., a specialty pharmaceutical company with offices in North America and Europe.

We intend to continue to seek similar agreements with strategic partners as to other products and product candidates. Our failure to do so or to obtain additional funding will have an adverse affect on our business prospects.

Manufacturing and Product Sales

We manufacture defibrotide, calcium heparin, sulglicotide and other miscellaneous pharmaceutical products at our manufacturing facility near Como, Italy, and we lease our affiliate Sirton's facility to manufacture urokinase. Urokinase and calcium heparin are active pharmaceutical ingredients used to make other drugs. Sulglicotide is intended to be used to treat peptic ulcers. During 2002, 2003, 2004 and the nine months ended September 30, 2005, 100%, 100%, 92% and 95%, respectively, of our total product sales came from sales of these products to Sirton. Our revenues from the sales of these products to date have been generated only in Italy and, in 2004, also in Korea and amounted to €5.9 million, €6.5 million, €3.1 million and €1.9 million in 2002, 2003, 2004 and the nine months ended September 30, 2005, respectively. In 2004 we completed an upgrade to our facilities that cost approximately €7.2 million which we believe will facilitate the FDA and European regulatory approval process for our product candidates and enable our future production. In anticipation of the renovations, we temporarily increased our production shifts and deliveries in 2003 and suspended our production for approximately seven months in 2004. Period to period comparisons of our results will therefore be difficult.

Risk Factors

We have generated limited revenues to date, most of which have been derived from sales to Sirton. Our general and administrative expenses have increased as we internalized certain of our administrative services which were

previously provided by Sirton and FinSirton and adapted to being a public reporting company. We do not have regulatory approvals for the sale of defibrotide to treat or prevent VOD and will be required to perform further clinical trials for these and other uses. The approval process for new drugs is lengthy and expensive and if we fail to raise additional funds in the future or enter into collaborative agreements, we may be unable to continue the development of our product candidates. Our most advanced product candidate, defibrotide to treat VOD with multiple-organ failure, will have a very limited market. See “Risk Factors.”

Corporate Information and Executive Offices

We were originally formed in 1993 as Pharma Research S.r.L., an Italian private limited company, to pursue research and development activities of prospective pharmaceutical specialty products. In December 2000, we changed from a private limited company to a corporation organized under the laws of the Republic of Italy. In July 2001 we changed our name to Gentium S.p.A. Under our current bylaws, the duration of our company will expire on December 31, 2050.

We are part of a group of pharmaceutical businesses founded in Italy in 1944 that has been involved in the research and development of drugs derived from DNA and DNA molecules since the 1970's. Our largest shareholder is FinSirton S.p.A., an Italian corporation. FinSirton is controlled by Dr. Laura Ferro, who is our Chief Executive Officer and President and one of our directors, and her family. We receive administrative and other services and lease office and manufacturing facilities from FinSirton and Sirton. The manufacturing facilities are 3,200 square meters in size.

Our principal executive offices are located at Piazza XX Settembre 2, 22079 Villa Guardia (Como), Italy. Our telephone number is +39 031 385111. Our website is located at www.gentium.it. The information contained on our website is not part of this prospectus. Our registered agent for service of process is CT Corporation System, located at 111 Eighth Avenue, 13th Floor, New York, New York 10011, telephone number (212) 894-8940.

United States and international trademark rights in "Gentium" and Italian trademark rights to "Pharma Research." We also have a number of patent registrations issued and pending in Italy, the United States and other countries. This prospectus also refers to brand names, trademarks, service marks, and trade names of other companies and organizations, and these brand names, trademarks, service marks, and trade names are the property of their respective holders.

This prospectus contains market data and industry forecasts that were obtained from industry publications.

SUMMARY FINANCIAL DATA

The following tables summarize our financial data, prepared using U.S. generally accepted accounting principles, for the periods presented. You should read the following financial information together with the information under "Selected Financial Data,""Operating and Financial Review and Prospects,""Risk Factors" and our financial statements and the notes to those financial statements appearing elsewhere in this prospectus. The summary financial data as of December 31, 2004 and for each of the three years ended December 31, 2004 are derived from our audited financial statements, which are included in this prospectus. The summary financial data as of September 30, 2005 and for each of the nine months ended September 30, 2004 and 2005 are derived from our unaudited financial statements, which are included in this prospectus. The summary financial data for the year ended December 31, 2001 is derived from our unaudited financial statements, which are not included in this prospectus. Our historical results are not necessarily indicative of results to be expected in any future period.

Certain reclassification of prior period amounts have been made to our financial statements to conform to the current period presentation.

Statement of Operations Data: *(000s omitted except per share data)*	**For The Years Ended December 31,**				**For The Nine Months Ended September 30,**	
	2001	**2002**	**2003**	**2004**	**2004**	**2005**
Revenues:					*(unaudited)*	
Sales to affiliates	€ 6,459	€ 5,915	€ 6,532	€ 2,870	€ 1,719	€ 1,900
Third party product sales	—	—	—	243	243	95
Total product sales	6,459	5,915	6,532	3,113	1,962	1,995
Other income and revenues	5	392	1,843	583	501	210
Total revenues	6,464	6,307	8,375	3,696	2,463	2,205
Operating costs and expenses:						
Cost of goods sold	2,531	2,135	2,435	2,579	1,453	1,721
Charges from affiliates	1,025	1,156	1,485	1,665	915	781
Research and development	2,206	1,753	2,253	2,922	2,461	3,117
General and administrative	793	864	854	815	602	1,375
Non-cash compensation	—	—	—	379	—	363
Depreciation and amortization	185	102	67	89	52	78
	6,740	6,010	7,094	8,449	5,483	7,435
Operating income (loss)	(276)	297	1,281	(4,753)	(3,020)	(5,230)
Other income	—	195	—	—	—	—
Foreign currency exchange gain (loss), net	—	268	156	(55)	42	(435)
Interest income (expense), net	(147)	(105)	(71)	(2,192)	(26)	(4,197)
Pre-tax income (loss)	(423)	655	1,366	(7,000)	(3,004)	(9,862)

Income tax expense (benefit):						
Current	145	128	243	65	48	48
Deferred	13	108	(84)	(37)	(28)	—
	158	236	159	28	20	48
Net income (loss)	€ (581)	€ 419	€ 1,207	€ (7,028)	€ (3,024)	€ (9,910)
Net income (loss) per share:						
Basic and Diluted	€ (0.12)	€ 0.08	€ 0.24	€ (1.41)	€ (0.60)	€ (1.62)

The following table summarizes certain of our balance sheet data at September 30, 2005 on an actual basis and on a pro forma basis adjusted to reflect our receipt and use of the net proceeds from a private placement in October 2005 of 1,551,125 of our ordinary shares at a price per share of $7.05 (approximately €5.83 based on the exchange rate on the date of closing) and warrants to purchase an aggregate of 620,450 ordinary shares after deducting placement fees of $656,126 (approximately €542,253) and estimated offering expenses of $363,975 (approximately €300,806), as if we had received and used the net proceeds on September 30, 2005.

(000's omitted)	**Pro Forma Condensed Balance Sheet As of September 30, 2005**		
	Historical (Unaudited)	**Pro Forma Adjustment**	**Pro Forma**
Assets			
Cash and cash equivalents	€ 7,012	€ 8,200	€ 15,212
Receivables	909		909
Inventories	1,683		1,683
Prepaid expenses and other current assets	1,075		1,075
Total Current Assets	10,679	8,200	18,879
Property, manufacturing facility and equipment, net	8,526		8,526
Intangible and other assets, net	845		845
	€ 20,050	€ 8,200	€ 28,250
Liabilities and Shareholders' Equity			
Payables, accruals, other current liabilities	€ 3,368	€	€ 3,368
Current maturities of long-term debt	895		895
Deferred income	350		350
Total Current Liabilities	4,613	—	4,613
Long-term debt, net of current maturities	2,577		2,577
Termination indemnities	693		693
Total Liabilities	7,883	—	7,883
Total Shareholders' Equity	12,167	8,200	20,367
	€ 20,050	€ 8,200	€ 28,250

The following table summarizes certain of our statement of operations data for the year ended December 31, 2004 on an actual basis and on a pro forma basis adjusted to reflect:

- our receipt of the net proceeds from the sale of $8.010 million of our Series A senior convertible promissory notes from October through January 2005 as if we had received the net proceeds on January 1, 2004; and

- our receipt and use of the net proceeds from the sale of 2,400,000 of our ordinary shares in June 2005 in our initial public offering and 300,000 of our ordinary shares in July 2005 from the exercise of part of the underwriters' over-allotment option, after deducting underwriting discounts and commissions and offering expenses, as if we had received and used the net proceeds on January 1, 2004.

	Pro Forma Condensed Statement of Operations For the Year Ended December 31, 2004		
(000s omitted except per share data)	**Historical (Audited)**	**Pro Forma Adjustments**	**Pro Forma**
Revenues:			
Sales to affiliates	€ 2,870	€	€ 2,870
Third party product sales	243		243
Total product sales	3,113		3,113
Other income and revenues	583		583
Total revenues	3,696		3,696
Operating costs and expenses:			
Cost of goods sold	2,579		2,579
Charges from affiliates	1,665		1,665
Research and development	2,922		2,922
General and administrative	815		815
Non-cash compensation	379		379
Depreciation and amortization	89		89
	8,449		8,449
Operating loss	(4,753)		(4,753)
Foreign currency exchange loss, net	(55)		(55)
Interest income (expense), net	(2,192)	3,784	(5,976)
Pre-tax loss	(7,000)	3,784	(10,784)
Income tax expense (benefit):			
Current	65		65
Deferred	(37)		(37)
	28		28
Net loss	€ (7,028)	€ 3,784	€ (10,812)

- The net proceeds of our initial public offering were used to repay part of our Series A senior convertible promissory notes, loans from our affiliate Sirton and for working capital. In addition, at the time of our initial public offering, the holder of $2.912 million of our Series A notes elected to convert its notes into our ordinary shares.

- If these transactions had occurred on January 1, 2004, the pro forma impact on our operating results for the year ended December 31, 2004 would have been that (i) we would not have incurred interest paid and accrued in the amount of €53 thousand and (ii) we would have incurred additional non-cash interest of €3.837 million from the write-off of the issue discount and debt issue costs associated with the portion of our Series A notes that were redeemed.

The following table summarizes certain of our statement of operations data for the nine months ended September 30, 2005 on an actual basis and on a pro forma basis adjusted to reflect:

- our receipt and use of the net proceeds from the sale of $1.912 million of our Series A notes in January 2005 as if we had received and used the net proceeds on January 1, 2005; and

- our receipt and use of the net proceeds from the sale of 2,400,000 of our ordinary shares in June 2005 in our initial public offering and 300,000 of our ordinary shares in July 2005 from the exercise of part of the underwriters' over-allotment option after deducting underwriting discounts and commissions and offering expenses, as if we had received and used the net proceeds on January 1, 2004.

	Pro Forma Condensed Statement of Operations For the Nine Months Ended September 30, 2005		
(000s omitted except per share data)	**Historical (Unaudited)**	**Pro Forma Adjustments**	**Pro Forma**
Revenues:			
Sales to affiliates	€ 1,900	€	€ 1,900
Third party product sales	95		95
Total product sales	1,995		1,995
Other income and revenues	210		210
Total revenues	2,205		2,205
Operating costs and expenses:			
Cost of goods sold	1,721		1,721
Charges from affiliates	781		781
Research and development	3,117		3,117
General and administrative	1,375		1,375
Non-cash compensation	363		363
Depreciation and amortization	78		78
	7,435		7,435
Operating loss	(5,230)		(5,230)
Foreign currency exchange loss, net	(435)		(435)
Interest income (expense), net	(4,197)	258	(3,939)
Pre-tax loss	(9,862)	258	(9,604)
Income tax benefit:			
Current	48		48
Deferred	—		—
	48		48
Net loss	€ (9,910)	€ 258	€ (9,652)

- The net proceeds of our initial public offering were used to repay part of our Series A senior convertible promissory notes, loans from our affiliate Sirton on and for working capital. In addition, at the time of our initial public offering, the holder of $2.912 million of our Series A notes elected to convert its notes into our ordinary shares.

- If these transactions had occurred on January 1, 2005, the pro forma impact on our operating results for the nine month period ended September 30, 2005 is that we would not have incurred interest paid and accrued in the amount of €258 thousand. Therefore, our operating results still reflect the non-cash interest expense from the write-off of the issue discount and debt issue costs associated with the redemption of a portion of our Series A notes.

RISK FACTORS

This offering involves a high degree of risk. You should carefully consider the risks described below, in conjunction with the other information and financial statements and related notes included elsewhere in this prospectus, before making an investment decision. You should pay particular attention to the fact that we conduct our operations in Italy and are governed by a legal and regulatory environment that in some respects differs significantly from the environment that prevails in other countries with which you may be familiar. Our business, financial condition or results of operations could be affected materially and adversely by any or all of these risks. In that event, the market price of our ordinary shares could decline and you could lose all or part of your investment.

Risks Relating to Our Business

We have generated limited revenues from commercial sales of our products to date, our revenues fluctuated significantly in 2003 compared to 2004 and in the nine months ended September 30, 2004 compared to the same period in 2005, and we do not know whether we will ever generate significant revenues or achieve profitability.

We are focused on product development and have generated limited revenue from commercial sales of our products to date. In 2003, we had revenues of €6.5 million and in 2004, we had revenues of €3.1 million, primarily from sales of active pharmaceutical ingredients and existing products to Sirton, our affiliate. Our 2004 revenues were substantially less than our 2003 revenues due to the need to temporarily cease operations for seven months in 2004 at our manufacturing facility for an upgrade to the facility and our increase in production at the facility in 2003 to stockpile inventory in anticipation of this cessation and because Sirton had a decrease in demand for some of the products we sell to them, as discussed below. In the nine months ended September 30, 2004, we had revenues of €2.463 million and in the nine months ended September 30, 2005 we had revenues of €2.205 million.

We do not expect our revenues to materially increase unless we are able to sell our product candidates, and we will continue to incur significant expenses as we research, develop, test and seek regulatory approval for these product candidates. While we were profitable in 2002 and 2003, we incurred a net loss of €581 thousand in 2001, a net loss of €7.0 million in 2004 and a net loss of €9.910 million for the nine months ended September 30, 2005. Our general and administrative expenses have increased as we added personnel to support our operations in connection with our development of our product candidates, internalized certain administrative services that were performed for us by our largest shareholder, FinSirton, and our affiliate, Sirton, and supported our operations in connection with being a public company. As a result, we anticipate incurring substantial and increasing losses for the foreseeable future. We cannot assure you that we will ever become profitable. If we fail to achieve profitability within the time frame expected by investors or securities analysts, the market price of our ordinary shares may decline.

Most of our revenues are from sales to Sirton, our affiliate; those sales have declined over the past several years and may continue to decline in the future.

Substantially all of our product sales in 2001, 2002 and 2003, approximately 92% of our product sales in 2004 and approximately 95% of our product sales in the nine months ended September 30, 2005 have been from the sale of our active pharmaceutical ingredients and products to Sirton, which has recently experienced financial difficulties. Sirton sells its finished products, including calcium heparin, primarily to one customer, Crinos, which sells them to the retail market. Calcium heparin, which is one of the active pharmaceuticals ingredients that we sell to Sirton to make into a finished product for sale by Crinos, has seen decreased demand over the past several years due to a new competitive product, low molecular weight heparin, made by Aventis and other companies. Also, Crinos has limited its sale of urokinase to a single dose, which has a more limited market than multiple doses. As a result, Sirton's demand for these products has decreased over the past several years, and may continue to decrease over the next several years until and unless both we and Sirton develop new customers. If we and Sirton are unsuccessful at developing new customers and the demand for our products continues to decrease, it could increase our need for additional capital, and our business

could be adversely affected.

We currently do not have any regulatory approvals to sell defibrotide to treat or prevent VOD or defibrotide to treat multiple myeloma or any of our other product candidates and we cannot guarantee that we will ever be able to sell any of these products anywhere in the world.

We must demonstrate that our product candidates satisfy rigorous standards of safety and effectiveness before the FDA, the European Commission and other regulatory authorities will approve the products for commercial marketing. We or others must conduct clinical trials of those products which must be approved by the FDA or other regulatory agencies. These trials are time consuming and expensive, and we cannot guarantee whether they will be successful. Currently, the only regulatory approvals we have relate to the use of defibrotide to prevent vascular disease with risk of thrombosis in Italy. We do not have approval to sell defibrotide to treat or prevent VOD, defibrotide to treat multiple myeloma or any of our other product candidates anywhere in the world. We will need to conduct significant additional research, preclinical testing and clinical testing before we can file applications with the FDA, the European Commission and other regulatory authorities for approval of our product candidates. In addition, to compete effectively, our future products must be easy to use, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives, and, as a result, may not be able to sell any of our product candidates anywhere in the world.

Our most advanced product candidate, defibrotide to treat VOD with multiple-organ failure, has a very limited market and will not generate a large amount of revenue.

Our most advanced product candidate is defibrotide to treat VOD with multiple-organ failure, which the FDA has designated an "orphan drug." Orphan drug status is granted to products that treat rare diseases or conditions and generally means that fewer than 200,000 people are affected by the disease or condition. We believe that as few as 1,500 people in the United States may need treatment for VOD with multiple-organ failure each year. As a result, we believe that there is a very limited market for this use of defibrotide, and we do not expect to generate a large amount of revenue from sales of defibrotide to treat VOD with multiple-organ failure.

The FDA and other regulatory authorities may require us to conduct a new clinical trial of defibrotide to treat VOD with multiple-organ failure using a control group.

The Dana-Farber Cancer Institute at Harvard University conducted a Phase II clinical trial in the United States for the use of defibrotide to treat VOD with multiple-organ failure that concluded in December 2005. Based on our review of more than 200 articles in the medical literature, we believe that the survival rate for this disease is only approximately 20%. As a result of this fact and the fact that we and the clinical investigators believe that there are no approved treatments available at this time, the clinical investigators did not establish a control group of patients who do not receive the drug, as is customarily done in the FDA approval process. The FDA has stated a preference for a double-blind study that utilizes a control group but indicated that they would review a trial using a historical control only. Our Phase III clinical trial that is currently underway uses historical control only. The FDA, upon reviewing this trial, may require us to conduct a new clinical trial using a control group and other regulatory authorities may take the same position. This could significantly delay the filing of a New Drug Application with the FDA or applications for other regulatory approval for this use because one or more of the clinical centers where the clinical trial is to be conducted may not be willing to conduct such a clinical trials on the basis that it is unethical to refuse treatment to patients when the treatment being investigated could potentially save their lives. The committee of clinical investigators who sponsored a Phase II/III clinical trial of defibrotide to treat VOD in Europe conducted by Consorzio Mario Negri Sud, which had a control group, cancelled the trial in October 2005 due to a lack of patients enrolling. We believe that patients were reluctant to enroll due to the possibility of being placed into the control group and not receiving treatment. A requirement for a control group would also require the expenditure of more funds on clinical trials and delay our ability to generate revenue from this product candidate.

Our additional product candidates are at early stages of development and will require clinical trials which may not be successful.

We intend to apply for FDA and other regulatory agency approval for our additional product candidates, including other uses of defibrotide, in the future, and these additional product candidates will require that we conduct clinical

trials and undergo the regulatory approval process. The commencement and completion of these clinical trials could be delayed or prevented by a variety of factors, including:

· delays in identifying and reaching agreement on acceptable terms with institutional review boards of clinical trial providers and prospective clinical trial sites;

· delays in obtaining FDA or other regulatory agency clearance to commence a clinical trial;

· delays in the enrollment of patients;

· lack of effectiveness of the product candidate during clinical trials; or

· adverse events or safety issues.

We do not know whether these future clinical trials will be initiated or completed at all. Significant delays in clinical trials will impede our ability to commercialize these additional product candidates and generate revenue, and could significantly increase our development costs.

We may be required to suspend or discontinue clinical trials, including due to adverse events or other safety issues that could preclude approval of our products or due to difficulty enrolling participants.

Our clinical trials may be suspended at any time for a number of safety-related reasons. For example, we may voluntarily suspend or terminate our clinical trials if at any time we believe that our product candidates present an unacceptable risk to the clinical trial patients. In addition, institutional review boards of clinical trial providers or regulatory agencies may order the temporary or permanent discontinuation of our clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, including if they present an unacceptable safety risk to patients.

Administering any product candidate to humans may produce undesirable side effects. VOD and VOD with multiple-organ failure are complications associated with high dose chemotherapy and stem cell transplantation. Adverse events involving vascular disorders, coagulation, and potentially life-threatening bleeding have been reported in patients with VOD treated with defibrotide which potentially could be related to the defibrotide therapy. Hypotension has been reported as a possibly related serious adverse event in the trials of defibrotide to treat VOD with multiple-organ failure. Also, we discontinued a 69-patient Phase I/II clinical trial of defibrotide to prevent deep vein thrombosis after hip surgery in Denmark in 2002 after three patients experienced hypotension after receiving the defibrotide intravenously. That trial was discontinued due to the hypotension and because defibrotide can also be administered orally to prevent deep vein thrombosis. These adverse events reports will be weighed by FDA and other regulatory authorities in determining whether defibrotide can, from a risk-benefit perspective, be considered to be safe and effective to treat VOD with multiple-organ failure, to prevent deep vein thrombosis or any other indication for which approval is sought.

It is possible that as further data are collected and analyzed, additional adverse events or safety issues could emerge which could impact conclusions relating to the safety of these additional product candidates. As one of our current products and many of our product candidates utilize or will utilize defibrotide, any problems that arise from the use of this drug would severely harm our business operations, since most of our anticipated primary revenue sources would be negatively affected.

Furthermore, the committee of clinical investigators who sponsored a Phase II/III clinical trial of defibrotide to treat VOD in Europe that was conducted by Consorzio Mario Negri Sud cancelled the trial in October 2005 due to a lack of enrollees. In addition, the National Institute of Tumors in Milan cancelled a Phase I clinical trial of defibrotide to increase the number of stem cells available for transplant in December 2005 due to a lack of eligible enrollees. We are co-sponsoring with the European Group for Blood and Marrow Transplantation a Phase II/III clinical trial in Europe of defibrotide to prevent VOD in children, which is scheduled to begin enrolling participants in the first quarter of 2006, and a Phase II/III clinical trial in Europe of defibrotide to prevent VOD and transplant associated microangiopathy in adults, which is scheduled to begin enrolling participants in the second quarter of 2006. The participants in both of these trials will randomly receive either defibrotide or no treatment. We may have difficulty enrolling participants in these trials as patients may be reluctant to take the risk of not receiving treatment with defibrotide. Our other clinical trials may also be discontinued if we or the sponsors are not successful in enrolling participants.

Our products could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements, if and when any of our product candidates are approved.

Any product for which we obtain marketing approval, together with the manufacturing processes, post-approval commitments, and advertising and promotional activities for such product, will be subject to continued regulation by the FDA and other regulatory agencies. Later discovery of previously unknown problems with our products or their manufacture, or failure to comply with regulatory requirements, may result in:

· restrictions on such products or manufacturing processes;

· withdrawal of the products from the market;

· voluntary or mandatory recalls;

· fines;

· suspension of regulatory approvals;

· product seizures; or

· injunctions or the imposition of civil or criminal penalties.

If we are slow to adapt, or unable to adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, we may lose marketing approval for our products when and if any of them are approved.

Our manufacturing facility is subject to continuing regulation by Italian authorities and is subject to inspection and regulation by the FDA and European regulatory. These authorities could force us to stop manufacturing our products if they determine that we are not complying with applicable regulations or require us to complete further costly alterations to our facility.

Although our main business is discovering, researching and developing drugs, we also manufacture drugs, active pharmaceutical ingredients and other products at our manufacturing facility located near Como, Italy. This facility is subject to continuing regulation by the Italian Health Authority and other Italian regulatory authorities. During a biannual inspection of our manufacturing facility by the Italian Health Authority in October 2004, the Italian Health Authority noted by way of observations certain deficiencies in regard to the operation of our facility. We are committed to complete appropriate corrective action prior to the next bi-annual inspection, and have kept the Italian Health Authority current with respect to the progress of our corrective actions, the majority of which has been completed. No penalties were imposed, our facility was not shut down and our manufacturing activities were not otherwise limited or curtailed as a result of the Italian Health Authorities' notation of these deficiencies.

Our manufacturing facility is subject to inspection and regulation by the FDA and European regulatory authorities with respect to manufacturing our product candidates for investigational use. Also, part of the process for obtaining approval from the FDA and European regulatory authorities for our product candidates is approval by those authorities of our manufacturing facility's compliance with current good manufacturing practices. After receiving initial approval, if any, the FDA or those European regulatory authorities will continue to inspect our manufacturing facility, including inspecting it unannounced, to confirm whether we are complying with the good manufacturing practices.

These regulators may require us to stop manufacturing our products and product candidates if they determine that we are not complying with applicable regulations or require us to complete costly alterations to our facility. We spent approximately €292 thousand in 2004 to correct the deficiencies noted by the Italian Health Authority and spent approximately €200 thousand in 2005 to complete these corrective actions. We spent approximately €7.2 million in 2004 to substantially upgrade our facility in anticipation of the FDA and European regulatory approval process for our product candidates.

If our third-party clinical trial vendors fail to comply with strict regulations, the clinical trials for our product candidates may be delayed or unsuccessful.

We do not have the personnel capacity to conduct or manage all of the clinical trials that we intend for our product candidates. We rely on third parties to assist us in managing, monitoring and conducting most of our clinical trials. We entered into a clinical trial agreement with the Dana-Farber Cancer Institute at Harvard University regarding a Phase II clinical trial of defibrotide to treat VOD with multiple-organ failure that concluded in December 2005. We have entered into similar arrangements with other clinical research organizations, including the European Group for Blood and Marrow Transplantation, which is co-sponsoring with us a Phase II/III clinical trial of defibrotide to prevent VOD in children in Europe and a Phase II/III clinical trial of defibrotide to prevent VOD and transplant associated microangiopathy in adults in Europe, both of which are scheduled to begin enrolling patients in 2006. We have entered into an agreement with Bradstreet Clinical Research & Associates, Inc. to perform clinical research project management services in connection with clinical trials conducted in the United States and agreements with KKS-UKT, GmbH and MDS Pharma Services Italy SpA to provide such services for our clinical trials in Europe. If

these third parties fail to comply with applicable regulations or do not adequately fulfill their obligations under the terms of our agreements with them, we may not be able to enter into alternative arrangements without undue delay or additional expenditures, and therefore the clinical trials for our product candidates may be delayed or unsuccessful.

Furthermore, the FDA can be expected to inspect some or all of the clinical sites participating in our clinical trials, or our third party vendors' sites, to determine if our clinical trials are being conducted according to current good clinical practices. If the FDA determines that our third-party vendors are not in compliance with applicable regulations, we may be required to delay, repeat or terminate the clinical trials. Any delay, repetition or termination of our clinical trials could materially harm our business.

Our failure to raise additional funds in the future may delay the development of certain of our product candidates and sale of our products.

The development and approval of our product candidates and the acquisition and development of additional products or product candidates by us, as well as the expansion of our research, regulatory and manufacturing operations, will require a commitment of substantial funds. Our future capital requirements are dependent upon many factors, some of which are beyond our control, including:

· the successful and continued development of our existing product candidates in preclinical and clinical testing;

· the costs associated with protecting and expanding our patent and other intellectual property rights;

· future payments, if any, received or made under existing or possible future collaborative arrangements;

· the timing of regulatory approvals needed to market our product candidates; and

· market acceptance of our products.

We will need additional funds before we have completed the development of our product candidates. We have no committed sources of additional funds. We cannot assure you that funds will be available to us in the future on favorable terms, if at all. If adequate funds are not available to us on terms that we find acceptable, or at all, we may be required to delay, reduce the scope of, or eliminate research and development efforts or clinical trials on any or all of our product candidates. We may also be forced to curtail or restructure our operations, obtain funds by entering into arrangements with collaborators on unattractive terms or relinquish rights to certain technologies or product candidates that we would not otherwise relinquish in order to continue independent operations.

We are currently dependent on third parties to market and distribute our products in finished dosage form, and we expect to continue to be dependent on third parties to market and distribute our products and product candidates.

Our internal ability to handle the marketing and distribution functions for our current products and our product candidates is limited and we do not expect to develop the capability to provide marketing and distribution for all of our future products. Our long-term strategy involves having alliances with third parties to assist in the marketing and distribution of our product candidates. We have entered into an agreement with Sigma-Tau Pharmaceuticals, Inc. to market defibrotide to treat VOD in North America, Central America and South America and will need to enter into similar agreements to market and distribute our other product candidates. We face, and will continue to face, intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions, for attracting investigators and sites capable of conducting our clinical trials and for licenses of proprietary technology. Moreover, these arrangements are complex to negotiate and time-consuming to document. Our future profitability will depend in large part on our ability to enter into effective marketing agreements and our product revenues will depend on those marketers' efforts, which may not be successful.

If we are unable to attract and retain key personnel, we may be unable to successfully develop and commercialize our product candidates or otherwise manage our business effectively.

We are highly dependent on our senior management, especially Dr. Laura Ferro, our President and Chief Executive Officer, and Dr. Massimo Iacobelli, our Senior Vice President and Scientific Director, whose services are critical to the successful implementation of our product acquisition, development and regulatory strategies. If we lose their services or the services of one or more of the other members of our senior management or other key employees, our

ability to successfully commercialize our product candidates or otherwise manage our business effectively could be seriously harmed. Dr. Ferro's employment agreement with us is for a period of three years with a two year renewal option and prohibits her from competing with us during the term of her employment and for a period of one year after the termination of her employment. Dr. Ferro's employment agreement provides that she is not obligated to spend more than 75% of her time working for our company. Cary Grossman, our Chief Financial Officer, is an independent contractor, rather than an employee. Mr. Grossman works for our company on an at-will basis, and has not committed to continue to work for us for any defined period of time. We have an understanding with Mr. Grossman the he will devote approximately 50% of his time working for our company. If Mr. Grossman's services are discontinued and we are not able to hire an appropriate full-time, permanent Chief Financial Officer on a timely basis, we may not be able to maintain effective internal controls, accurately report our financial results or prevent fraud. As a result, our operating results could be harmed, we may fail to meet our reporting obligations and potential shareholders could lose confidence in our financial reporting, which would harm our business and the trading price of our shares.

Replacing key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of specific skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel. In addition, under Italian law, we must pay our employees a severance amount based on their salary and years of service if they leave their employment, even if we terminate them for cause or they resign.

In order to expand our operations, we will need to hire additional personnel and add corporate functions that we currently do not have. Our ability to manage our operations and growth will require us to continue to improve our operational, financial and management controls and reporting system and procedures, or contract with third parties to provide these capabilities for us.

Our independent registered public accounting firm reported a material weakness in our internal controls and we may not be able to remedy this material weakness or prevent future weaknesses. If we fail to maintain effective internal controls, we may not be able to accurately report our financial results or prevent fraud. As a result, potential shareholders could lose confidence in our financial reporting, which would harm our business and the trading price of our ordinary shares.

Our independent registered public accounting firm has informed us that our financial statement close process and the transformation of our Italian statutory financial statements into U.S. generally accepted accounting principles (U.S. GAAP) has not reduced to an acceptably low level the risk that errors in amounts that would be material in relation to those financial statements may occur and may not be detected within a timely period by management in the normal course of business. Our independent registered public accounting firm considered these deficiencies in determining the nature, timing and extent of their procedures in their audit of our annual financial statements, and those deficiencies did not affect their report on our annual financial statements included herein.

The preparation of our U.S. GAAP based financial statements is a manual process which involves the transformation of our Italian statutory financial statements into U.S. GAAP through a significant number of complex accounting adjustments and processes. This process also requires an ongoing review and update of the applicable U.S. GAAP that should be applied to the underlying Italian financial statements. This process is complicated, time-consuming and requires significant attention and time of our senior accounting personnel. Moreover, U.S. GAAP accounting adjustments tend to result in large differences between our Italian statutory and U.S. GAAP based financial statements. Finally, U.S. GAAP is a very dynamic set of financial statement guidelines, which is subject to constant change, interpretation, refinement and rigor, therefore requiring dedicated internal financial reporting resources.

A key component of remedying the material weaknesses in our internal control structure is the identification and retention, on a full time basis, of a finance professional with both Italian and U.S. GAAP accounting knowledge. In February 2005 we hired Salvatore Calabrese, whom we believe fits the aforementioned role, as our Vice-President, Finance. Mr. Calabrese is a full-time, permanent employee. If we determine that Mr. Calabrese is not an appropriate choice, we may not be able to maintain effective internal control, accurately report our financial results or prevent fraud. As a result, our operating results could be harmed, we may fail to meet our reporting obligations and potential shareholders could lose confidence in our financial reporting, which would harm our business and the market price of our shares.

The addition of Mr. Calabrese in and of itself is not enough to address the material weakness issues raised by our independent registered auditors, due to the fact that there are additional structural issues identified by our independent registered auditors that are significant enough to warrant material weakness status. The following highlights the areas identified:

· For the first six months of 2005, we still relied on FinSirton for most of the data processing related to our significant processes, such as inventory costing, payroll and general ledger; after that we established our accounting, controlling and reporting departments. However, we have limited control over the information technology system related to the input or output of data. Additionally, we have no direct control over the security of data and access controls related to the control environment.

· Our process for budgeting, awarding, tracking and verifying research and development costs has historically been handled outside of the general accounting system. We have not historically had controls surrounding this process to closely monitor such areas as actual costs versus budgeted costs, actual costs billed versus the contractual amounts and the timing of when those costs have been incurred. We are addressing this issue and have implemented additional procedures, such as the review by Mr. Calabrese of all research and development expenditures on a monthly basis and establishing our own internal control department.

· Our overall control environment is geared towards a small sized, family owned Italian company. We have historically not been required to close our accounting records on a monthly or even quarterly basis. The current process is extremely time consuming and manual intensive, and requires us to verify and reconcile between various sets of records, some of which are not under our control, in order to arrive at a draft set of Italian statutory financial statements, which are subsequently converted into U.S. GAAP financial statements with a similarly manual intensive process. Mr. Calabrese is the only member of our permanent management team that has the relative knowledge regarding U.S. GAAP. Although we are making progress in addressing these issues, such as the hiring of Mr. Calabrese and establishing our own accounting, controlling and reporting departments, the movement towards a more formalized information system that is independent of FinSirton and the implementation of an internal structure to assume the necessary tasks required of us, we have not achieved the point where we are able to address these tasks on our own.

Any failure to implement new or improved internal controls, or resolve difficulties encountered in their implementation, could harm our operating results or cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

Our revenues, expenses and results of operations have been and will continue to be subject to significant fluctuations, which makes it difficult to compare our operating results from period to period.

In 2003, 2004 and the nine months ended September 30, 2005, our revenues have fluctuated significantly due to the need to temporarily cease operations at our manufacturing facility for an upgrade to the facility for seven months in 2004 and increase production at the facility in 2003 to stockpile inventory in anticipation of this cessation. Our revenues have also fluctuated due to changes in the amounts of each of our products that we sell in different periods. Until we have successfully developed and commercialized a product candidate, we expect that substantially all of our revenues will result from the sale of our existing products. We expect that our operating results will vary significantly from quarter to quarter and year to year as a result of the timing and extent of:

· our research and development efforts;

· the revenues generated from the sale or licensing of our products;

· the execution or termination of collaborative arrangements;

· the receipt of grants;

· the initiation, success or failure of clinical trials; and

· the manufacture of our product candidates, or other development related factors.

Some of Series A senior convertible promissory notes we issued in the fourth quarter of 2004 and the first quarter of 2005 were converted into our ordinary shares upon the closing of our initial public offering in June 2005 and the remainder were repaid in June and July 2005. Our results of operations in 2004 and for the nine months ended

September 2005 reflect and our full year 2005 results of operations will reflect the interest expense we incurred on those notes. That interest expense included the amortization of the debt issue costs and of the original issue discount resulting from the inclusion of the warrants with the notes and the amortization of the value of the beneficial conversion feature resulting from the effective conversion price since the conversion ratio, which is equal to the principal amount of the notes divided by $8.10 (ninety percent (90%) of the initial offering price per ADS in our initial public offering), was less than the fair value of our ordinary shares at the time of issuance of the notes, which was $10.00. During 2004 and the nine months ending September 30, 2005, we incurred €1.828 million and €4.095 million, respectively, of interest expense on these notes (including amortization of original issue discount and debt issue costs). As a result, our interest expense, pre-tax income (loss) and net income (loss) for those periods was and will be less than it would have otherwise have been.

Accordingly, our revenues and results of operations for any period may not be comparable to the revenues or results of operations for any other period. If our operating results do not match the expectations of securities analysts and investors as a result of these and other factors, the trading price of our ADSs will likely be adversely affected.

Most of our manufacturing capability is located in one facility that is vulnerable to natural disasters, telecommunication and information system failures, terrorism and similar problems, and we are not insured for losses caused by all of these incidents.

We conduct most of our manufacturing operations in one facility located in Villa Guardia, near Como, Italy. This facility could be damaged by fire, floods, earthquake, power loss, telecommunication and information system failures, terrorism or similar events. Our insurance covers losses to our facility, including the buildings, machinery, electronic equipment and goods, for approximately €12 million, but does not insure against all of the losses listed above, including terrorism and some types of flooding. Although we believe that our insurance coverage is adequate for our current and proposed operations, there can be no guarantee that it will adequately compensate us for any losses that may occur. We are not insured for business interruption and we have no replacement manufacturing facility readily available.

We obtain office and manufacturing space and certain administrative, financial, information technology, human resources, regulatory and quality control services from affiliates. This structure creates inherent conflicts of interest that may adversely affect us.

Our largest shareholder is FinSirton, which owns approximately 39% of our ordinary shares. Dr. Ferro, who is our Chief Executive Officer and President and one of our directors, and members of her family control FinSirton. FinSirton provides some of our office space, and corporate, payroll and information technology services. Sirton, which is a wholly owned subsidiary of FinSirton, has been and currently is our principal customer. Sirton also provides us with a number of business services such as, quality control and regulatory services, and leases us office and manufacturing space.

If either of these affiliates failed to perform services for us adequately or caused us damage through their negligent conduct, our management would be presented with inherent conflicts of interest due to their ownership and oversight of FinSirton. We may have limited recourse in the event of such conflicts, and our business may be adversely affected by their occurrence.

Our industry is highly competitive and subject to rapid technological changes. As a result, we may be unable to compete successfully or to develop innovative products, which could harm our business.

Our industry is highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. While we are unaware of any other products or product candidates that treat or prevent VOD or the apoptosis that our product candidate oligotide is designed to treat, we believe that other companies have products or are currently developing products to treat some of the same disorders and diseases that our other product candidates are designed to treat. These companies include AnorMED Inc., AstraZeneca International, British Biotech plc, Abbott Laboratories, The Bayer Group, GlaxoSmithKline plc, Bristo-Myers Squibb Company, Eli Lilly Company, Boehringer Ingelheim, Axcan Pharma Inc., The Proctor & Gamble Company, Solvay Pharmaceuticals, Inc., Millenium Pharmaceuticals, Inc., ARIAD Pharmaceuticals, Inc., Celgene Corp., Titan Pharmaceuticals, Inc., Cell Genesys, Inc., Human Genome Sciences, Inc., Chugai Pharmaceutical Co., Ltd., The National Cancer Institute, Seattle Genetics, Inc., EntreMed, Inc., NeoRxx Corporation, Xcyte Therapies, Inc., Amgen, Inc., CuraGen Corporation, Aesgen, Inc. and Endo Pharmaceutical Holdings Inc.

In addition, low molecular weight heparin, made by Aventis and other companies, competes with calcium heparin, which is one of the active pharmaceutical ingredients that we sell to Sirton which makes it into a finished product for

sale by Crinos.

Many of these competitors have substantially greater research and development capabilities and experience, and greater manufacturing, marketing and financial resources, than we do. In addition, these companies' products and product candidates are in more advanced stages of development than ours or have been approved for sale by the FDA and other regulatory agencies. As a result, these companies may be able to develop their product candidates faster than we can or establish their products in the market before we can. Their products may also prove to be more effective, safer or less costly than our product candidates. This could hurt our ability to recognize any significant revenues from our product candidates.

In May 2003, the FDA designated defibrotide as an orphan drug to treat VOD. If the FDA approves the New Drug Application that we intend to file before approving a New Drug Application filed by anyone else for this use of defibrotide, the orphan drug status will provide us with limited market exclusivity for seven years from the date of the FDA's approval of our New Drug Application. However, a marketing authorization may be granted for the same therapeutic indications to a similar medicinal product if we give our consent to the second applicant, we are unable to supply sufficient quantities of defibrotide, or the second applicant can establish in its application that the second medicinal product, although similar to defibrotide, is safer, more effective or otherwise clinically superior. In that case, our product would not have market exclusivity. Additionally, while we are not aware of any other company researching defibrotide for this use, if another company does develop defibrotide for this use, there is no guarantee that the FDA will approve our New Drug Application before approving anyone else's defibrotide product for this use, in which case the first product approved would have market exclusivity and our product would not be eligible for approval until that exclusivity expires.

In July 2004, the European Commission designated defibrotide as an orphan medicinal product to both treat and prevent VOD. If the European regulators grant us a marketing authorization for those uses of defibrotide, we will have limited market exclusivity for those uses for ten years after the date of the approval. However, a marketing authorization may be granted for the same therapeutic indications to a similar medicinal product if we give our consent to the second applicant, we are unable to supply sufficient quantities of defibrotide, or the second applicant can establish in its application that the second medicinal product, although similar to defibrotide, is safer, more effective or otherwise clinically superior. In that case, our product would not have market exclusivity.

If we are unable to adequately protect our intellectual property, our ability to compete could be impaired.

Our long-term success largely depends on our ability to create and market competitive products and to protect those creations. Our pending patent applications, or those we may file in the future, may not result in patents being issued. Until a patent is issued, the claims covered by the patent may be narrowed or removed entirely, and therefore we may not obtain adequate patent protection. As a result, we may face unanticipated competition, or conclude that without patent rights the risk of bringing products to the market is too great, thus adversely affecting our operating results.

Because of the extensive time required for the development, testing and regulatory review of a product candidate, it is possible that before any of our product candidates can be approved for sale and commercialized, our relevant patent rights may expire or remain in force for only a short period following commercialization. Our issued United States patents expire between 2008 and 2016, and our United States patents for which we have submitted applications will expire between 2008 and 2025. Our United States patent covering defibrotide expires in 2010, and our U.S. patent covering the chemical process for extracting defibrotide expires in 2008. Our European patent covering both defibrotide and the chemical process for extracting defibrotide expires in 2007. There may be no opportunities to extend these patents and thereby extend FDA approval exclusivity, in which case we could face increased competition for our products that are derived from defibrotide. Patent expiration could adversely affect our ability to protect future product development and, consequently, our operating results and financial position.

We also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. We intend to eventually license or sell our products in China, Korea and other countries which do not have the same level of protection of intellectual property rights as exists in the United Sates and Europe. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Risks Related to Ownership of the ADSs

Our largest shareholder exercises significant control over us, which may make it more difficult for you to elect or replace directors or management and approve or reject mergers and other important corporate events.

Our largest shareholder, FinSirton, owns approximately 39% of our ordinary shares. Dr. Laura Ferro, who is our Chief Executive Officer and President and one of our directors, and members of her family control FinSirton. As a result, Dr. Ferro and her family, through FinSirton, will substantially control the outcome of all matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other important corporate events. They may exercise this ability in a manner that advances their best interests and not necessarily yours. In particular, Dr. Ferro may use her control over FinSirton's shareholdings in our company to resist any attempts to replace her or other members of our board of directors or management or approve or reject mergers and other important corporate events. Also, the concentration of our beneficial ownership may have the effect of delaying, deterring or preventing a change in our control, or may discourage bids for the ADSs or our ordinary shares at a premium over the market price of the ADSs. The significant concentration of share ownership may adversely affect the trading price of the ADSs due to investors' perception that conflicts of interest may exist or arise.

If a significant number of ADSs are sold into the market, the market price of the ADSs could significantly decline, even if our business is doing well.

Our executive officers (other than Cary Grossman, our Chief Financial Officer), directors and current largest shareholder, FinSirton, have agreed with the underwriters of our initial public offering to a lock-up of their ordinary shares for a period of 18 months after the effective date of the registration statement relating to our initial public offering of securities, provided, however, that if the average price per ADS of our ADSs equals or exceeds 200% of the initial public offering price of the ADSs in our initial public offering for a minimum of twenty continuous trading days, the ordinary shares may be released from the lock-up at the request of the holder, which could result in the release from the lock-up restrictions of the 3,750,000 outstanding shares held by FinSirton and any shares that underlie options that we may grant to these officers and directors in the future. Our Chief Financial Officer, Cary Grossman, has agreed with the underwriters to a lock-up of 85,000 ordinary shares issuable upon exercise of certain of his options for a period of 365 days after the effective date of the registration statement relating to our initial public offering of securities. The holders of 359,505 ordinary shares issued upon conversion of our Series A senior convertible promissory notes and 452,948 ordinary shares issuable upon exercise of the related warrants have agreed with the underwriters to a lock-up of those ordinary shares for a period of 270 days after the effective date of the registration statement relating to our initial public offering of securities. Three of our other shareholders have agreed with the underwriters to a lock-up of their 1,250,000 outstanding ordinary shares for a period of 180 days after the effective date of the registration statement relating to our initial public offering of securities. Sales of a substantial number of ADSs representing these ordinary shares in the public market could depress the market price of the ADSs and impair our ability to raise capital through the sale of additional equity securities. The underwriters, in their sole discretion and at any time without notice, may release all or any portion of the ordinary shares held by our officers, directors, and existing shareholders subject to these lockup agreements. Further, in addition to the ordinary shares registered in the registration statement of which this prospectus forms a part, we have agreed to register (upon request) 1,159,505 outstanding ordinary shares currently held by two of our shareholders, 66,000 shares issuable upon conversion of warrants issued in connection with our Series A senior convertible promissory notes held by one of our securityholders and 151,200 ordinary shares issuable upon exercise of purchase options we granted to the underwriters of our initial public offering for resale in the market. We intend to register ADSs representing such ordinary shares in addition to the ordinary shares themselves, and such registration and ultimate sale of the securities in the markets may adversely affect the market for the ADSs.

Risks Relating to Being an Italian Corporation

We are restricted under Italian law as to the amount of debt securities that we may issue relative to our equity, we may need to restore the ratio of our debt to our equity by raising more equity.

We were incorporated under the laws of the Republic of Italy. The principal laws and regulations that apply to our operations, those of Italy and the European Union, are different from those of the United States. Italian law provides

that we may not issue debt securities for an amount exceeding twice the amount of the sum of the aggregate par value of our ordinary shares (which we call our capital), our legal reserve and any other disposable reserves appearing on our latest Italian GAAP balance sheet approved by our shareholders. The legal reserve is a reserve to which we allocate 5% of our net income each year until it equals at least 20% of our capital. One of the other reserves that we maintain on our balance sheet is a "share premium reserve", meaning amounts paid for our ordinary shares in excess of the capital. At September 30, 2005, the sum of our capital, legal reserves and other reserves on our Italian GAAP balance sheet was €23.614 million. If we issue debt securities in the future, until such debt securities are repaid in full, we may not voluntarily reduce our capital or our reserves (such as by declaring dividends) if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt. If our equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of our equity, some legal scholars are of the opinion that the ratio must be restored by a recapitalization of our company. If our equity is reduced, we could recapitalize by issuing new shares or having our shareholders contribute additional capital to our company, although there can be no assurance that we would be able to find purchasers for new shares or that any of our current shareholders would be willing to contribute additional capital.

The process of seeking to raise additional funds is cumbersome, subject to the verification of a notary public as to compliance with our bylaws and applicable law and may require prior approval of our shareholders at an extraordinary meeting of shareholders.

In order to issue new equity or debt securities convertible into equity, with some exceptions, we must increase our authorized capital. In order to do so, our board must meet and resolve to recommend to our shareholders that they approve an amendment to our bylaws to increase our capital. Our shareholders must then approve that amendment to our bylaws in a formal meeting duly called, with the favorable vote of the required majority, which may change depending on whether the meeting is held on a first or subsequent call. These meetings take time to call. In addition, a notary public must verify the compliance of the capital increase with our bylaws and applicable Italian law. Further, under Italian law, our existing shareholders and any holders of convertible securities sometimes have preemptive rights to acquire any such shares on the same terms as are approved concurrent with the new increase of the authorized capital pro rata based on their percentage interests in our company. Also, our shareholders can authorize the board of directors to increase our capital, but the board may exercise such power for only five years. If the authorized capital is not issued by the end of those five years, the authorized capital expires, and our board and shareholders would need to meet again to authorize a new capital increase. Italian law also provides that if the shareholders vote to increase our capital, dissenting, abstaining or absent shareholders representing more than 5% of the outstanding shares of our company may, for a period of 90 days following the filing of the shareholders' approval with the Registry of Companies, challenge such capital increase if the increase was not in compliance with Italian law. In certain cases (if, for example, a shareholders' meeting was not called), any interested person may challenge the capital increase for a period of 180 days following the filing of the shareholders' approval with the Registry of Companies. Finally, once our shareholders authorize a capital increase, we must issue all of those authorized shares before the shareholders may authorize a new capital increase, unless the shareholders vote to cancel the previously authorized shares. These restrictions could limit our ability to issue new equity or convertible debt securities on a timely basis.

If we suffer losses that reduce our capital to less than €120 thousand, we would need to either recapitalize, change our form of entity or be liquidated.

Italian law requires us to reduce our shareholders' equity and, in particular, our capital (aggregate par value of our ordinary shares) to reflect on-going losses. We are also required to maintain a minimum capital of €120 thousand. At September 30, 2005, our capital was approximately €8.060 million. If we suffer losses from operations that would reduce our capital to less than €120 thousand, then either we must increase our capital (which we could do by issuing new shares or having our shareholders contribute additional capital to our company) or convert the form of our company into an S.r.l., which has a lower capital requirement of €10 thousand. If we did not take these steps, a court could liquidate our company.

You may not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise your right to vote.

Except as described in this prospectus and in the deposit agreement for the ADSs, with our depositary, holders of the ADSs will not be able to exercise voting rights attaching to the ordinary shares evidenced by the ADSs on an individual basis. Holders of the ADSs will have the right to instruct the depositary as their representative to exercise the rights attached to the ordinary shares represented by the ADSs. You may not receive voting materials in time to instruct the depositary to vote, and it is possible that you, or persons who hold their ADSs through brokers, dealers or other third parties, will not have the opportunity to exercise a right to vote.

You may not be able to participate in rights offerings and may experience dilution of your holdings as a result.

We may from time to time distribute rights to our shareholders, including rights to acquire our securities. Under our deposit agreement for the ADSs with our depositary, the depositary will not offer those rights to ADS holders unless

both the rights and the underlying securities to be distributed to ADS holders are either registered under the Securities Act of 1933, as amended, or exempt from registration under the Securities Act with respect to all holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or underlying securities or to endeavor to cause such a registration statement to be declared effective. In addition, we may not be able to take advantage of any exemptions from registration under the Securities Act. Accordingly, holders of our ADSs may be unable to participate in our rights offerings and may experience dilution in their holdings as a result.

You may be subject to limitations on transfer of your ADSs.

Your ADSs represented by the ADRs are transferable on the books of the depositary. However, the depositary may close its transfer books at any time or from time to time when it deems expedient in connection with the performance of its duties. In addition, the depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary deem it advisable to do so because of any requirement of law or of any government or governmental body, or under any provision of the deposit agreement, or for any other reason.

Due to the differences between Italian and U.S. law, the depositary (on your behalf) may have fewer rights as a shareholder than you would if you were a shareholder of a U.S. company.

We are incorporated under the laws of the Republic of Italy. As a result, the rights and obligations of our shareholders are governed by Italian law and our bylaws, and are in some ways different from those that apply to U.S. corporations. Some of these differences may result in the depositary (on your behalf) having fewer rights as a shareholder than you would if you were a shareholder of a U.S. corporation. We have presented a detailed comparison of the Italian laws applicable to our company against Delaware law in *"Comparison Of Italian And Delaware Corporate Laws*." We compared the Italian laws applicable to our company against Delaware law because Delaware is the most common state of incorporation for U.S. public companies.

Italian labor laws could impair our flexibility to restructure our business.

In Italy, our employees are protected by various laws giving them, through local and central works councils, rights of consultation with respect to specific matters regarding their employers' business and operations, including the downsizing or closure of facilities and employee terminations. These laws and the collective bargaining agreements to which we are subject could impair our flexibility if we need to restructure our business.

FORWARD-LOOKING STATEMENTS

This prospectus may contain forward-looking statements that involve substantial risks and uncertainties regarding future events or our future performance. When used in this prospectus, the words "anticipate,""believe,""estimate,""may,""intent,""continue,""will,""plan,""intend," and "expect" and similar expressions ident forward-looking statements. You should read statements that contain these words carefully because they discuss our future expectations, contain projections of our future results of operations or of our financial condition or state other "forward-looking" information. We believe that it is important to communicate our future expectations to our investors. Although we believe that our expectations reflected in any forward-looking statements are reasonable, these expectations may not be achieved. The factors listed in the section captioned "Risk Factors," as well as any cautionary language included in this prospectus or incorporated by reference, provide examples of risks, uncertainties and events that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. Before you invest in our ordinary shares, you should be aware that the occurrence of the events described in the "Risk Factors" section and elsewhere in this prospectus could have a material adverse effect on our business, performance, operating results and financial condition. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements set forth in this prospectus. Except as required by federal securities laws, we are under no obligation to update any forward-looking statement, whether as a result of new information, future events, or otherwise.

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. We are offering to sell and seeking offers to buy our ordinary shares only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our

ordinary shares.

USE OF PROCEEDS

We will not receive any proceeds from the sale by the selling security holders of the securities offered in this prospectus.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our ordinary shares. We currently intend to retain all available funds to support our operations and to finance the growth and development of our business. We are not subject to any contractual restrictions on paying dividends. Under Italian law and our bylaws, our payment of any annual dividend must be proposed by our board of directors and is subject to the approval of our shareholders at the annual ordinary shareholders' meeting. Before dividends may be paid out of our net income in any year, we must allocate an amount equal to 5% of the net income to our legal reserve until such reserve is at least equal to 20% of the aggregate par value of our issued shares, which we call our "capital." If a loss in our capital occurs, we may not pay dividends until the capital is reconstituted or reduced by the amount of such losses. We may pay dividends out of available retained earnings from prior years, provided that after such payment, we will have a legal reserve at least equal to the legally required minimum of 20% of the capital. We may not approve or pay dividends until this minimum is met. If the minimum is met, the board of directors proposes the issuance of a dividend and the shareholders approve that issuance, the shareholders' resolution will specify the manner and the date for their payment.

Any dividend we declare will be paid to the holders of ADSs, subject to the terms of the deposit agreement, to the same extent as holders of our ordinary shares, less the fees and expenses payable under the deposit agreement. Any dividend we declare will be distributed by the depositary to the holders of the ADSs. Cash dividends on our ordinary shares, if any, will be paid in U.S. dollars. See "Description of American Depositary Shares."

If we issue debt securities in the future, until those debt securities are repaid in full, we may not declare dividends if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt.

The board of directors may not approve interim dividends at times between our annual ordinary shareholders' meetings. Any future determination relating to dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including our future earnings, capital requirements, financial condition, future prospects and other factors as the board of directors may deem relevant.

Under Italian law, Italian companies are required to supply to the Italian tax authorities certain information regarding the identity of non-resident shareholders in connection with the payment of dividends. Shareholders are required to provide their Italian tax identification number, if any, or alternatively, in the case of legal entities, their name, country of establishment and address, or in the case of individuals, their name, address and place and date of birth, or in the case of partnerships, the information required for individuals with respect to one of their representatives. In the case of ADSs owned by non-residents of Italy, we understand that the provision of information concerning the depositary, in its capacity as holder of record of the ordinary shares underlying the ADSs, will satisfy this requirement. However, beneficial U.S. ADS holders are entitled to a reduction of the withholding taxes applicable to dividends paid to them under the income tax convention currently in effect between the United States and Italy. In order for you to benefit from that reduction, we are required to furnish certain information concerning you to the Italian tax authorities, and therefor any claim by you for those benefits would need to be accompanied by the required information.

EXCHANGE RATE INFORMATION

Fluctuations in the exchange rates between the euro and the dollar will affect the dollar amounts received by owners of ADSs on conversion by the depositary of dividends, if any, paid in euros on the ordinary shares represented by the ADSs. Moreover, such fluctuations may also affect the dollar price of the ADSs on the American Stock Exchange. The following table sets forth information regarding the exchange rates of U.S. dollars per euro for the periods indicated, calculated by using the average of the noon buying rates on the last day of each month during the periods presented.

	U.S. Dollar per Euro	
Year	**Average**	**Period End**
2000	0.9207	0.9388
2001	0.8909	0.8901
2002	0.9495	1.0485
2003	1.1411	1.2597
2004	1.2478	1.3538
2005	1.2400	1.1842

Source: Federal Reserve Statistical Release H.10

The following table sets forth information regarding the high and low exchange rates of U.S. dollars per euro for the periods indicated using the noon buying rate on each day of such period.

	U.S. Dollar per Euro	
Month	**High**	**Low**
July 2005	1.2200	1.1917
August 2005	1.2434	1.2147
September 2005	1.2538	1.2011
October 2005	1.2148	1.1914
November 2005	1.2067	1.1667
December 2005	1.2041	1.1699
January 2006 (through January 25, 2006)	1.2287	1.1980

Source: Federal Reserve Statistical Release H.10

On January 25, 2006, the noon buying rate was €1.00 to $1.2252.

We publish our financial statements in euro. This prospectus contains translations of euros into U.S. dollars at specified rates solely for the convenience of the reader. No representation is made that the euro amounts referred to in this prospectus could have been or could be converted into U.S. dollars at any particular rate or at all.

CAPITALIZATION AND INDEBTEDNESS

The following table summarizes our capitalization as of September 30, 2005:

- on an actual basis; and
- on a pro forma basis to reflect our issuance of and our receipt and use of the net proceeds from a private placement in October 2005 of 1,551,125 of our ordinary shares at a price per share of $7.05 and warrants to purchase an aggregate of 620,450 ordinary shares after deducting placement fees of $656,126 and estimated offering expenses of $363,975, as if we had received and used the net proceeds on September 30, 2005.

You should read the following table in conjunction with our financial statements and related notes appearing elsewhere in this prospectus.

	As of September 30, 2005 Actual *(unaudited)*	Pro Forma For Private Placement
Long-term debt:		
Mortgage loans secured by real property	€ 2,323	€ 2,323
Loans secured by equipment	700	700
Other	449	449
	3,472	3,472
Less current maturities	895	895
	2,577	2,577
Shareholders' equity:		
Ordinary shares, par value €1.00 per share, 11,976,803 shares authorized; 8,059,505 shares issued and outstanding, actual; 9,610,630, shares issued and outstanding, pro forma	8,060	9,611
Additional paid-in capital	26,925	33,574
Accumulated deficit	(22,818)	(22,818)
Total Shareholders' Equity	12,167	20,367
Total Capitalization	€ 14,744	€ 22,944

The pro forma capitalization excludes:

- 503,298 ordinary shares issuable at $9.52 per share upon exercise of our outstanding warrants issued in connection with the Series A notes;
- 620,450 ordinary shares issuable at $9.69 per share upon exercise of warrants issued in connection with the October 2005 private placement of ordinary shares;
- 93,068 ordinary shares issuable at $9.69 per share upon exercise of warrants issued to the placement agent of our October 2005 private placement of ordinary shares and warrants.
- 982,000 ordinary shares issuable upon exercise of our options that were outstanding at September 30, 2005; and

· 578,000 ordinary shares issuable upon exercise of options available for future grant under our existing equity incentive plans at September 30, 2005.

SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with "Operating and Financial Review and Prospects" and our financial statements and the related notes appearing elsewhere in this prospectus. The selected financial data as of December 31, 2003 and December 31, 2004 and for each of the three years ended December 31, 2004 are derived from our audited financial statements, which are included in this prospectus. The selected financial data as of September 30, 2004 and 2005 and for each of the nine month periods ended September 30, 2004 and 2005 have been derived from our unaudited financial statements, which are included in this prospectus. The selected financial data as of December 31, 2001 and December 31, 2002 and for the year ended December 31, 2001 has been derived from our unaudited financial statements, which are not included in this prospectus. Our historical results are not necessarily indicative of results to be expected in any future period.

We have not included statement of operations selected financial data for the year ended December 31, 2000 or balance sheet selected financial data for December 31, 2000 because the cost and time to create the data necessary to produce that financial data would place an unreasonable effort and expense on us, we do not believe that the data would be indicative of future operating results and we do not believe that the additional information would be useful for your review of our historical operating results.

Certain reclassification of prior period amounts have been made to our financial statements to conform to the current period presentation.

Statement of Operations Data: *(000s omitted except per share data)*	**For The Years Ended December 31,**				**For The Nine Months Ended September 30,**	
	2001	**2002**	**2003**	**2004**	**2004**	**2005**
Revenues:					*(unaudited)*	
Sales to affiliates	€ 6,459	€ 5,915	€ 6,532	€ 2,870	€ 1,719	€ 1,900
Third party product sales	—	—	—	243	243	95
Total product sales	6,459	5,915	6,532	3,113	1,962	1,995
Other income and revenues	5	392	1,843	583	501	210
Total revenues	6,464	6,307	8,375	3,696	2,463	2,205
Operating costs and expenses:						
Cost of goods sold	2,531	2,135	2,435	2,579	1,453	1,721
Charges from affiliates	1,025	1,156	1,485	1,665	915	781
Research and development	2,206	1,753	2,253	2,922	2,461	3,117
General and administrative	793	864	854	815	602	1,375
Non-cash compensation	—	—	—	379	—	363
Depreciation and amortization	185	102	67	89	52	78
	6,740	6,010	7,094	8,449	5,483	7,435
Operating income (loss)	(276)	297	1,281	(4,753)	(3,020)	(5,230)
Other income	—	195	—	—	—	—

Foreign currency exchange gain (loss), net	—	268	156	(55)	42	(435)
Interest income (expense), net	(147)	(105)	(71)	(2,192)	(26)	(4,197)
Pre-tax income (loss)	(423)	655	1,366	(7,000)	(3,004)	(9,862)
Income tax expense (benefit):						
Current	145	128	243	65	48	48
Deferred	13	108	(84)	(37)	(28)	—
	158	236	159	28	20	48
Net income (loss)	€ (581)	€ 419	€ 1,207	€ (7,028)	€ (3,024)	€ (9,910)
Net income (loss) per share:						
Basic and Diluted	€ (0.12)	€ 0.08	€ 0.24	€ (1.41)	€ (0.60)	€ (1.62)

The following table summarizes certain of our balance sheet data at September 30, 2005 on an actual basis and on a pro forma basis adjusted to reflect our receipt and use of the net proceeds from a private placement in October 2005 of 1,551,125 of our ordinary shares at a price per share of $7.05 (approximately €5.83 based on the exchange rate on the date of closing) and warrants to purchase an aggregate of 620,450 ordinary shares after deducting placement fees of $656,126 (approximately €542,253) and estimated offering expenses of $363,975 (approximately €300,806), as if we had received and used the net proceeds on September 30, 2005.

(000's omitted)	**Pro Forma Condensed Balance Sheet As of September 30, 2005**		
	Historical (Unaudited)	**Pro Forma Adjustment**	**Pro Forma**
Assets			
Cash and cash equivalents	€ 7,012	€ 8,200	€ 15,212
Receivables	909		909
Inventories	1,683		1,683
Prepaid expenses and other current assets	1,075		1,075
Total Current Assets	10,679	8,200	18,879
Property, manufacturing facility and equipment, net	8,526		8,526
Intangible and other assets, net	845		845
	€ 20,050	€ 8,200	€ 28,250
Liabilities and Shareholders' Equity			
Payables, accruals, other current liabilities	€ 3,368	€ —	€ €3,368
Current maturities of long-term debt	895		895
Deferred income	350		350
Total Current Liabilities	4,613	—	4,613
Long-term debt, net of current maturities	2,577		2,577
Termination indemnities	693		693
Total Liabilities	7,883	—	7,883
Total Shareholders' Equity	12,167	8,200	20,367
	€ 20,050	€ 8,200	€ 28,250

The following table summarizes certain of our statement of operations data for the year ended December 31, 2004 on an actual basis and on a pro forma basis adjusted to reflect:

- our receipt of the net proceeds from the sale of $8.010 million of our Series A senior convertible promissory notes from October through January 2005 as if we had received the net proceeds on January 1, 2004; and

- our receipt and use of the net proceeds from the sale of 2,400,000 of our ordinary shares in June 2005 in our initial public offering and 300,000 of our ordinary shares in July 2005 from the exercise of part of the underwriters' over-allotment option after deducting underwriting discounts and commissions and offering expenses, as if we had received and used the net proceeds on January 1, 2004.

	Pro Forma Condensed Statement of Operations For the Year Ended December 31, 2004		
(000s omitted except per share data)	**Historical (Audited)**	**Pro Forma Adjustments**	**Pro Forma**
Revenues:			
Sales to affiliates	€ 2,870	€	€ 2,870
Third party product sales	243		243
Total product sales	3,113		3,113
Other income and revenues	583		583
Total revenues	3,696		3,696
Operating costs and expenses:			
Cost of goods sold	2,579		2,579
Charges from affiliates	1,665		1,665
Research and development	2,922		2,922
General and administrative	815		815
Non-cash compensation	379		379
Depreciation and amortization	89		89
	8,449		8,449
Operating loss	(4,753)		(4,753)
Foreign currency exchange loss, net	(55)		(55)
Interest income (expense), net	(2,192)	3,784	(5,976)
Pre-tax loss	(7,000)	3,784	(10,784)
Income tax expense (benefit):			
Current	65		65
Deferred	(37)		(37)
	28		28
Net loss	€ (7,028)	€ 3,784	€ (10,812)

- The net proceeds of our initial public offering were used to repay part of our Series A senior convertible promissory notes, loans from our affiliate Sirton and for working capital. In addition, at the time of our initial public offering, the holder of $2.912 million of our Series A notes elected to convert its notes into our ordinary shares.

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If these transactions had occurred on January 1, 2004, the pro forma impact on our operating results for the year ended December 31, 2004 is that (i) we would not have incurred interest paid and accrued in the amount of €53 thousand and (ii) we would have incurred additional non-cash interest of €3.837 million from the write-off of the issue discount and debt issue costs associated with the portion of our Series A notes that were redeemed.

The following table summarizes certain of our statement of operations data for the nine months ended September 30, 2005 on an actual basis and on a pro forma basis adjusted to reflect:

- our receipt and use of the net proceeds from the sale of $1.912 million of our Series A notes in January 2005 as if we had received and used the net proceeds on January 1, 2005; and

- our receipt and use of the net proceeds from the sale of 2,400,000 of our ordinary shares in June 2005 in our initial public offering and 300,000 of our ordinary shares in July 2005 from the exercise of part of the underwriters' over-allotment option, after deducting underwriting discounts and commissions and offering expenses, as if we had received and used the net proceeds on January 1, 2004.

	Pro Forma Condensed Statement of Operations For the Nine Months Ended September 30, 2005		
(000s omitted except per share data)	**Historical (Unaudited)**	**Pro Forma Adjustments**	**Pro Forma**
Revenues:			
Sales to affiliates	€ 1,900	€	€ 1,900
Third party product sales	95		95
Total product sales	1,995		1,995
Other income and revenues	210		210
Total revenues	2,205		2,205
Operating costs and expenses:			
Cost of goods sold	1,721		1,721
Charges from affiliates	781		781
Research and development	3,117		3,117
General and administrative	1,375		1,375
Non-cash compensation	363		363
Depreciation and amortization	78		78
	7,435		7,435
Operating loss	(5,230)		(5,230)
Foreign currency exchange loss, net	(435)		(435)
Interest income (expense), net	(4,197)	258	(3,939)
Pre-tax loss	(9,862)	258	(9,604)
Income tax expense:			
Current	48		48
Deferred	—		—
	48		48
Net loss	€ (9,910)	€ 269	€ (9,652)

- The net proceeds of our initial public offering were used to repay part of our Series A senior convertible promissory notes, loans from our affiliate Sirton on and for working capital. In addition, at the time of our initial public offering, the holder of $2.912 million of our Series A notes elected to convert its notes into our ordinary shares.

- If these transactions had occurred on January 1, 2005, the pro forma impact on our operating results for the nine month period ended September 30, 2005 is that we would not have incurred interest paid and accrued in the amount of €258 thousand. Therefore, our operating results still reflect the non-cash interest expense from the write-off of the issue discount and debt issue costs associated with the redemption of a portion of our Series A notes.

OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion together with the financial statements, related notes and other financial information included elsewhere in this prospectus. This discussion may contain predictions, estimates and other forward-looking statements that involve risks and uncertainties, including those discussed under "Risk Factors" and elsewhere in this prospectus. These risks could cause our actual results to differ materially from any future performance suggested below.

Background

We are a biopharmaceutical company focused on the research, discovery and development of drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. In 1986, our founding company received approval to sell in Italy a drug called "defibrotide" to treat deep vein thrombosis, and, in 1993, it received approval to manufacture and sell defibrotide to both treat and prevent all vascular disease with risk of thrombosis. Our primary focus is on development of defibrotide for other uses in the United States and Europe, including to treat and prevent VOD and to treat multiple myeloma. In addition to defibrotide, we sell urokinase and calcium heparin, which are active pharmaceutical ingredients used to make other drugs, sulglicotide, which is intended to be used to treat peptic ulcers, and other miscellaneous pharmaceutical products. We have also developed a formulation of the drug mesalazine to treat inflammatory bowel disease. We will need to raise additional financing and/or enter into collaborative or licensing agreements in the future to fund continuing research and development for our product candidates.

We are part of a group of pharmaceutical businesses founded in Italy in 1944 that has been involved in the research and development of drugs derived from DNA and DNA molecules since the 1970's. Our largest shareholder, FinSirton, is controlled by Dr. Laura Ferro, who is our Chief Executive Officer and President and one of our directors, and her family. We receive certain administrative and other services and lease office and manufacturing space from FinSirton and Sirton, a wholly-owned subsidiary of FinSirton.

Overview

We manufacture defibrotide at our facility. Currently, we sell the defibrotide to our affiliate, Sirton. Sirton focuses on processing the defibrotide for either oral administration or intra-venous administration and sells the finished products to Crinos S.p.A., a subsidiary of Stada Arzneimittel AG. Crinos markets defibrotide in Italy to both treat and prevent vascular disease with thrombosis under a semi-exclusive license agreement with us. We also manufacture and sell to Sirton two active pharmaceutical ingredients, urokinase and calcium heparin, used by Sirton to make generic drugs, and sulglicotide, which is intended to be used to treat peptic ulcers. We sell sulglicotide to unrelated third parties and are actively working on developing other customers for these products. We also manufacture a variety of other miscellaneous pharmaceutical products.

For each of the three years ended December 31, 2004 and the nine months ended September 30, 2005, the sale of defibrotide, urokinase, calcium heparin, sulglicotide and our other products to Sirton amounted to approximately 100%, 100%, 92% and 95%, respectively, of our total product sales. The price of defibrotide to Sirton is based on comparable sale prices in years prior to 2002 to unrelated third-parties. The price for urokinase, calcium heparin, sulglicotide and our other products is based on comparable market prices charged by other manufacturers.

Sirton sells its finished products, including calcium heparin, primarily to one customer, Crinos, which sells them to the retail market. Calcium heparin, which is a by-product of manufacturing defibrotide, has seen decreased demand over the past several years due to a new competitive product, low molecular weight heparin, made by Aventis and other companies. Also, Crinos has limited its sale of urokinase to a single dose, which has a more limited market than

multiple doses. As a result, Sirton's demand for these products has decreased over the past several years, and may continue to decrease over the next several years until and unless both we and Sirton develop new customers outside of Crinos's exclusive area. Despite the fact that Sirton has recently experienced financial difficulties which could impact our business, we believe that we can continue to operate without a significant change in our operations or any disposal of our assets.

We have also generated revenue from the receipt of research grants, from the sale of rights to our intellectual property, and from licensing agreements. Our licensing agreements have included up-front payments, some of which are paid based on achieving defined milestones and royalties from product sales in the licensed territories. Our revenues by type are as described below:

(in thousands)	For The Years Ended December 31, 2002	2003	2004	For The Nine Months Ended September 30, 2004	2005
Product sales:				*(Unaudited)*	
Defibrotide	€ 3,270	€ 4,012	€ 1,424	€ 934	€ 1,348
Urokinase	1,942	1,784	1,316	671	488
Calcium heparin	269	579	51	30	125
Sulglicotide	153	147	243	253	16
Other	281	10	79	74	18
Total product sales	5,915	6,532	3,113	1,962	1,995
Other income	392	1,843	583	501	210
Total Revenue	€ 6,307	€ 8,375	€ 3,696	€ 2,463	€ 2,205

Of our product sales in the periods shown in the table above, all were sales in Italy to our affiliate Sirton except for 7.8% during the year ended December 31, 2004, which were sales of sulglicotide in Korea. Substantially all of our other income was for licensing the rights to our product candidates in the United States and Canada.

Our cost of goods sold consists of material costs, direct labor and related benefits and payroll burden, utilities, depreciation of our facility and other indirect costs of our facility.

The gross margin from our current revenues contributes towards our general and administrative expenses, research and development expenses, and capital expenditures. Our general and administrative expenses include compensation for our executive officers, office facilities, accounting and human resources, information technology services, professional fees and other corporate expenses, including public company expenses. Some of these services are provided pursuant to contracts with Sirton and FinSirton. We have implemented plans to decrease our reliance on shared services from these affiliates over time. As of September 30, 2005, we are providing our own purchasing, logistic, quality assurance, accounting, controlling and reporting services and continue to obtain corporate services, payroll services, information technology services, infrastructure costs and quality control services and regulatory activities from these affiliates.

We expect to continue to incur net losses as we continue the development of our product candidates, apply for regulatory approvals and expand our operations.

Research and Development Expenses

Our research and development expenses consist primarily of costs associated with research, preclinical development and clinical trials for our product candidates. During the years ended December 31, 2002, 2003 and 2004 and the nine months ended September 30, 2004 and 2005, we had three major categories of research projects relating to our advanced product candidates: defibrotide to treat VOD, defibrotide to prevent VOD and assorted other projects. The table below presents our research and development expenses by project for each of the years ended December 31, 2002, 2003 and 2004 and the nine months ended September 30, 2004 and 2005.

(in thousands)	For The Years Ended December 31, 2002	2003	2004	For The Nine Months Ended September 30, 2004	2005
				(Unaudited)	
Defibrotide to treat VOD	€ 1,626	€ 2,077	€ 2,521	€ 2,124	€ 2,805
Defibrotide to prevent VOD	—	25	112	94	118
Others	127	151	289	243	194
Total	€ 1,753	€ 2,253	€ 2,922	€ 2,461	€ 3,117

The Dana-Farber Cancer Institute at Harvard University sponsored and completed in December 2005 a Phase II clinical trial in the United States of defibrotide to treat VOD with multiple-organ failure. We started a Phase III clinical trial of this product candidate in the United States in December 2005, which we are sponsoring. We do not anticipate obtaining FDA or European regulatory approval of this product candidate before 2007 at the earliest. The table above also includes research and development expenses that we incurred in connection with a Phase II/III clinical trial of defibrotide to treat VOD in Europe and Israel that was sponsored by a committee of clinical investigators and conducted by Consorzio Mario Negri Sud. The committee of clinical investigators terminated this trial in October 2005.

Defibrotide to prevent VOD is also currently in a Phase II/III clinical trial of children in Europe sponsored by our company and the European Group for Blood and Marrow Transplantation. We expect to begin a Phase II/III clinical trial of defibrotide to prevent VOD and transplant associated microangiopathy in adults in Europe in early 2006 which will be sponsored by our company and the European Group for Blood and Marrow Transplantation. We do not anticipate obtaining European regulatory approval of this product candidate before 2009.

An independent Phase I/II clinical trial in Italy of defibrotide, in combination with melphalan, prednisone and thalidomide, to treat patients with advanced and refractory multiple myeloma started in December 2005. As a result, no costs associated with development of this product candidate are reflected in the table above. This clinical trial is being conducted at approximately 10 cancer centers in Italy, starting with Hospital Molinette of Torino, and the principal investigator is Dr. Mario Boccadoro, M.D., at the Division of Hematology, University of Turin, Italy.

The table above includes research and development expenses that we incurred in connection with a Phase I clinical trial of defibrotide to mobilize and increase the number of stem cells available in patients' and donors' blood for subsequent stem cell transplantation sponsored by the National Institute of Tumors of Milan. The National Institute of Tumors of Milan terminated this trial in December 2005. We cannot estimate when, if ever, we will be able to obtain European regulatory approval of this product candidate.

We expect to continue to increase our research and development expenses for the research and development of defibrotide to treat and prevent VOD and the treatment of multiple myeloma and possibly for other indications for defibrotide. This will involve sponsoring or funding, or both, clinical trials in both the United States and Europe. Development timelines and costs are difficult to estimate and may vary significantly for each product candidate and from quarter to quarter. The process of seeking regulatory approvals, and the subsequent compliance with applicable regulations, requires the expenditure of substantial resources. We expect that we will need additional funds before we have completed the development of our product candidates. We may seek to raise these funds through licensing and other collaboration agreements or through the sale of debt or equity securities. There can be no assurance that we will be successful in raising additional funds or that if we are, it will be on favorable terms.

A further discussion of the risks and uncertainties associated with developing our product candidates and certain consequences of failing to do so are set forth in the risk factors under the heading "Risks Relating to Our Business" as well as other risk factors.

Critical Accounting Policies and Estimates

Our financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. Actual results could differ from those estimates.

We believe the following policies to be the most critical to an understanding of our financial conditions and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently

uncertain.

Revenue Recognition

Currently, our primary source of revenue is from the sale of products to our affiliate, Sirton. We recognize revenue from product sales when ownership of the product is transferred to and accepted by the customer, the sales price is fixed and determinable, and collectibility is reasonably assured. Provisions for returns and other adjustments related to sales are provided in the same period the related sales are recorded on the basis of historical rates of return. Historically our returns have been insignificant due to our most significant customer also being an affiliate. However, given our intent to grow our non-affiliate revenues, we expect that in the future we will be required to periodically estimate the amount of goods subject to return.

Licensing and royalty agreements generally contemplate that our technology or intellectual property will be utilized to commercialize or produce certain pharmaceutical products and that we will receive certain fees pursuant to these agreements. Up-front payments related to licensing agreements are deferred and recognized ratably over the life of the agreement. Royalty revenues are recognized in proportion to the underlying sales. We also derive revenues from research and development agreements with co-development partners. We initially defer milestone revenues on such arrangements and subsequently recognize them as income in proportion to the costs incurred for the related development phase and in accordance with the contract terms. Performance milestone payments are not subject to forfeiture. We recognize revenue from these contractual arrangements according to Staff Accounting Bulletin No. 104, "Revenue Recognition." When necessary, we divide our agreements into separate units of accounting as required by Emerging Issues Task Force No. 00-21, "Revenue Arrangements with Multiple Deliverables" before using the applicable revenue recognition policy for each arrangement within the agreement. Accordingly, we recognize revenues on performance milestones contracts only when we have met specific targets or milestones set forth in the contracts. We defer and recognize as revenue non-refundable payments received in advance that are related to future performance over the life of the related research project.

We have used and expect to continue to enter into arrangements that have multiple deliverables. The timing and amount of revenue recognition is subject to our estimates of the relative fair values of the individual components of an agreement. In connection with recording revenue, we must make estimates and assumptions determining the expected conversion of the revenue streams to cash collected. The cash conversion estimation process requires that our management make assumptions based on historical results, future expectations, the economic and competitive environment and changes in the credit worthiness of customers, and other relevant factors. If these assumptions prove to be incorrect, our actual conversion rate of recorded revenue to cash may be lower than expected and we would be required to increase our allowance for doubtful accounts.

Our current estimate of bad debt expense is zero, as approximately 95% of our product sales are with one affiliate. If we increased our estimate of bad debt to 1% of sales, our operating results would have been lower by approximately €59 thousand, €65 thousand and €31 thousand for the three years ended December 31, 2004, respectively, and €19 thousand and €20 thousand for the nine months ended September 30, 2004 and 2005, respectively. These amounts would have a material impact on our results of operation and our shareholder's equity, but no impact on our cash flow in those periods.

Inventories

We state inventories at the lower of cost or market, determining cost on an average cost basis. We periodically review inventories and reduce items that we consider outdated or obsolete to their estimated net realizable value. We estimate reserves for excess and obsolete inventories based on inventory levels on hand, future purchase commitments, and current and forecasted product demand. Our reserve level, and as a result our overall profitability, is therefore subject to our ability to reasonably forecast future sales levels versus quantities on hand and existing purchase commitments. Forecasting of demand and resource planning are subject to extensive assumptions that we must make regarding, among other variables, expected market changes, overall demand, pricing incentives and raw material availability. Significant changes in these estimates could indicate that inventory levels are excessive, which would require us to reduce inventories to their estimated net realizable value. We capitalize inventory costs associated with certain by-products, based on management's judgment of probable future commercial use and net realizable value. We could be required to permanently write down previously capitalized costs related to commercial inventory upon change in such judgment, a delay in commercialization, delay of approval by regulatory bodies, or other potential factors. In the highly regulated industry in which we operate, raw materials, work in progress and finished goods inventories have expiration dates that must be factored into our judgments about the recoverability of inventory cost. Additionally, if our estimate of a product's demand and pricing is such that we may not fully recover the cost of inventory, we must consider that in our judgment as well. In the context of reflecting inventory at the lower of cost or market, we will record a permanent inventory write-down as soon as a need for such a write down is determined.

Impairment of Long-lived Assets

Our long-lived assets consist primarily of product rights and property and equipment. In accordance with Statement of Financial Accounting Standards No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets (SFAS 144), we evaluate our ability to recover the carrying value of long-lived assets used in our business, considering changes in the business environment or other facts and circumstances that suggest their value may be impaired.

To assess impairment of property, manufacturing facility and equipment and amortizing intangible assets for purposes of U.S. generally accepted accounting principles, we use the guidance outlined in SFAS 144. If, based on the preceding discussion, our management has concluded that impairment indicators exist, we will initially review by assessing the undiscounted cash flows expected to be derived from the asset or group of assets, comparing the lowest level of total expected undiscounted cash flow to the carrying value. If the carrying value of the asset or the group of assets exceeds the sum of the undiscounted cash flows, impairment is considered to exist. An impairment charge is assessed by comparing the assets' fair value to the carrying value. Fair value can be calculated by a number of different approaches, including discounted cash flow, comparables, market valuations or quoted market prices. The process and steps required to assess the possible impairments of assets, including the identification of possible impairment indicators, assessing undiscounted cash flows, selecting the appropriate discount rate, the calculation of the weighted average cost of capital and the discounts or premiums inherent in market prices requires a substantial amount of management discretion and judgment. If actual results differ from these estimates, or if we adjust these estimates in future periods, operating results could be significantly affected.

Research and Development Expenses

We have several activities and cost drivers that we collectively refer to as "research and development." These activities include salaries and benefits of our direct employees, facility costs, overhead costs, clinical trial costs and related trial product manufacturing costs, contracted services, subcontractor costs and other research and or developmental related costs. Research and development costs, including any upfront payments and milestones paid to collaborators, are expensed as incurred. The timing of upfront fees and milestone payments in the future may cause variability in future research and development expenses. Clinical trial costs include costs associated with contract research organizations. The billing that we receive from contract research organizations for services rendered can lag for several months. We accrue the estimated costs of the contract research organizations related services based on our estimate of management fees, site management and monitoring costs and data management costs. Our research and development department is in continuous communication with our contract research organizations suppliers to assess both their progress on the underlying study and the reasonableness of their cost estimates. Differences between estimated trial costs and actual have not been material to date, and any changes have been made when they become known. Under this policy, research and development expense can vary due to accrual adjustments related to the underlying clinical trials and the expenses incurred by the contract research organizations. For the years ended December 31, 2002, 2003 and 2004, we have incurred research and development expenses of €1.753 million, €2.253 million and €2.922 million, respectively. For the nine months ended September 30, 2004 and 2005, we have incurred research and development expenses of €2.461 million and €3.117 million, respectively. As of September 30, 2005, we had €2.169 million of future payables under outstanding contracts with various contract research organizations. Most of these contracts are on a cost plus basis or actual cost basis.

Share-Based Compensation

We have adopted the fair value based method of accounting for share-based employee compensation in accordance with the provisions of Statement of Financial Accounting Standards No. 123R, "Share Based Payment" (SFAS 123R). SFAS 123R requires us to estimate a significant number of variables in order to derive a fair value of an equity based instrument. For example, the risk of the underlying equity instruments deliverable (i.e., our ordinary shares) as compared to the market as a whole, is generally reflected in our unique "Beta". This is a unique measurement to each company, and requires several assumptions. The most common and generally accepted valuation models related to option pricing also include many significant assumptions related to such variables as dividend yields, share prices and the estimated life of the option before being exercised. The actual selection of which valuation model to use requires judgment, as there are several models to choose from.

In using the option pricing model that we have selected, changes in the underlying assumptions have the following effect on the resulting fair value output:

An increase to the:	Results in a fair value estimate that is:
Price of the underlying share	Higher
Exercise price of option	Lower
Expected volatility of stock	Higher
Expected dividends on stock	Lower
Risk-free interest rate	Higher
Expected term of option	Higher

In our current valuation, we consider the volatility factor to be critical. We have used a weighted average 50% factor based on what we believe is a representative sample of similar biopharmaceutical companies. However, this sample is not perfect as it omits, for example, Italian companies, due to the fact that there are a limited number of companies such as ourselves publicly traded in the U.S. market. If we increased our volatility factor to 80%, the fair value of our stock options granted in 2004 and the nine months ended September 30, 2005 would have increased by €46 thousand and €1.364 million, respectively, and would have resulted in €29 thousand and €88 thousand in additional compensation expense in 2004 and the nine months ended September 30, 2005, respectively. Therefore, significant changes to these estimates could have a material impact on the results of our operations.

Accounting for income taxes

We use the liability method of accounting for income taxes, as set forth in Statement of Financial Accounting Standards No. 109, "Accounting for Income Taxes." Under this method, we recognize deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities and net operating loss carry-forwards, all of which we calculate using presently enacted tax rates. We establish valuation allowances when necessary to reduce deferred tax assets to the amount that we expect to be realized.

In our accompanying financial statements we have reserved for all of our deferred tax assets as we currently believe that it is more likely than not that the assets will not be recoverable during their estimated life. In establishing our deferred tax position, in particular deferred tax assets, we only establish the tax asset if we believe that it is probable that this asset will be an allowable deduction in our tax jurisdiction. The assessment of the "recoverability" of that asset is a separate exercise, which uses the "more likely than not" criteria. In Italy, which is currently the only taxing jurisdiction where we are required to file a tax return, we have assessed that due to the limited lives of our net operating losses (limited to 5 years), we believe that these assets will not be recoverable before expiration. Although we have paid some corporate income taxes in the past, the significant amount of other tax assets in conjunction with the higher level of expected expenditures, the already existing net operating losses and limited taxable income expected in the near future resulted in our estimating that a complete valuation allowance was necessary. Significant changes either to the underlying facts, such as an increase in the net operating loss life in Italy, or our estimates, such as our ability to generate meaningful taxable income, could result in changes to our existing valuation allowance. Such changes could have a material impact on our results of operations or financial position.

Recent Accounting Pronouncements

In May 2005, the FASB issued Statement of Financial Accounting Standard No 154, "Accounting Changes and Error Corrections" (SFAS 154), which replaces APB Opinion No. 20, "Accounting Changes," and supersedes FASB Statement No. 3, "Reporting Accounting Changes in Interim Financial Statements - an amendment of APB Opinion No. 28." SFAS 154 requires retrospective application to prior periods' financial statements of changes in accounting principle, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. When it is impracticable to determine the period-specific effects of an accounting change on one or more individual prior periods presented, SFAS 154 requires that the new accounting principle be applied to the balances of assets and liabilities as of the beginning of the earliest period for which retrospective application is practicable and that a corresponding adjustment be made to the opening balance of retained earnings for that period rather than being reported in an income statement. When it is impracticable to determine the cumulative effect of applying a change in accounting principle to all prior periods, SFAS 154 requires that the new accounting principle be applied as if it were adopted prospectively from the earliest date practicable. SFAS 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. We do not expect the provisions of SFAS 154 to have a significant impact on our results of operations.

In July 2005, the FASB published an Exposure Draft of a proposed Interpretation, “Accounting for Uncertain Tax Positions.” The Exposure Draft seeks to reduce the significant diversity in practice associated with recognition and measurement in the accounting for income taxes. It would apply to all tax positions accounted for in accordance with SFAS 109, “Accounting for Income Taxes.” The Exposure Draft requires that a tax position meet a “probable recognition threshold” for the benefit of the uncertain tax position to be recognized in the financial statements. This threshold is to be met assuming that the tax authorities will examine the uncertain tax position. The Exposure Draft contains guidance with respect to the measurement of the benefit that is recognized for an uncertain tax position, when that benefit should be recognized, and other matters. This proposed interpretation would clarify the accounting for uncertain tax positions in accordance with SFAS 109. The FASB staff is considering the comment letters that have been received and is determining the plan for deliberations. The FASB board expects to issue a final interpretation, which would include amendments to SFAS 109, in the first quarter of 2006. We are currently evaluating the impact this proposed interpretation would have on our results of operations.

Results of Operations

The following tables set forth our results of operations expressed as a percentage of total product sales:

	For The Years Ended December 31,					
	2002		2003		2004	
000s omitted	Amount	Percent	Amount	Percent	Amount	Percent
Sales to affiliates	€ 5,915	100.0%	€ 6,532	100.0%	€ 2,870	100.0%
Third party product sales					243	8.5
Total product sales	5,915	100.0	6,532	100.0	3133	108.5
Other income and revenues	392	6.6	1,843	28.2	583	20.3
Total Revenues	6,307	106.6	8,375	128.2	3,696	128.8
Operating costs and expenses:						
Cost of goods sold	2,135	36.1	2,435	37.3	2,579	89.9
Charges from affiliates	1,156	19.5	1,485	22.7	1,665	58.0
Research and development	1,753	29.6	2,253	34.5	2,922	101.8
General and administrative	864	14.6	854	13.1	815	28.4
Non-cash compensation	—	—	—	—	379	13.2
Depreciation and amortization	102	1.7	67	1.0	89	3.1
	6,010	101.6	7,094	108.6	8,449	294.4
Operating income (loss)	297	5.0	1,281	19.6	(4,753)	(165.6)
Other income	195	3.3	—	—	—	—
Foreign currency exchange gain (loss), net	268	4.5	156	2.4	(55)	(1.9)
Interest income (expense), net	(105)	(1.8)	(71)	(1.1)	(2,192)	(76.4)
Pre-tax income (loss)	655	11.0	1,366	20.9	(7,000)	(243.9)
Income tax expense (benefit)						
Current	128	2.1	243	3.7	65	2.3
Deferred	108	1.8	(84)	(1.3)	(37)	(1.3)
Total income tax expense	236	3.9	159	2.4	28	1.0
Net income (loss)	€ 419	7.1%	€ 1,207	18.5%	€ (7,028)	(244.8)%

	For the Nine Months Ended September 30,			
	2004		2005	
	Unaudited		*Unaudited*	
000s omitted	**Amount**	**Percent**	**Amount**	**Percent**
Sales to affiliates	€ 1,719	87.6%	€ 1,900	95.2%
Third party product sales	243	12.3	95	4.8
Total product sales	1,962	100.0	1,995	100.0
Other income and revenues	501	25.5	210	10.5
Total Revenues	2,463	125.5	2,205	110.5
Operating costs and expenses:				
Cost of goods sold	1,453	74.1	1,721	86.3
Charges from affiliates	915	46.6	781	39.1
Research and development	2,416	123.1	3,117	156.2
General and administrative	602	30.7	1,375	68.9
Non-cash compensation	—	—	363	18.2
Depreciation and amortization	52	2.7	78	3.9
	5,483	279.5	7,435	372.7
Operating loss	(3,020)	(153.9)	(5,230)	(262.2)
Foreign currency exchange gain (loss), net	42	2.1	(435)	(21.8)
Interest income (expense), net	(26)	(1.3)	(4,197)	(210.4)
Pre-tax loss	(3,004)	153.1	(9,862)	(494.3)
Income tax expense (benefit)				
Current	48	2.4	48	2.4
Deferred	(28)	(1.4)	—	—
Total income tax expense	20	1.0	48	2.4
Net loss	€ (3,024)	(154.1)%	€ (9,910)	(496.7)%

Nine Months Ended September 30, 2005 Compared to Nine Months Ended September 30, 2004

Product sales.

Our sales were €1.995 million for the nine month period ended September 30, 2005 compared to €1.962 million in the comparable 2004 period. The timing of manufacturer orders can cause variability in sales. Total product sales in 2005 were in line with the prior period although sales to our affiliate increased 10.5% to €1.900 million and sales to third parties decreased 61% to €95 thousand. Sales to affiliates increased due to higher sales volume of the Company's main product, defibrotide, which represents 68% (or €1.348 million) and 48% (or €934 thousand) of the total product sales in the nine months period ended September 30, 2005 and 2004, respectively. The increase in affiliate sales of defibrotide was partially offset by a decrease in sales of urokinase which decreased from 34% (or €671 thousand) to 24% (or €488 thousand) of the total product sales. The decrease is due to Crinos, the principal customer of our affiliate Sirton, selling urokinase in only a single dose, which has a more limited market than multiple doses. Third party product sales decreased primarily due to lower sales volume of sulglicotide to a Korean customer. The Korean customer delayed the launch of a new product which uses sulglicotide. We expect future growth in sulglicotide revenue due to the expected launch of the Korean customer's product in 2006.

Cost of goods sold.

Our cost of goods sold was €1.721 million for the nine month period ended September 30, 2005 compared to €1.453 million in the comparable 2004 period. During the nine months ended September 30, 2005, we wrote down €130 thousand of inventory which was charged to cost of goods sold. We wrote down the inventory to adjust cost to its estimated net realizable value. Cost of goods sold as percent of product sales was 86% in 2005 and 74% in 2004. The increase in costs as a percentage of sales was due to the inventory write-off, a price decrease for our products defibrotide and urokinase, and higher production cost such as depreciation and quality control specification associated with the revamping of our facilities.

Other income and revenues

Our other income and revenues was €210 thousand for the nine month period ended September 30, 2005 compared to €501 thousand in the comparable 2004 period. In 2004, the Company recognized a milestone payment of €273 thousand under its license agreement with Sigma-Tau Pharmaceuticals, Inc. due to the issuance of an investigational new drug application for the Phase III pivotal study of defibrotide to treat VOD.

Research and development expenses.

We incurred research and development expenses of €3.117 million for the nine month period ended September 30, 2005 compared to €2.461 million in the comparable 2004 period. The increase was primarily related to the timing and amount of research and development expenses for the development of defibrotide to treat and prevent VOD and performance of related obligations under our license agreement with Sigma-Tau. Also contributing to the increase were growth in headcount and outside services to support increased activity in our clinical trials, including the preparation of regulatory filings and clinical production costs.

General and administrative expenses.

Our general and administrative expenses were €1.375 million for the nine month period ended September 30, 2005 compared to €602 thousand in the comparable 2004 period. The increase in 2005 was primarily due to increased headcount and facilities related expenses, general corporate expenses of being a public company and increase in internally provided administrative services to replace administrative services previously provided by affiliates.

Depreciation and amortization expense.

Depreciation and amortization expense was €78 thousand for the nine month period ended September 30, 2005 compared to €52 thousand in the comparable 2004 period. Depreciation expense excludes depreciation on our manufacturing facilities which are included in cost of goods sold.

Interest income (expense), net.

The components of interest expense have changed primarily due to the effects of our issuance of our Series A senior convertible promissory notes in the fourth quarter of 2004 and first quarter of 2005. In the 2005 period, interest expense on the Series A notes was €4.095 million, including non-cash interest expense of €3.837 million from amortization of the issue discount and issue cost. Interest expense for the 2004 period is net of interest which was capitalized as part of our manufacturing facility overhaul. The increase in interest expense was partially offset by income resulting from higher level of invested funds due to the completion of a public offering that closed in June 2005.

Net loss.

Our net loss was €9.910 million for the nine month period ended September 30, 2005 compared to €3.024 million in the comparable 2004 period. The increase was primarily due to the increase in interest expense, stock based compensation, research and development and general and administrative expenses and a decrease in other income and revenue.

Year Ended December 31, 2004 Compared to Year Ended December 31, 2003

Sales revenue.

Our sales were €3.11 million for the year ended December 31, 2004 compared to €6.53 million for the comparable period in 2003, a decrease of 52%. The decrease was primarily due to a need to temporarily cease operations at our manufacturing facility from February 2004 through August 2004 to complete a major facility overhaul and upgrade. A decline in sales to our principal customer and affiliate, Sirton, due to decreased demand by Sirton's principal customer, Crinos, also contributed to the decrease, slightly offset by an increase in revenues of €243 thousand from sales of sulglicotide.

Cost of goods sold.

Our cost of goods sold was €2.57 million for the year ended December 31, 2004 compared to €2.43 million for the comparable period in 2003. Our cost of goods sold as a percentage of product sales increased to 83% in 2004 from 37% in 2003. The increase in costs as a percentage of product sales was primarily due to the absorption of the fixed portion of our production costs by a reduced level of sales and the cost of materials for testing batches of product as we restarted our facility after the upgrade.

Other income and revenues.

Our other income and revenues was €583 thousand for the year ended December 31, 2004, compared to €1.84 million for the comparable period in 2003. Other income is primarily due to our recognition of revenues for performance milestone payments received under our license agreement with Sigma Tau Pharmaceuticals, Inc. and upfront payments recognized ratably over the expected life of the research period.

Research and development expenses.

We incurred research and development expenses of €2.92 million for the year ended December 31, 2004 compared to €2.25 million for the comparable period in 2003. The expenses were primarily for the development of defibrotide to treat and prevent VOD. The difference between the periods is primarily due to the timing and expenses incurred for clinical trials.

General and administrative expense.

Our general and administrative expense was €815 thousand for the year ended December 31, 2004 compared to €854 thousand for the comparable period in 2003. The slight decrease in expenses incurred is mainly due to the overhaul of our manufacturing facilities in 2004.

Depreciation and amortization expense.

Depreciation and amortization expense was €89 thousand for the year ended December 31, 2004 compared to €67 thousand for the comparable period in 2003. Depreciation expense excludes depreciation on our manufacturing facilities which are included in cost of goods sold.

Interest income (expense), net.

Interest expense was €2.20 million for the year ended December 31, 2004 compared to €77 thousand for the comparable period in 2003. Interest expense increased because of our increased borrowings, including our new mortgage, our equipment financing, loans from our affiliate, Sirton, and the issuance of our Series A senior convertible promissory notes. In 2004, interest expense included non-cash interest expense from the amortization of the beneficial conversion feature of our Series A notes of €1.77 million and amortization of debt issue costs in the aggregate amount of €1.775 million. Interest expense for the 2004 period is net of interest which was capitalized as part of our manufacturing facility overhaul.

Income taxes.

Income tax expense was €28 thousand on a pre-tax loss of €7.0 million for the year ended December 31, 2004. We incurred income tax expense of €159 thousand for the comparable 2003 period on a pre-tax income of €1.366 million. In the 2004 period, the primary difference between our income taxes at statutory rates and as reported relates to the difference in the basis of assets. We had a deferred tax asset from net operating loss carry forwards that was offset by a valuation allowance due to our current and expected future losses. In the 2003 period, the primary difference between our income taxes at statutory rates and as reported is due to the effect of net operating loss carry forwards.

Net income (loss).

Our net loss was €7.02 million for the year ended December 31, 2004 compared to a net income of €1.2 million for the comparable 2003 period. The increased loss was primarily due to the decrease in revenues and the related decrease in gross margin and the increase in general and administrative expenses.

Year Ended December 31, 2003 Compared to Year Ended December 31, 2002

Product sales

Our product sales were €6.53 million in 2003 compared to €5.92 million in 2002, an increase of 10.4%. The increase was primarily due to increased sales to Sirton during the second half of 2003 in anticipation of the need to temporarily cease operations at our manufacturing facility for an upgrade to the facility in 2004.

Cost of goods sold.

Our cost of goods sold was €2.43 million in 2003 and €2.13 million 2002. Our cost of goods sold as a percentage of sales increased to 37.3% in 2003 from 36.1% in 2002. The increase in costs as a percentage of sales was primarily due to a change in the mix of our product revenues.

Other income and revenues

Our other income and revenues was €1.84 million in 2003 compared to €392 thousand in 2002. The increase was primarily due to our recognition of revenues for milestone payments received under our license agreement with Sigma Tau Pharmaceuticals, Inc.

Research and development expenses.

We incurred research and development expenses of €2.25 million in 2003 compared to €1.75 million in 2002. The increase was primarily related to the timing and amount of research and development expenses for the development of defibrotide to treat and prevent VOD and performance of related obligations under our license agreement with Sigma Tau Pharmaceuticals, Inc.

General and administrative expenses.

Our general and administrative expenses were €854 thousand in 2003, consistent with €864 thousand in 2002.

Depreciation and amortization expense.

Depreciation and amortization expense was €67 thousand in 2003 compared to €102 thousand in 2002. The decrease was because some of assets were fully depreciated in 2002.

Interest income (expense), net.

Interest expense was €77 thousand in 2003 compared to €105 thousand in 2002. The decrease was due to reductions in the principal balance of our mortgage debt.

Income taxes.

Income tax expense was €159 thousand in 2003 compared to €236 thousand in 2002. The primary difference between income taxes at statutory rates and income taxes as reported was due to valuation allowances against our deferred tax assets as a result of our expected future operating losses.

Net income (loss).

Our net income in 2003 was €1.2 million compared to €419 thousand in 2002. The increase was primarily due to the increase in other income partially offset by higher research and development expenses.

Liquidity and Capital Resources

For the three years ended December 31, 2003 we funded our operations principally from operating cash flow, which included research grants, and the sale and licensing of intellectual property. For the year ended December 31, 2004, we used €4.119 million of cash in operating activities and we spend €5.341 million on capital expenditures. We funded our operations in 2004 principally with loans from our affiliate, Sirton, in the amount of €3.0 million, short-term

borrowings from a financial institution in the amount of €2.690 million and the proceeds of our Series A notes in the amount of $6.098 million. We used €800 thousand of the proceeds of the sale of the Series A notes to repay a portion of the loans we owed to our affiliate, Sirton, during the year ended December 31, 2004.

From January 2005 through the closing of our initial public offering in June 2005, described below, we funded our operations and repaid an additional €700 thousand of the loans we owed to Sirton with additional proceeds of the sale of our Series A notes in the amount of $1.912 million and capital contributions from our then-majority shareholder, FinSirton, in the amount of €3.9 million. We also used part of the proceeds of the sale of the Series A notes to pay for part of the costs of our initial public offering.

In June 2005 we completed an initial public offering of 2.4 million of our ordinary shares generating gross proceeds of $21.6 million. In addition, the holder of $2.912 million of our Series A notes converted its notes into 359,505 of our ordinary shares concurrent with the closing of our initial public offering. In July 2005, the underwriters of our initial public offering exercised part of their over-allotment option by purchasing an additional 300,000 of our ordinary shares generating additional gross proceeds of $2.7 million. We repaid the remaining €1.5 million of the loans we owed to Sirton and the remaining $5.098 million of our Series A notes with the proceeds of the initial public offering and over-allotment option exercise. These proceeds also funded our operations through September 30, 2005.

In October 2005, we completed a private placement of 1,551,125 of our ordinary shares at a price of $7.05 per share, together with warrants to purchase 620,450 ordinary shares, for aggregate gross proceeds of $10.9 million.

We expect to devote substantial resources to continue our research and development efforts, on regulatory expenses, and to expand our licensing and collaboration efforts. Our funding requirements will depend on numerous factors including:

· whether we are able to commercialize and sell defibrotide for the uses for which we are developing it;

· the scope and results of our clinical trials;

· advancement of other product candidates in development;

· the timing of, and the costs involved in, obtaining regulatory approvals;

· the cost of manufacturing activities;

· the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims and other patent-related costs, including litigation costs and results of such litigation; and

· our ability to establish and maintain additional collaborative arrangements.

We do not expect our revenues to increase significantly until we successfully obtain FDA and European regulatory marketing approval for, and begin selling, defibrotide to treat VOD with multiple-organ failure. We believe that some of the key factors that will affect our internal and external sources of cash are:

· our ability to obtain FDA and European regulatory marketing approval for and to commercially launch defibrotide to treat VOD with multiple-organ failure;

· the success of our other clinical and pre-clinical development programs, including development of defibrotide to prevent VOD and to treat multiple myeloma;

· the receptivity of the capital markets to financings of biotechnology companies; and

· our ability to enter into additional strategic agreements with corporate and academic collaborators and the success of such relationships.

In 2005, we expect to use approximately €9.0 million of cash to fund operations and working capital requirements, including research and development, and to incur capital expenditures of approximately €1.2 million.

We believe that our cash is sufficient for our present requirements but we will need to raise additional financing and/or enter into collaborative or licensing agreements in the future to fund continuing research and development for our product candidates, as well as any mergers or acquisitions in which we may engage. Changes in our operating plans, delays in obtaining approval to market our product candidates, lower than anticipated revenues, increased expenses or other events, including those described in “Risk Factors,” may cause us to seek additional debt or equity financing on an accelerated basis. Financing may not be available on acceptable terms, or at all, and our failure to raise capital when needed could negatively impact our growth plans and our financial condition and results of operations. Additional equity financing may be dilutive to the holders of our ordinary shares and debt financing, if available, may involve significant cash payment obligations and covenants and/or financial ratios that restrict our ability to operate our business.

Italian law provides for limits and restrictions on our issuance of debt securities. We may not issue debt securities for an amount exceeding twice the amount of the sum of the aggregate par value of our ordinary shares (which we call our capital), our legal reserve and any other disposable reserves appearing on our latest balance sheet approved by our shareholders. The legal reserve is a reserve to which we allocate 5% of our net income each year until it equals at least 20% of our capital. One of the other reserves that we maintain on our balance sheet is a “share premium reserve”, meaning amounts paid for our ordinary shares in excess of the capital. At September 30, 2005, the sum of our capital, legal reserves and other reserves on our Italian GAAP balance sheet was €23.614 million. If we issue debt securities in the future, we may not voluntarily reduce our capital or our reserves (such as by declaring dividends) if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt. If our equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of our equity, some legal scholars are of the opinion that the ratio must be restored by a recapitalization of our company. If our equity were reduced, we could recapitalize by means of issuing new shares or having our shareholders contribute additional capital to our company, although there can be no assurance that we would be able to find purchasers for new shares or that any of our shareholders would be willing to contribute additional capital.

In order to issue new equity or debt securities convertible into equity, with some exceptions, we must increase our authorized capital. In order to do so, our board must meet and resolve to recommend to our shareholders that they approve an amendment to our bylaws to increase our capital. Our shareholders must then approve that amendment to our bylaws in a formal meeting duly called, with the favorable vote of the required majority, which may change depending on whether the meeting is held on a first or subsequent call. These meetings take time to call. In addition, a notary public must verify the compliance of the capital increase with our bylaws and applicable Italian law. Further, under Italian law, our existing shareholders and any holders of convertible securities sometimes have preemptive rights to acquire any such shares on the same terms as are approved concurrent with the new increase of the authorized capital pro rata based on their percentage interests in our company. Also, our shareholders can authorize the board of directors to increase our capital, but the board may exercise such power for only five years. If the authorized capital is not issued by the end of those five years, the authorized capital expires, and our board and shareholders would need to meet again to authorize a new capital increase. Italian law also provides that if the shareholders vote to increase our capital, dissenting, abstaining or absent shareholders representing more than 5% of the outstanding shares of our company may, for a period of 90 days following the filing of the shareholders' approval with the Registry of Companies, challenge such capital increase if the increase was not in compliance with Italian law. In certain cases (if, for example, a shareholders' meeting was not called), any interested person may challenge the capital increase for a period of 180 days following the filing of the shareholders' approval with the Registry of Companies. Finally, once our shareholders authorize a capital increase, we must issue all of those authorized shares before the shareholders may authorize a new capital increase, unless the shareholders vote to cancel the previously authorized shares. These restrictions could limit our ability to issue new equity or convertible debt securities on a timely basis.

If we are unable to obtain additional financing, we may be required to reduce the scope of, or delay or eliminate some or all of our planned research, development and commercialization activities, which could harm our financing condition and operating results.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Contractual Obligations and Commitments

Our major contractual obligations and commitments relate to our real estate mortgages, other financing from banks and financial institutions and various service agreements (including those related to our clinical trials).

The following table summarizes our long-term commitments as of December 31, 2004.

(000s omitted)	**Total**	**1 Year**	**2 Years**	**3 Years**	**4 Years**	**5 Years**	**More than 5 Years**
Long-Term Debt Obligations:							
Mortgage loans	€ 2,629	€ 374	€ 655	€ 400	€ 400	€ 400	€ 400
Loans from Sirton	2,200	2,200	—	—	—	—	—
Equipment loans	831	175	175	175	175	131	—
Research loan	482	32	66	67	68	69	180
Series A Notes	4,477	4,477					
	10,619	7,258	896	642	643	600	580
Purchase Obligations and Operating Leases:							
	1,603	951	163	163	163	163	—

Inter-company services and lease						
Clinical research	840	477	131	120	106	6	—
Consultants	198	198	—	—	—	—	—
	2,641	1,626	294	283	269	169	—
Total	€ 13,260	€ 8,884	€ 1,190	€ 925	€ 912	€ 769	€ 580

We have a mortgage loan with Banca Nazionale del Lavoro that was originally granted for €1.549 million in May 1999 and bears interest at the six-month Euribor rate plus 1.0%. The loan is secured by some of our real property and was originally granted to our affiliate, Sirton, but we assumed it in 2002 in connection with a corporate reorganization of Sirton. We are required to make installment payments on the loan every six months until the final maturity in February 2006. At December 31, 2004, the amount outstanding under this loan was €357 thousand. At September 30, 2005, the amount outstanding under this loan was €119 thousand.

We have another mortgage loan with Banca Nazionale del Lavoro originally granted for €1.291 million in November 1996 that bears interest at the six-month Euribor rate plus 1.75%. The loan is secured by a mortgage on some of our real property and was originally granted to our affiliate, Sirton, but we assumed it in 2002 as part of the corporate reorganization of Sirton. We are required to make installment payments on the loan every six months until the final maturity in October, 2006. At December 31, 2004, the amount outstanding under this loan was €272 thousand. At September 30, 2005, the amount outstanding under this loan was €204 thousand.

We received a loan commitment from the Minister for University and Research for up to €653 thousand granted through San Paolo-IMI Bank. The loan is for financing research and development of defibrotide to treat and prevent VOD, and it bears interest at 1.0% per annum. In order to receive advances on the loan, we must provide the Minister with documentation supporting research and development expenses. We will need to repay this loan in installments every six months beginning six months after the completion of the related research and development, but no later than January 2012. At December 31, 2004, the amount outstanding under this loan was €482 thousand and €171 thousand was available for advance under the loan. At September 30, 2005, the amount outstanding under this loan was €450 thousand.

During 2004, we received a series of loans from our affiliate, Sirton, in the aggregate amount of €3.0 million. These loans bore interest at 3.5% per annum and mature on October 1, 2008. We repaid €800 thousand in 2004 and €700 thousand in January 2005 from the net proceeds of our Series A senior convertible promissory notes, and the remaining €1.5 million in June 2005 with the proceeds of our initial public offering.

On July 9, 2004, we obtained a loan in the approximate amount of €487 thousand from Cassa di Risparmio di Parma e Piacenza. The loan was obtained pursuant to Law No. 1329 of 28 November 1965 (Legge Sabatini), a law that facilitates the purchase and the lease of new production equipment. The loan is secured by a lien on our equipment and machinery. At December 31, 2004, the amount outstanding under this loan was €463 thousand. On August 4, 2004, we obtained an additional loan in the amount of €388 thousand from Cassa di Risparmio di Parma e Piacenza under the same terms and conditions. At December 31, 2004, the amount outstanding under this loan was €368 thousand. At September 30, 2005, the amount outstanding under both of these loans was €700 thousand.

On July 20, 2004, we obtained a third mortgage loan in the amount of €2.0 million from Banca Nazionale del Lavoro. The mortgage loan is secured by real estate owned by us and real estate owned by Sirton, and by a guarantee executed by FinSirton. In addition, payment of up to €1.0 million of our trade payables to Sirton is subordinated and made junior in right of payment to the prior payment in full in cash of the mortgage loan. No payment or prepayment of up to €1.0 million of the trade payables to Sirton may be made until our obligations under the mortgage loan are performed in full. Amounts due under the mortgage loan bear interest at the six-month Euribor rate plus 1.40%. The mortgage loan will mature on August 6, 2010. At December 31, 2004 and September 30, 2005, the amount outstanding under this loan was €2.0 million.

Our commitments for clinical research consist of fixed price contracts with third-party research organizations related to clinical trials for the development of defibrotide and related consulting services for advice regarding FDA issues, including our obligations under our trial and research agreements with the European Blood and Marrow Transplantation Group, Loyola University, Ospede San Matteo, MDS Pharma Services Italy SpA and our Consorzio Mario Negri Sud. Our research agreement with Consorzio Mario Negri Sud was cancelled in October 2005 due to a

lack of participants in the clinical trial.

From October 2004 through January 2005, we completed a private placement of $8.010 million of Series A senior convertible promissory notes. $2.912 million in principal amount of notes were converted into an aggregate of 359,505 ordinary shares at the closing of our initial public offering. We repaid the remainder of these notes with the net proceeds of our initial public offering. The notes bore interest at a per annum rate of 7% through March 31, 2005, 10% from April 2005 until maturity and the one-month LIBOR rate plus 12% after maturity.

Quantitative and Qualitative Disclosures about Market Risk

Market risk represents the risk of loss arising from adverse changes in market rates and foreign exchange rates. The carrying amounts of cash and cash equivalents, accounts receivable and other receivables, and the interest rate on our debt with floating rates represents our principal exposure to credit risk in relation to our financial assets.

As of September 30, 2005, substantially all of our cash and cash equivalents were held in accounts at financial institutions located in the Republic of Italy and the United States that we believe are of acceptable credit quality. We use interest rate swaps on our floating rate mortgage debt to hedge the risk of rising rates. We do not believe we are exposed to material risks due to changes in interest rates, although our future interest income may fluctuate in line with changes in interest rates. The risk associated with fluctuating interest rates is principally confined to our cash deposits in banks and our floating rate debt (to the extent we are not protected by interest rate hedges) and, therefore, we believe that our current exposure to interest rate risk is minimal.

Substantially all of our current revenue generating operations are transacted in, and substantially all of our assets and liabilities are denominated in the euro. In the future, we expect to transact business in the United States dollar and other currencies. The value of the euro against the United States dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions. Any change in the value of the euro relative to other currencies that we transact business with in the future could materially and adversely affect our cash flows, revenues and financial condition. To the extent we hold assets denominated in United States dollars, any appreciation of the euro against the United States dollar could result in a charge to our operating results and a reduction in the value of our United States dollar denominated assets upon remeasurement.

Trends

As a result of the temporary cessation of operations from February through August of 2004 in connection with the upgrade of our manufacturing facility, comparison of our operating results in 2004 and 2005 may not be meaningful.

Currently, our primary source of revenue is from the sale of products to our affiliate, Sirton. Sirton manufactures finished products from, in part, our products, and sells those products primarily to one customer, Crinos. Sirton sells its finished products, including calcium heparin, primarily to one customer, Crinos, which sells them to the retail market. Calcium heparin has seen decreased demand over the past several years due to a new competitive product, low molecular weight heparin, made by Aventis and other companies. Also, Crinos has limited its sale of urokinase to a single dose, which has a more limited market than multiple doses. As a result, Sirton's demand for these products of ours has decreased over the past several years, and may continue to decrease over the next several years until and unless both we and Sirton develop new customers.

On November 11, 2003, we entered into a Supply Agreement with Samil Pharm. Co., Ltd., a Korean corporation. Under this agreement, we supply Samil with sulglicotide, and Samil has the following purchase obligations:

Period	Purchase Amount
January 20, 2004 to June 20, 2005	at least 1,600 kilograms
June 20, 2005 to June 20, 2006	at least 2,600 kilograms
June 20, 2006 to June 20, 2007	at least 3,400 kilograms
After June 20, 2007	to be renegotiated

In any given period, excess purchases by Samil may be applied as a reduction of the immediately following period's minimum purchases or as compensation for a failure to purchase the immediately preceding period's minimum purchase, at Samil's choice. For the nine months period ended September 30, 2005 we have not received any orders for sulglicotide from Samil. Samil informed us that it experienced a delay in the launch of its product that uses

sulglicotide because of further market analyses required in order to properly position the product into the Korean market. We expect future growth in sulglicotide revenue due to the expected launch of Samil's product in 2006. However, we cannot be certain that Samil will launch its product in 2006, if ever.

In connection with the issue of our Series A senior convertible promissory notes, we incurred debt issues costs which are amortized over the term of the notes and included in interest expense. In addition, we recorded original issue discount on the notes due to the beneficial conversion feature of the notes and related detachable warrants. As of September 30, 2005, all of the notes have been repaid or converted into our ordinary shares. We incurred interest expense in the nine months ended September 30, 2005 on the notes in the amount of €4.095 million, including amortization of the issue costs and issue discount of €3.837 million.

As a public reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, as well as new rules subsequently implemented by the Securities and Exchange Commission and the American Stock Exchange, have required changes in corporate governance practices of public companies. We expect these new rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We also expect these new rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance.

BUSINESS

OVERVIEW

We are a biopharmaceutical company focused on the research, discovery and development of drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. In 1986, our founding company received approval to sell in Italy a drug called "defibrotide" to treat deep vein thrombosis, and, in 1993, it received approval to manufacture and sell defibrotide to both treat and prevent all vascular disease with risk of thrombosis. In addition to defibrotide, we sell urokinase and calcium heparin, which are active pharmaceutical ingredients used to make other drugs, sulglicotide, which is intended to be used to treat peptic ulcers, and other miscellaneous pharmaceutical products. We have also developed a formulation of the drug mesalazine to treat inflammatory bowel disease.

We are building upon our extensive experience with defibrotide, which our predecessors discovered over 18 years ago, to develop it for a variety of additional uses, including to treat and prevent hepatic Veno-Occlusive Disease, or VOD, a condition in which some of the veins in the liver are blocked as a result of toxic cancer treatments such as chemotherapy. A severe form of VOD with multiple-organ failure is a potentially devastating complication with a survival rate after 100 days of only approximately 20%, according to our review of more than 200 published medical articles. Results from a Phase II clinical trial conducted at Harvard University's Dana-Farber Cancer Institute of VOD with multiple-organ failure that concluded in December 2005 showed that the survival rate after 100 days was approximately 39% after treatment with defibrotide. We believe that there is no drug approved by the FDA or European regulators to treat or prevent VOD.

In May 2003, the FDA designated defibrotide as an orphan drug for use to treat VOD and made grants of $525 thousand to Dana-Farber supporting research into the use of defibrotide to treat VOD with multiple-organ failure. We have supported this research with a grant of $450 thousand to Dana-Farber. In July 2004, the European Commission granted us orphan medicinal product designation for the use of defibrotide to both treat and prevent VOD.

Due to the historically low survival rate and lack of treatments for this condition, we believe there is an immediate need for a drug to treat VOD with multiple-organ failure. The FDA has a "fast track" designation program which is designed to facilitate the development and expedite their review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. The FDA has approved our application for "fast track" designation for defibrotide to treat VOD with multiple-organ failure occurring after stem cell transplantation by means of injection. The FDA approval process for defibrotide for this use remains dependent upon the successful completion of clinical trials.

If we are successful in obtaining FDA approval and/or European regulatory approval for the initial use of defibrotide, we expect that the cash flows from operations generated by this use of defibrotide will contribute towards our working capital requirements and funding for the further development of defibrotide for other uses and our ultimate goal of FDA and European regulatory approval for other uses of defibrotide, including to prevent VOD and treat multiple myeloma. However, we will need to raise additional funds by either issuing new debt or equity securities or entering into licensing or similar collaborative arrangements in order to complete the development of these other uses of defibrotide.

If we are successful in bringing these advanced product candidates to market, we intend to use the cash flow from operations generated by them and our current products to continue to discover and develop additional uses of defibrotide, such as to prevent deep vein thrombosis in markets outside of Italy, and to develop other drugs, such as oligotide (which we believe may protect against damage to blood vessel wall cells caused by a particular cancer treatment) and Gen 301 (which we believe may prevent and treat oral ulcers that often develop during and after cancer

treatments). These product candidates will be very expensive to develop, and it is likely that we will need to either raise additional funds through debt and/or equity financings, or enter into licensing or similar collaborative arrangements, or both, in addition to cash flow we may generate from operations, to complete these developments.

Our strategy is to continue to enter into collaborative and strategic agreements to assist us in the development, manufacturing and marketing of our products and product candidates. To date, we have licensed the right to market defibrotide in North America, Central America and South America, upon regulatory approval, to treat VOD to Sigma-Tau Pharmaceuticals, Inc., which markets drug treatments for rare conditions and diseases. Sigma-Tau Pharmaceuticals, Inc. is an United States subsidiary of Sigma Tau Finanziaria S.p.A., an international family of pharmaceutical companies. We sold the rights to develop and sell our formulation of mesalazine in Canada, upon approval by Health Canada, and the United States, upon FDA approval, to Axcan Pharma, Inc., a specialty pharmaceutical company with offices in North America and Europe. We licensed the right to distribute mesalazine in Italy to Crinos, a subsidiary of Stada Arzneimittel AG. Crinos also markets defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement with us. We intend to continue to seek similar agreements with strategic partners as to other products and product candidates.

We manufacture defibrotide, calcium heparin, sulglicotide and other miscellaneous pharmaceutical products at our manufacturing facility near Como, Italy, and we lease our affiliate Sirton's facility to manufacture urokinase. Urokinase and calcium heparin are active pharmaceutical ingredients used to make other drugs. Sulglicotide is intended to be used to treat peptic ulcers. Almost all of our revenues during the past three years have come from sales of these products to Sirton. Our revenues from the sales of these products to date have been generated only in Italy and, in 2004, also in Korea and amounted to €5.9 million, €6.5 million, €3.1 million and €2.0 million in 2002, 2003, 2004 and the nine months ended September 30, 2005, respectively. In 2004 we completed an upgrade to our facilities that cost approximately €7.2 million which we believe will facilitate the FDA and European regulatory approval process for our product candidates and enable our future production. In anticipation of the renovations, we temporarily increased our production shifts and deliveries in 2003 and suspended our production for approximately seven months in 2004. Period to period comparisons of our results will therefore be difficult.

MARKET OVERVIEW

The American Cancer Society estimated that in 2005 approximately 1.4 million new patients in the United States will be diagnosed with cancer and that there will be approximately 570,000 patient deaths attributable to these cancers. Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Most cancer patients will receive one or more of chemotherapy, radiation therapy and hormone therapy.

Chemotherapy, radiation therapy and hormone therapy treatments for cancer are used to target and kill cancer cells. In some cases, the therapy treats the cancer directly; in other cases, it is administered to prepare the patient for a stem cell or bone marrow transplant, which treats cancer or other diseases. Unfortunately, these therapies often have significant negative side effects, including damage to the cells that line the blood vessel walls. The damage to these cells can lead to various disorders of the vascular system. Some patients may not be able to continue with cancer treatments because they develop these vascular system complications; other patients considered at high risk of developing these vascular system complications may not receive optimal cancer treatments or any treatment at all.

VOD. One of the disorders of the vascular system that can result from chemotherapy, radiation therapy and hormone therapy is VOD. VOD is a condition in which the damage to the cells that line the walls of small veins in the liver causes swelling of those walls, which blocks some of those veins. VOD can cause damage to the liver and, in its severe form, leads to failure of the liver and other organs (multiple-organ failure), which usually results in death. Based on our review of more than 200 articles in the medical literature, we believe that the 100 day survival rate for VOD with multiple-organ failure is only approximately 20% and that approximately 20% of people who receive stem cell or bone marrow transplants contract VOD. The International Bone Marrow Transplant Registry estimates that approximately 45,000 people worldwide received blood and bone marrow transplants in 2002. VOD poses a severe risk to the victim's health. We believe that there are no FDA or European regulatory approved treatments at this time for VOD.

Multiple myeloma. Multiple myeloma is a cancer of the plasma cell. The American Cancer Society estimates that about 15,980 new cases of multiple myeloma will be diagnosed in the U.S. during 2005. Approximately 11,300 Americans are expected to die of multiple myeloma in 2005. The 5-year survival rate for patients with multiple myeloma is approximately 32%.

STRATEGY

Our goal is to research, discover, develop and manufacture drugs derived from DNA extracted from natural sources and drugs which are synthetic oligonucleotides (molecules chemically similar to natural DNA) to treat and prevent of a variety of vascular diseases and conditions related to cancer and cancer treatments. The primary elements of our strategy include:

· **Obtain FDA approval to use defibrotide to treat VOD with multiple-organ failure.** The Dana-Farber investigator presented the results from its Phase II clinical trial of defibrotide in patients with VOD with multiple-organ failure at the 47th Annual Meeting of the American Society of Hematology held on December 12, 2005. Results show that the survival rate after 100 days for the 142 patients for whom that information was available was approximately 39% after 100 days as compared to the historical 100 day survival rate of approximately 20%. The FDA has approved our application for "fast track" designation for defibrotide to treat VOD with multiple-organ failure occurring after stem cell transplantation by means of injection. The FDA approval process for defibrotide for this use remains dependent upon the successful completion of clinical trials.

· **Obtain European regulatory approval to use defibrotide to treat VOD with multiple-organ failure.** We believe that we may be able to use results from U.S. clinical trials of defibrotide to treat VOD with multiple-organ failure to apply for European regulatory approval of this product candidate without the need to replicate the clinical trials in Europe.

· **Expand approval of defibrotide to include prevention of VOD in Europe and the United States.** A preliminary study indicated that defibrotide may provide safe and effective protection against VOD. We are cosponsoring a Phase II/III clinical trial for this use of defibrotide in children in Europe and a Phase II/III clinical trial in Europe for both the prevention of VOD and the prevention of transplant associated microangiopathy in adults. We intend to start a Phase II/III clinical trial in the United States of this product candidate in late 2006 or early 2007. If the clinical trials confirm the preliminary indications, we intend to pursue further development in Europe and the United States, and ultimately to apply for FDA and European regulatory approval for this use.

· **Expand approval of defibrotide to include treatment of multiple myeloma.** Based on preclinical studies conducted at the Jerome Lipper Multiple Myeloma Center at Harvard University's Dana Farber Cancer Institute, a Phase I/II clinical study of defibrotide to treat multiple myeloma started in December 2005 which we expect will include approximately 10 cancer centers in Italy. The principal investigator for the clinical trial is Dr. Mario Boccadoro, M.D., Division of Hematology, University of Turin, Italy.

· **Discover and develop additional product candidates.** We and others have conducted preclinical studies of other uses of defibrotide and of other drugs in our pipeline. We plan to continue to develop these product candidates and to further expand the possible markets for our products and product candidates. If we are successful in bringing our initial product candidates to market, our cash flow from operations will fund some of the costs needed to develop these product candidates. These product candidates will be very expensive to develop, and we will need to either raise additional funds through debt and/or equity financings, or enter into strategic partnerships, or both, to complete these developments.

· **Increase our marketing capacity through strategic partnerships.** We have already entered into a strategic license agreement with Sigma-Tau Pharmaceuticals, Inc. to market defibrotide to treat VOD in North America, Central America and South America upon regulatory approval and have granted Sigma-Tau Pharmaceuticals, Inc. a right of first refusal to market defibrotide to prevent VOD, to mobilize and increase the number of stem cells available for transplant and in non-intravenous forms. We intend to pursue similar agreements with Sigma-Tau Pharmaceuticals, Inc. and other strategic partners to market defibrotide in other jurisdictions and to market our other product candidates. We expect that these collaborations will allow us to focus our resources on research, development and manufacturing.

ADVANCED PRODUCT CANDIDATES

We have extensive experience developing and manufacturing drugs derived from DNA extracted from natural sources and drugs which are synthetic oligonucleotides. Our most advanced product candidates utilize defibrotide, a drug that our founding company discovered and we currently manufacture and license to others for sale in Italy, to treat and prevent VOD and to treat multiple myeloma and mobilize. Our most advanced product candidates and their stages of development are set forth below.

The FDA's designation of a product candidate as an orphan drug means that if the FDA approves our New Drug Application for that product candidate before approving a New Drug Application filed by anyone else for that product candidate, we will have limited market exclusivity for that product candidate for seven years from the date of the FDA's approval of our New Drug Application. If the FDA were to approve a New Drug Application filed by someone else for a product candidate prior to the FDA approving our New Drug Application for the product candidate, our ability to market the product candidate would be restricted by their orphan drug exclusivity. Similarly, the

Commission of the European Communities designation of a product candidate as an orphan medicinal product means that if the European regulators grant us a marketing authorization for that product candidate, we will have limited market exclusivity for that product candidate for ten years after date of the approval. If the European regulators were to grant a marketing authorization filed by someone else for a product candidate prior to the European regulators granting a marketing authorization for the product candidate, our ability to market the product candidate could be restricted.

The following table sets forth the clinical trials of our advanced product candidates completed or being conducted to date.

Product candidate	Intended use	Orphan drug designation	Territory and status of clinical trial	Sponsor of clinical trial	Centers participating in clinical trial	Number of patients participating in clinical trials
Defibrotide	Treat VOD with multiple-organ failure	Orphan drug designation in the United States and Europe	United States, Phase I/II, results published in 2002	Investigator at Dana-Farber Cancer Institute at Harvard University	Dana-Farber Cancer Institute, Boston Brigham and Women's Hospital, Boston The Children's Hospital, Boston Massachusetts General Hospital, Boston Beth Israel Deaconess Medical Center, Boston Columbia University, New York Loyola University Medical Center, Chicago University of Colorado Health Center, Denver Duke University Medical Center, Durham Johns Hopkins Oncology Center, Baltimore Fred Hutchinson Cancer Research Center, Seattle.	88
	Treat VOD with multiple-organ failure		United States, Phase II, results published in December 2005	Investigator at Dana-Farber Cancer Institute at Harvard University	Dana-Farber Cancer Institute, Boston Brigham and Women's Hospital, Boston The Children's Hospital, Boston Massachusetts General Hospital, Boston Beth Israel Deaconess Medical Center, Boston Fred Hutchinson Cancer Research Center, Seattle Duke University Medical Center, Durham Johns Hopkins Oncology Center, Baltimore Memorial Sloan Kettering Cancer Center, New York City of Hope, Duarte	142

	Treat VOD with and without multiple-organ failure		Europe, "Compassionate use" study, results published in 2000	Committee of clinical investigators	Christie Hospital, Manchester Royal Free Hospital, London Ospedali Riuniti, Bergamo University Hospital, Munich University Hospital, Graz	40
	Treat VOD with multiple-organ failure		United States, Phase III, started in December 2005	Gentium	Dana-Farber Cancer Institute, Boston Brigham and Women's Hospital, Boston The Children's Hospital, Boston Massachusetts General Hospital, Boston Beth Israel Deaconess Medical Center, Boston Fred Hutchinson Cancer Research Center, Seattle Duke University Medical Center, Durham Johns Hopkins Oncology Center, Baltimore Memorial Sloan Kettering Cancer Center, New York City of Hope, Duarte Children Hospital of Philadelphia MD Anderson Cancer Center, Houston	0 at December 31, 2005, patients scheduled to be enrolled beginning by first quarter of 2006
Defibrotide	Prevent VOD	Orphan drug designation in Europe	Switzerland, preliminary pilot clinical study completed	University Hospital of Geneva	University Hospital of Geneva	104
			Europe, Phase II/III, pediatric	European Group for Blood and Marrow Transplantation and Gentium	Pediatric Hematology Centers of Frankfurt, Ulm, Tübingen, Jena, Kiel, Düsseldorf, München, Muenster, Hannover, Dresden, Hamburg, Zürich, Genf, Bern, Graz, Wien, Tivka,	0 at December 31, 2005; patients scheduled to be enrolled beginning by first quarter of 2006

				Israel, Leiden, Utrecht, Goeteborg, Upsala, Huddinge, Lund; London, Bristol, Genua, Monza	
		Europe, Phase II/III, adult, anticipated for 2006	European Group for Blood and Marrow Transplantation and Gentium	Trial has not started	0 at December 31, 2005; patients scheduled to be enrolled beginning by second quarter of 2006
Defibrotide	Treat multiple myeloma	United States, preclinical studies, completed	Investigator at Dana-Farber Cancer Institute at Harvard University	Dana-Farber Cancer Institute at Harvard University	0 (study was in rodents)
		Italy, Phase I/II started in December 2005	Investigator at the University of Turin	Approximately 10 centers, beginning with Hospital Molinetter of Tornio	0 at December 31, 2005; patients scheduled to be enrolled beginning by first quarter of 2006

Defibrotide to treat VOD with multiple-organ failure

Our leading product candidate is defibrotide to treat VOD, and in particular VOD with multiple-organ failure. In May 2003, the FDA designated defibrotide as an orphan drug to treat VOD. In July 2004, the Commission of the European Communities designated defibrotide to treat and prevent VOD as an orphan medicinal product, which is similar to being designated an orphan drug by the FDA.

In 2000, the British Journal of Hematology published the results of a 40 patient "compassionate use" study of defibrotide to treat VOD conducted in 19 centers in Europe from December 1997 to June 1999. 19 patients, or 47.5%, survived more than 100 days. The publication indicated that four of the 19 patients who survived more than 100 days subsequently died. 28 patients were judged likely to die or had evidence of multiple-organ failure, and 10, or 36%, of these patients survived more than 100 days. The 100 day survival rate is a milestone generally used to determine transplant success. This publication stated that the defibrotide was generally safely administered with no significant side-effects.

In 2002, the results from 88 patients with VOD with multiple-organ failure following stem cell transplants who were treated with defibrotide from March 1995 to May 2001 were published in *Blood*, the Journal of the American Society of Hematology. This publication reported data on 19 patients treated under individual Investigational New Drug Applications and on a subsequent 69 patient multi-center Phase I/II clinical trial that was conducted under an Investigational New Drug Application filed by a Dana-Farber investigator. The primary goal of the trial was the assessment of the potential effectiveness of the drug and its side effects, if any. All patients in the clinical trial received defibrotide on an emergency basis. This publication stated that 31 patients, or 35.2%, of those patients survived at least 100 days after stem cell transplant with minimal adverse side effects, primarily transient mild hypotension. Thirteen of those 31 patients who had survived more than 100 days had died by October 2001, the latest date for which survival information was available. No mortality from VOD or other toxicity related to the cancer treatment was seen more than 134 days after treatment with defibrotide, with the most common cause of later death being relapse.

The Dana-Farber investigator also sponsored, under its Investigational New Drug Application, a Phase II clinical trial in the United States of defibrotide which enrolled 145 stem cell transplant patients with VOD with multiple-organ failure at eight cancer centers. This trial was funded by us and $525 thousand in grants from the orphan drug division of the FDA. The purpose of this trial was to evaluate the effectiveness of this drug, including the effect of the drug on the survival rate of patients with VOD with multiple-organ failure, the effective dosage and potential adverse side effects.

The Dana-Farber investigator presented the results from this Phase II clinical trial at the 47th Annual Meeting of the American Society of Hematology on December 12, 2005. Results show that the survival rate after 100 days for the 142 patients for whom that information was available was approximately 39% after 100 days with minimal adverse events as compared to the historical 100 day survival rate of approximately 20%. We do not have information about the survival rate after 100 days.

The FDA has approved our application for "fast track" designation for defibrotide to treat VOD with multiple-organ failure occurring after stem cell transplantation by means of injection. The FDA approval process for defibrotide for this use remains dependent upon the successful completion of clinical trials. Fast track designation may shorten and facilitate the approval process.

We started a Phase III clinical trial in the United States for this use in December 2005. We are the sponsor and will conduct the Phase III clinical trial and any additional clinical trials required by the FDA under our own Investigational New Drug Application that we submitted to the FDA in December 2003, instead of under Dana-Faber's Investigational New Drug Application. Sponsoring and conducting the additional clinical trials under our own Investigational New

Drug Application will allow us to communicate directly with the FDA regarding the development of this drug for marketing approval.

Consorzio Mario Negri Sud had been conducting a multi-center Phase II/III clinical trial in Europe and Israel of defibrotide to treat VOD after stem cell transplants that was sponsored by a committee of clinical investigators. The trial was scheduled to include approximately 340 patients, of which approximately 60 had been enrolled at December 31, 2004. We were funding the costs of this clinical trial. The committee of clinical investigators cancelled the trial in October 2005 due to a lack of patients enrolled in the trial. This trial included a randomly selected control group. We believe that patients may have been reluctant to enroll due to the possibility of being placed in the control group and not receiving treatment.

Defibrotide to prevent VOD

We believe there is a significant market opportunity for defibrotide to prevent VOD for patients at risk of developing VOD. Based on our experience researching VOD, we believe that many recipients of high doses of chemotherapy, radiation therapy or hormone therapy or of therapies that prepare for stem cell transplants have an elevated risk of developing VOD. We believe that there are no FDA or European regulatory approved drugs to prevent VOD at this time.

A preliminary pilot clinical study in Switzerland by the University Hospital of Geneva on defibrotide, in patients at high risk of VOD, suggested that defibrotide may provide effective and safe prevention against VOD. The study tested patients who received stem cell transplants. None of 52 successive transplant patients who received defibrotide as a preventative agent developed VOD. By comparison, 10 of 52 patients who underwent transplants in the same center before the study developed VOD, which was fatal in three cases. The study report indicated that mild to moderate toxicity such as mild nausea, fever and abdominal cramps was documented, although the report stated that it was difficult to determine whether the toxicity was directly attributable to the defibrotide, the chemotherapy that preceded the stem cell transplants or other drugs used during the stem cell transplants. The study report did not indicate the number of patients who experienced this toxicity.

We are cosponsoring with the European Group for Blood and Marrow Transplantation, a not-for-profit scientific society, a Phase II/III clinical trial in Europe of defibrotide to prevent VOD in children. We expect this study to include 270 patients enrolled by several centers in Europe beginning by the first quarter of 2006, who will randomly receive either defibrotide or no treatment.

We are also co-sponsoring with the European Group for Blood and Marrow Transplantation a second Phase II/III clinical trial in Europe of defibrotide to prevent VOD and transplant associated microangiopathy in adults. We expect this trial to include approximately 300 patients enrolled by several centers in Europe beginning by the second quarter of 2006, who will randomly receive either defibrotide or no treatment.

We intend to initiate development of defibrotide to prevent VOD in the United States by starting a clinical trial of this product candidate in late 2006 or early 2007.

Defibrotide to treat multiple myeloma.

Preclinical studies conducted by the Myeloma Center of the Dana-Farber Cancer Institute at Harvard University on human multiple myeloma in rodents suggests that defibrotide’s effect on the cells of blood vessel walls may help increase the effectiveness of other treatments for multiple myeloma. In particular, the overall survival rate of rodents with human multiple myeloma increased and tumor volume decreased when the animals were administered defibrotide in combination with other chemotherapy agents. The Myeloma Center of Dana-Farber is conducting additional preclinical studies of defibrotide’s effects on multiple myeloma.

An independent Phase I/II clinical study of defibrotide to treat multiple myeloma in combination with melphalan, prednisone, and thalidomide (MPT) started in December 2005 which we expect to include approximately 10 cancer

centers in Italy. The principal investigator for the clinical trial is Dr. Mario Boccadoro, M.D., Division of Hematology, University of Turin, Italy. We will pay part of the costs of this trial. The trial is scheduled to be a dose-escalating, multi-center, non-comparative, open label study designed to assess the safety and the efficacy of Defibrotide with MPT regimen as a salvage treatment in advanced refractory MM patients. The Phase I component of the trial will combine oral MPT with escalating doses of defibrotide to determine the maximum tolerated dosage of defibrotide combined with MPT in 24 patients (three cohorts of eight patients). In the Phase II component of the trial, the oral MPT regimen will be combined with the maximum tolerated dosage of defibrotide and administered to 20 consecutive patients to assess response rate and clinical efficacy.

ADDITIONAL PRODUCT CANDIDATES

We and other unrelated institutions have conducted preclinical studies of other uses of defibrotide and of other drugs in our pipeline. We plan to continue to develop our product candidates to further expand our possible markets. If we are successful in bringing our advanced product candidates to market, we intend to use our cash flow from operations generated by them and our current products to continue to fund some of the costs needed to develop these product candidates. These product candidates will be very expensive to develop, and we will need to either raise additional funds through debt and/or equity financings, or enter into strategic partnerships, or both, to complete these developments.

Product Candidate	Intended Use	Stage of Development
Defibrotide	Mobilize and increase the number of stem cellsa available in patients' and donors' blood for subsequent stem cell transplantation	Preclinical completed in Italy; Phase I trial in Italy cancelled due to lack of enrollees
Defibrotide	Oral administration to prevent deep vein thrombosis outside Italy	Phase I/II completed in Denmark
Mesalazine	Treat inflammatory bowel disease	Phase III in United States and Canada
Oligotide	Protect against damage (apoptosis) of cells of the blood vessel walls caused by fludarabine, a chemotherapy agent	Preclinical in Germany
Gen 301	Prevent and treat mucositis	Preclinical in England

Defibrotide to mobilize and increase the number of stem cells available in patients' and donors' blood for subsequent stem cell transplantation

We believe that we may be able to further expand our market for defibrotide to include its use to mobilize and increase the number of stem cells available for transplant. A stem cell transplant is a medical procedure that involves collecting stem cells from the blood of a patient before chemotherapy, radiation therapy or hormone therapy or a compatible donor intravenously and then re-administering them to the patient after the treatment. Stem cell transplants are used to treat side effects of certain cancer therapies. One side effect of chemotherapy, radiation therapy and hormone therapy is that these treatments can permanently damage the bone marrow, which inhibits or halts the production of blood cells and can be life threatening. There are many different types of blood cells, but they all develop from stem cells. Most of these stem cells are found in the bone marrow (the soft inside part of the bone), although some are found in the blood (peripheral blood stem cells). Doctors may use stem cell transplants to regenerate bone marrow after these cancer therapies. Stem cell transplants can also be used to treat some cancers directly, in addition to treating this side effect of some cancer treatments.

Peripheral blood stem cell transplants are less invasive than bone marrow transplants, which require a surgical procedure to remove bone marrow from the patient's or donor's bones. However, since blood is not as rich in stem cells as bone marrow, the availability of adequate amounts of peripheral blood stem cells from the patient or a compatible donor is critical to the effectiveness of a peripheral blood stem cell transplant.

Preclinical studies conducted by The National Institute of Tumors of Milan in rodents and non-human primates (rhesus monkeys) used defibrotide in combination with G-CSF, a drug commonly used to cause stem cells to migrate (mobilize) from the bone marrow into the blood circulatory system for collection and transplant. The preclinical study in rodents showed a statistically significant increase in certain types of stem cells available for transplant. The preclinical study in primates showed that the number of stem cells available for transplant increased by a factor of six.

The National Institute of Tumors of Milan was conducting a Phase I clinical trial in Italy to evaluate the safety and effectiveness of defibrotide to increase the number of stem cells available for transplant when used with G-CSF in humans. The primary objective of this study was to determine the dose of defibrotide to be injected over a 24-hour period by continuous intra-venous injection necessary to increase the number of stem cells to the level that was obtained in the rhesus monkeys study. Patients who did not achieve a target number of stem cells available for transplant after an initial treatment with G-CSF were eligible to be enrolled for this study. The strict enrollment criteria led to difficulties in enrolling patients and the National Institute of Tumors of Milan cancelled this trial in December 2005 for this reason.

Defibrotide to prevent deep vein thrombosis

We and our predecessors have manufactured and marketed defibrotide in Italy to treat deep vein thrombosis since 1986 and to both treat and prevent all vascular disease with risk of thrombosis since 1993. These uses of defibrotide both involve intra-venous injection and oral administration. Beginning in 2002, we licensed the right to sell defibrotide to treat and prevent all vascular disease with risk of thrombosis in Italy to Crinos.

Vascular disease with risk of thrombosis refers to several serious cardiovascular conditions, one of which is deep vein thrombosis. Deep vein thrombosis is a blockage of the veins in the legs that can have many causes, including hip surgery, pregnancy, cancer and cancer therapies and injuries. Deep vein thrombosis can lead to pulmonary embolism, the dislodging and migration of blood clots to the lungs, which is often fatal.

Our future plans include the development of oral administration of defibrotide to prevent deep vein thrombosis for markets outside of Italy. We concluded a 69-patient Phase I/II clinical trial of defibrotide to prevent deep vein thrombosis after hip surgery in Denmark in 2002. In this clinical trial, the defibrotide was administered through intra-venous infusion for up to two days followed by oral administration for a further three to six days. This trial was discontinued after three patients receiving defibrotide through intra-venous infusion experienced hypotension, a serious adverse event. No serious adverse events were noted in patients receiving defibrotide orally. Based on the results of this trial and prior use of defibrotide to prevent deep vein thrombosis in Italy, we nonetheless believe that defibrotide may be safe and effective to prevent deep vein thrombosis. We believe that the largest market opportunity for this use of defibrotide involves administering it orally, as this would allow patients to take the drug at home instead of a hospital. We would need to conduct additional clinical trials in markets outside of Italy to explore the safety and effectiveness of oral administration of defibrotide for this use.

Mesalazine

Inflammatory bowel disease, or ulcerative colitis, is a disease that causes inflammation and lesions in the large intestine. We have created a gel formulation of mesalazine, an anti-inflammatory product intended to treat the disease. In 2002 we sold to Axcan the exclusive rights to develop and market in Canada, upon Health Canada approval, and the United States, upon FDA approval, our formulation of mesalazine to be developed to treat inflammatory bowel disease. Axcan is a Canadian pharmaceutical company that specializes in gastrointestinal therapies and markets its products through its own sales force in North America and Europe. In addition to certain upfront payments aggregating €1.258 million, Axcan has agreed to pay us deferred consideration in the amount of 4% of Axcan’s net sales of mesalazine in Canada and the United States during the first ten years of its commercialization.

Axcan completed an open-label, randomized 180-patient Phase III study to assess the evolution of the clinical symptoms of inflammatory bowel disease during the induction of remission by our formulation of mesalazine in 2005. This study was supported by two 50-patient placebo-controlled studies. Axcan has reported that they expect to “launch” the formulation in 2006 if it is approved by Health Canada and/or the FDA. We believe that patients will tolerate our formulation of mesalazine better than other companies’ formulations.

We also licensed the rights to develop and sell our formulation of mesalazine in Italy to Crinos, which has a right of first refusal to license the rights for substantially all other European countries.

Oligotide

We are developing oligotide, another product derived from natural DNA. One particular chemotherapy agent, fludarabine, is used to treat chronic lymphocytic leukemia. Fludarabine interferes with the growth of cancer cells, but it also causes damage, specifically apoptosis (a series of events in a cell that leads to its death), to blood vessel wall cells, which is an undesirable toxic effect of the chemotherapy. Researchers at the University of Regensburg,

Germany, performed preclinical studies showing that oligotide, when used in combination with fludarabine, reduced the level of apoptosis in the cells of blood vessel walls to approximately the same level normally found in cells that have not been treated with fludarabine. We believe there is a potential market for oligotide to be used in conjunction with fludarabine and other cancer therapies to reduce the undesirable toxic effects of these cancer therapies. We may conduct further research on oligotide to investigate its effectiveness in protecting blood vessel cell walls against cancer therapies.

Gen 301

Some cancer therapies, such as chemotherapy and radiation therapy, can cause mucositis. Mucositis is a condition in which the lining of the digestive system becomes inflamed and ulcerated, often resulting in sores in the mouth. Patients with these oral ulcerations suffer from pain and have an associated risk of developing life-threatening infections because the patients also have a diminished natural immune system following chemotherapy or radiation therapy. Gen 301 is another product derived from pig intestines that we are developing and investigating in preclinical studies to prevent and treat this complication. *Oral Complications in Cancer Chemotherapy, Cancer Incidence, and Mortality in the U.S.*, a 2003 article in *Dental Article Review and Testing*, states that mucositis occurs in approximately 40% of cancer patients who receive chemotherapy and 80% of patients who receive certain stem cell transplants. 50% of patients who develop oral ulcerations require intervention that often includes modifying or discontinuing the chemotherapy. *Oral Mucositis and the Clinical and Economic Outcomes of Hematopoietic Stem-Cell Transplantation*, by Stephen T. Sonis, et. al. (2001) estimates that there is an additional cost of more than approximately €31 thousand for every patient that develops oral ulcerations during the 100-day post transplant period.

We are currently investigating Gen 301 in preclinical studies on a rodent model of mucositis caused by radiation therapy.

CURRENT PRODUCTS

Our revenues from the sales of our current products were €6.5 million, €5.9 million, €6.5 million, €3.1 million and €2.0 million in 2001, 2002, 2003, 2004 and the nine months ended September 30, 2005, respectively. We and our predecessors have manufactured defibrotide since 1986 using a manufacturing process on which we hold a U.S. patent and a European patent granted in 1991 and license others to sell it in Italy. In addition to defibrotide, we manufacture and sell in Italy urokinase and calcium heparin, which are active pharmaceutical ingredients used to make other drugs, sulglicotide, which is intended to treat peptic ulcers, and other miscellaneous pharmaceutical products. We have also developed a formulation of the drug mesalazine to treat inflammatory bowel disease.

Defibrotide

Currently, we manufacture defibrotide for Sirton, our affiliate. Sirton focuses on processing the defibrotide for either oral administration or intra-venous administration and sells the finished products to Crinos. Crinos markets defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement. We have the right to grant a second license in Italy but only to a third party that has been expressly approved by Crinos.

Urokinase

Urokinase is made from human urine and has the potential to dissolve fibrin clots and, as such, is used to treat various vascular disorders such as deep vein thrombosis and pulmonary embolisms. We sell urokinase to Sirton, who uses it as an ingredient in the manufacture of generic drugs. Sirton sells the final formulated generic drugs to other companies, which then sell the drugs to hospitals and pharmacies.

Heparin Calcium

Heparin calcium is made from pig intestines and prevents the blood from clotting. Decreasing clot formation diminishes the likelihood of strokes and heart attacks. Heparin calcium has numerous uses including the treatment of certain types of lung, blood vessel, and heart disorders, and administration during or after certain types of surgery, such as open heart and bypass surgeries. Other uses include the flushing of catheters and other medical equipment. Heparin calcium and its salts are also part of many topical preparations to treat various inflammatory disorders. We

sell heparin calcium to Sirton, who uses it as an ingredient in the manufacture of generic drugs. Sirton sells the final formulated generic drugs to other companies, which then sell the drugs to hospitals and pharmacies.

Sulglicotide

Sulglicotide is developed from pig intestines and appears to have ulcer healing and gastrointestinal protective properties. The effects of this drug have prompted us to commission a preclinical investigation by Epistem Ltd., an United Kingdom contract research organization specializing in studies of mucositis caused by anticancer or radiation therapies, into its function in potential prevention and treatment of mucous membrane damage. We also sell sulglicotide to Sirton for use in contract manufacturing of Gliptide, a drug marketed in Italy to treat peptic ulcers. We expect to sell sulglicotide to Samil, a Korean company, for use in manufacturing a product of Samil's for sale in Korea.

OUR STRATEGIC ALLIANCES

License and Distribution Agreements

On December 7, 2001, we entered into a License and Supply Agreement with Sigma-Tau Industrie Pharmaceutiche Reunite S.p.A., which later assigned the contract to an affiliate, Sigma Tau Pharmaceuticals, Inc., which markets drug treatments for rare conditions and diseases. Sigma Tau Industrie Pharmaceutiche Reunite S.p.A. and Sigma Tau Pharmaceuticals, Inc. are subsidiaries of Sigma Tau Finanziaria S.p.A., an international family of pharmaceutical companies. Under this agreement, we have licensed the right to market defibrotide in the United States to treat VOD to Sigma-Tau Pharmaceuticals, Inc. This license expires on the earlier of the eighth year of our launch of the product or the expiration of the U.S. patent regarding the product, which expires on 2010.

In return for the license, Sigma-Tau Pharmaceuticals, Inc. agreed to pay us an aggregate of $4.9 million, of which it has paid us $4.0 million to date. It will owe us an additional $550 thousand within 30 days of the end of a Phase III pivotal study, and $350 thousand within 30 days of obtaining an FDA New Drug Application or Biologic License Application and other approvals necessary for the marketing of defibrotide in the United States. We will not recognize the amounts due for these performance criteria until the performance obligations are fully satisfied. If we unilaterally discontinue development of defibrotide to treat VOD (after written notice to Sigma-Tau Pharmaceuticals, Inc.) and then resume the development, substantially availing our company of the stages previously completed, either independently or with a third party, within 36 months of the discontinuation, then we will be required to promptly reimburse Sigma-Tau Pharmaceuticals, Inc. for the amounts received. We do not have any intention to discontinue the development of this product candidate.

If during the drug development stages we realize that the activities to bring the product to completion would require a material increase of expenditures, either party can terminate the agreement. If we or Sigma-Tau Pharmaceuticals, Inc. terminates the agreement for that reason and we then resume the development, substantially availing our company of the stages previously completed, either independently or with a third party, within 36 months of the termination, we will be required to promptly reimburse Sigma-Tau Pharmaceuticals, Inc. for the amounts received. We are not aware of any factors that would require a material increase of expenditures for the remaining development activities.

Sigma-Tau Pharmaceuticals, Inc. must purchase all of its defibrotide for this use from us at a price equal to the higher of €50.00 per unit or 31% of its net sales of defibrotide, and must also pay us a royalty equal to 7% of its net sales of defibrotide. We also granted Sigma-Tau Pharmaceuticals, Inc. an exclusive, irrevocable right of first refusal to market defibrotide to prevent VOD, to mobilize and increase the number of stem cells available in patients' and donors' blood for subsequent stem cell transplantation, and in non-intravenous forms for these indications.

We have entered into an agreement with Sigma-Tau Pharmaceuticals, Inc. to expand Sigma-Tau's current license and right of first refusal to market defibrotide in the United States to all of North America, Central America and South America.

On October 9, 2002, we entered into a Purchase Agreement with Sirton and Axcan, a specialty pharmaceutical company with offices in North America and Europe. Under this agreement, we and Sirton sold the rights to develop, make, use and sell our formulation of mesalazine in the United States, upon FDA approval, and Canada, upon Health Canada approval, to Axcan in consideration for Axcan paying us:

· €170 thousand upon execution of the agreement;

· €300 thousand within 60 days of filing New Drug Application for our formulation of mesalazine with the FDA;

· €750 thousand within 60 days of Axcan's receipt of marketing approval for our formulation of mesalazine in the United States by the FDA; and

· 4% of Axcan's net sales of the product in the United States and Canada during the first ten years of its commercialization.

To date, Axcan has paid us an aggregate of €170 thousand. In addition to the above amounts, Axcan agreed to pay Sirton an aggregate of €280 thousand in consideration for certain intellectual property related to our formulation of mesalazine transferred by Sirton to Axcan in connection with the purchase. We and Sirton also granted Axcan a right of first refusal to purchase or license the rights to exploit, register, promote or commercialize our formulation of mesalazine in territories outside of substantially all European countries.

On May 17, 2002, we, Sirton (then known as Crinos Industria Farmacobiologica S.p.A.), SFS Stada Financial Services Ltd. and Crinos S.p.A. entered into an Umbrella Agreement. Under this Umbrella Agreement, Sirton spun off its marketing and sales division, including the brand-name "Crinos" to Crinos S.p.A., a newly formed subsidiary of Stada Arzneimittel AG. As part of the sale, we granted Crinos S.p.A. a semi-exclusive license to market defibrotide in Italy to treat and prevent of vascular disease with risk of thrombosis for no consideration. We have the right to grant a second license in Italy but only to a third party that has been expressly approved by Crinos. This agreement remains valid until the later of the expiration of the patent on defibrotide in Italy in 2009, and the date there is no market remaining for defibrotide, as determined in good faith by the parties. We also granted Crinos S.p.A. a right of first refusal for an exclusive or semi-exclusive license to market defibrotide in Italy for additional uses approved in the future, as well as for all uses in all European countries. Crinos S.p.A. can exercise this right of first refusal free of charge within 45 days of Gentium sending written notice of an offer to market or co-market defibrotide for a new use or in a new European country. As a further part of the sale, we granted Crinos S.p.A. a semi-exclusive license to market mesalazine in Italy. We have the right to grant a second license in Italy but only to a third party that has been expressly approved by Crinos. This agreement remains valid until the later of the expiration of the patent on mesalazine in Italy in 2015, and the date there is no market remaining for mesalazine, as determined in good faith by the parties. We also granted Crinos a right of first refusal for an exclusive or semi-exclusive license to market mesalazine in Italy for additional uses approved in the future, as well as for all uses in all other European countries. Crinos can exercise this right of first refusal free of charge within 45 days of Gentium sending written notice of an offer to market or co-market mesalazine for a new therapeutic use or in a new European country.

On July 15, 2004, we entered into a License Agreement with Crinos, pursuant to which we granted Crinos a non-exclusive license to use the know-how and the patent to market defibrotide under the trademark "Noravid" in Italy for both current and future uses as approved by the Italian Ministry of Health. This License Agreement is in addition to the license included as part of the Umbrella Agreement discussed above. In return for the license, Crinos will pay us a 3% royalty on its net sales of defibrotide in Italy. To date, Crinos has not sold defibrotide under the trademark "Noravid" and thus has not paid us any amounts under this License Agreement. Crinos is required to purchase the defibrotide exclusively from Sirton (we sell defibrotide to Sirton under a Supply Agreement). We provide Crinos with the existing technical information, know how and scientific assistance which Crinos needs to market, promote, and sell defibrotide. The agreement remains valid until the expiration of the patent in 2009, but can be extended for renewable three year periods if the parties, in good faith, determine that defibrotide still has a market life after the patent expires.

On June 11, 2002, we entered into a License and Supply Agreement with Abbott S.p.A., pursuant to which we granted Abbott a semi-exclusive license to use the know-how and the patent to market our formulation of mesalazine under the trademark "Quota" in Italy. We also agreed to transfer our Italian regulatory approvals for mesalazine and the trademark "Quota" to Abbott under this agreement. In return, Abbott paid us €155 thousand when we signed the agreement, and paid us another €155 thousand when we transferred our Italian regulatory approvals for mesalazine to them. Abbott is required to purchase our formulation of mesalazine exclusively from us. We are required, upon Abbott's request, to purchase the active ingredient used in our formulation of mesalazine from Abbott. We provide Abbott with the existing technical information, know how and scientific assistance which Abbott needs to market, promote, and sell our formulation of mesalazine. The agreement remains valid until the later of the expiration of the final patent on our formulation of mesalazine in Italy in 2016 or ten years from Abbott's first third-party sale of our formulation of mesalazine (not including quantities distributed solely for research purposes, clinical trials, samples, or promotions), but is automatically renewed for an additional period of the same number of years unless either party gives notice within 180 days of the date the agreement would terminate. We also granted Abbott a right of first refusal for a semi-exclusive license to market additional formulations of mesalazine in Italy. Abbott can exercise this right of first refusal free of charge within 60 days of Gentium sending Abbott written notice of an offer to co-market new formulations of mesalazine received by Gentium from a third party.

On January 2, 2004 we entered into an Active Ingredient Supply Agreement with Sirton, pursuant to which we manufacture defibrotide for Sirton in consideration for €1,446.00 per unit of defibrotide for injection, and €650.00 per unit of oral defibrotide, for a period of one year. The agreement automatically renews each year unless one party gives written notice of its intent to terminate the agreement at least one month prior to the annual termination date. Sirton processes and sells the defibrotide to Crinos. This agreement was renewed for 2005.

On November 11, 2003, we entered into a Supply Agreement with Samil Pharm. Co., Ltd., a Korean corporation. Under this agreement, we supply Samil with sulglicotide. From January 20, 2004 to June 20, 2005, Samil must purchase at least 1,600 kilograms of sulglicotide. From June 20, 2005 to June 20, 2006, Samil must purchase at least 2,600 kilograms of sulglicotide. From June 20, 2006 to June 20, 2007, Samil must purchase at least 3,400 kilograms of sulglicotide. After June 20, 2006, both parties will renegotiate quantity and price. In any given period, excess purchases by Samil may be applied as a reduction of the immediately following period's minimum purchases or as compensation for a failure to purchase the immediately preceding period's minimum purchases, at Samil's choice. Samil must submit purchase orders at least 90 days prior to a requested delivery date, and the minimum quantity which they can order is one batch (120 kilograms) or a multiple thereof. The price of the sulglicotide was originally set at €460/kilogram for between 0 and 2,000 kilograms, €452/kilogram for 2,001 to 3,000 kilograms, €440/kilogram for 3,001 to 4,000 kilograms, and €420/kilogram for 4,001 to 5,000 kilograms. These prices will change based on inflation and raw material price increases. For the nine months period ended September 30, 2005, we have not received any orders for sulglicotide from Samil. Samil informed us that it experienced a delay in the launch of its product that uses sulglicotide because of further market analyses required to properly position the product into the Korean market. This agreement expires on June 20, 2014. The agreement automatically renews for two year periods unless either party giving notice of termination at least 180 days before the expiration of the initial term of the agreement or any successive two year period.

Clinical Trial Agreements

On February 26, 2004, we entered into a Trial Agreement with the European Blood and Marrow Transplantation Group. Under this agreement, the European Blood and Marrow Transplantation Group is conducting a clinical trial of defibrotide to prevent VOD in children after stem cell transplants, in consideration for €476 thousand to be paid over five years. Through September 30, 2005, we have not made any payments to the European Blood and Marrow Transplantation Group. We can terminate the clinical trial and the contract prior to completion of the clinical trial, but we would have to make pro-rata payments to the European Blood and Marrow Transplantation Group based on then enrolled eligible patients.

In December 2005, we entered into a letter of intent with MDS Pharma Services SpA, an Italian research organization. The letter of intent contemplates that we will enter into a formal agreement with MDS pursuant to which MDS will manage the clinical and regulatory aspects of our clinical trials of defibrotide to prevent VOD in children and adults that we are cosponsoring with the European Blood and Marrow Transplantation Group.

On June 14, 2000, Sirton (then known as Crinos Industria Farmacobiologica S.p.A.) entered into a Research Agreement with Consorzio Mario Negri Sud. We succeeded to Sirton's interest in this agreement as part of a corporate restructuring of the FinSirton companies in 2002. Under this agreement, Consorzio was conducting a Phase II/III clinical trial in Europe and Israel of defibrotide to treat VOD after stem cell transplants. In October, 2005, the sponsor cancelled this contract due to a lack of patients being enrolled in the trial. We do not owe Consorzio any additional amounts in connection with this agreement.

On March 19, 2004 we entered into a General Consulting Agreement with Bradstreet Clinical Research & Associates, Inc., a New Jersey-based clinical research organization. Under this agreement, Bradstreet provides us with clinical and regulatory consulting services. Bradstreet provides estimated project budgets to us to determine the manner in which the services are to be provided and the number of hours required to provide the services. We pay Bradstreet on an hourly basis after Bradstreet presents us with monthly invoices and corresponding timesheets. Bradstreet is also entitled to reimbursement of its reasonable and customary expenses, including travel expenses. Through September 30, 2005, we have paid Bradstreet an aggregate of approximately $801 thousand. The agreement is effective for an indefinite period of time, but either party may terminate the agreement by giving 60 days' notice to the other party.

On April 20, 2004 we entered into a Consulting Agreement with KKS-UKT, GmbH, a German clinical research organization. Under this agreement, KKS provided us with clinical and regulatory consulting services. KKS provides estimated project budgets to us to determine the manner in which the services will be performed. This agreement expired on April 20, 2005 and we renewed it for a subsequent six month period. Through September 30, 2005, we have paid KKS an aggregate of €10 thousand under this agreement.

RESEARCH AND DEVELOPMENT

We discover, research and conduct initial development of our product candidates at our facilities in Italy, and also hire consultants to do so in various countries in Europe and the United States. We typically conduct preclinical laboratory and animal studies of product candidates either ourselves or through other research facilities. We typically cosponsor or engage other entities, such as the Dana-Farber Cancer Institute at Harvard University, to sponsor clinical trials of our product candidates. In certain cases, where we believe the development costs will be substantial, we may enter into strategic partnerships to help us develop those product candidates. We expense research and development costs as incurred. The following table shows our research and development expenses for each of our advanced product candidates.

(in thousands)	For The Years Ended December 31, 2002	2003	2004	For The Nine Months Ended September 30, 2005
				Unaudited
Defibrotide to treat VOD	€ 1,626	€ 2,077	€ 2,521	€ 2,805
Defibrotide to prevent VOD	—	25	112	118
Others	127	151	289	194
Total	€ 1,753	€ 2,253	€ 2,922	€ 3,117

SEASONALITY

Seasonality does not affect our business.

INTELLECTUAL PROPERTY RIGHTS AND PATENTS

As of December 31, 2005, we had seven issued U.S. patents, four pending U.S. patent applications, 28 issued foreign patents and 88 pending foreign patent applications. These include the following. The United States Patent & Trademark Office issued a patent covering our manufacturing process of defibrotide in 1991. In April 2001, we filed a patent application with the United States Patent & Trademark Office and corresponding patent applications in certain foreign countries regarding the use of defibrotide in stem cell transplants. These United States patents expire between 2008 and 2024.

Patent rights and other proprietary rights are important in our business. We have sought, and intend to continue to seek, patent protection for our inventions and rely upon patents, trademarks, trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain a competitive advantage.

However, the patent positions of companies like ours involve complex legal and factual questions and, therefore, their enforceability cannot be predicted with any certainty. Our patents, those licensed to us, and those that may be issued to us in the future may be challenged, invalidated or circumvented, and the rights granted under them may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be approved for sale and commercialized, our relevant patent rights may expire or remain in force for only a short period following commercialization.

REGULATORY MATTERS

Overview

The preclinical and clinical testing, manufacture, labeling, storage, distribution, promotion, sale, import and export, reporting and record-keeping of our product candidates are subject to extensive regulation by governmental authorities in the United States, principally the FDA and corresponding state agencies, and regulatory agencies in foreign countries.

Non-compliance with applicable regulatory requirements can result in, among other things, injunctions, seizure of products, total or partial suspension of product manufacturing and marketing, failure of the government to grant approval, withdrawal of marketing approvals, civil penalty actions and criminal prosecution. Except as discussed below, we believe that we are in substantial compliance in all material respects with each of the currently applicable

laws, rules and regulations mentioned in this section. During a biannual inspection of our manufacturing facility by the Italian Health Authority in October 2004, the Italian Health Authority noted by way of observations certain deficiencies in regard to the operation of our facility. We are committed to complete appropriate corrective action prior to the next bi-annual inspection, and have kept the Italian Health Authority current with respect to the progress of our corrective actions, the majority of which has been completed. Also, a regional Italian regulatory inspector, during an April 2005 inspection of our manufacturing facility, requested that we install an exhaust vent on one of our machines. We have installed this device. In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets their current good manufacturing practices, or GMP, including requirements for equipment verification and validation of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but we have recently completed an approximately €7.2 million major overhaul and upgrade in anticipation of such an inspection. We are not aware of any other situation that could be characterized as an incidence of non-compliance in the last three years.

United States Regulatory Approval

FDA regulations require us to undertake a long and rigorous process before any of our product candidates may be marketed or sold in the United States. This regulatory process typically includes the following general steps:

· our performance of satisfactory preclinical laboratory and animal studies under the FDA's good laboratory practices regulations;

· our obtaining the approval of independent Institutional Review Boards at each clinical site to protect the welfare and rights of human subjects in clinical trials;

· our submission to and acceptance by the FDA of an Investigational New Drug Application (IND) which must become effective before human clinical trials may begin in the United States;

· our successful completion of a series of adequate and well-controlled human clinical trials to establish the safety, purity, potency and effectiveness of any product candidate for its intended use;

· our submission to, and review and approval by, the FDA of a marketing application prior to any commercial sale or shipment of a product; and

· our development and demonstration of manufacturing processes which conform to FDA-mandated current good manufacturing practices.

This process requires a substantial amount of time and financial resources. In 2002, the FDA announced a reorganization that has resulted in the shift of the oversight and approval process for certain therapeutic biologic drugs and the related staff from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research. Our initial product candidate, defibrotide to treat VOD with multiple-organ failure, is being regulated through the latter.

Preclinical Testing

Preclinical tests generally include laboratory evaluation of a product candidate, its chemistry, formulation, stability and toxicity, as well as certain animal studies to assess its potential safety and effectiveness. We must submit the results of these preclinical tests, together with manufacturing information, analytical data and the clinical trial protocol, to the FDA as part of an Investigational New Drug Application, which must become effective before we may begin any human clinical trials. An application automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within this 30-day time period, raises concerns or questions about the intended conduct of the trials and imposes what is referred to as a clinical hold. If one or more of our products is placed on clinical hold, we would be required to resolve any outstanding issues to the satisfaction of the FDA before we could begin clinical trials. Preclinical studies generally take several years to complete, and there is no guarantee that an Investigational New Drug Application based on those studies will become effective, allowing clinical testing to begin.

In addition to FDA review of an application, each clinical institution that desires to participate in a proposed clinical trial must have the clinical protocol reviewed and approved by an independent Institutional Review Board. The independent Institutional Review Boards consider, among other things, ethical factors, informed consent and the selection and safety of human subjects. Clinical trials must be conducted in accordance with the FDA's good clinical practices requirements.

In addition to FDA review of an Investigational New Drug Application, clinical trials must meet requirements for Institutional Review Board oversight, informed consent and the FDA's good clinical practices. Prior to commencement

of each clinical trial, the sponsor must submit to the FDA a clinical plan, or protocol, accompanied by the approval of the committee responsible for overseeing clinical trials at one of the clinical trial sites. The FDA, and/or the Institutional Review Board at each institution at which a clinical trial is being performed, may order the temporary or permanent discontinuation of a clinical trial at any time if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients.

The sponsor must submit to the FDA the results of the pre-clinical and clinical trials, together with, among other things, detailed information on the manufacturing and composition of the product, in the form of New Drug Application or a Biologics License Application. Once the submission has been accepted for filing, the FDA has 180 days to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification.

Clinical Trials

Human clinical trials are typically conducted in three sequential phases that may overlap, including the following:

Phase I

In Phase I clinical trials, a product candidate is typically given to either healthy people or patients with the medical condition for which the new drug is intended to be used. The main purpose of the trial is to assess a product candidate's safety and the ability of the human body to tolerate the product candidate, and may also assess the dosage, absorption, distribution, excretion and metabolism of the product candidate.

Phase II

During Phase II, a product candidate is given to a limited number of patients with the disease or medical condition for which it is intended to be used in order to:

· further identify any possible adverse side effects and safety risks;

· assess the preliminary or potential effectiveness of the product candidate for the specific targeted disease or medical condition; and

· assess dosage tolerance and determine the optimal dose for a Phase III trial.

Phase III

If and when one or more Phase II trials demonstrate that a specific dose or range of doses of a product candidate is likely to be effective and has an acceptable safety profile, one or more Phase III trials are generally undertaken to demonstrate clinical effectiveness and to further test for safety in an expanded patient population with the goal of evaluating the overall risk-benefit relationship of the product candidate. The successful demonstration of clinical effectiveness and safety in one or more Phase III trials is typically a prerequisite to the filing of an application for FDA approval of a product candidate.

After approval, the FDA may also require a Phase IV clinical trial to continue to monitor the safety and effectiveness of the product candidate.

Post-Approval Regulations

If a product candidate receives regulatory approval, the approval is typically limited to specific clinical uses. Subsequent discovery of previously unknown problems with a product may result in restrictions on its use or even complete withdrawal of the product from the market. Any FDA-approved products manufactured or distributed by us are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse events or experiences. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies, and are subject to periodic inspections by the FDA and state agencies for compliance with current good manufacturing practice, or GMP, which impose rigorous procedural and documentation requirements

upon us and our contract manufacturers. Failure to comply with these requirements may result in, among other things, total or partial suspension of production activities, failure of the FDA to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals.

If the FDA approves one or more of our product candidates, we and our contract manufacturers must provide certain updated safety and effectiveness information. Product changes, as well as changes in the manufacturing process or facilities where the manufacturing occurs or other post-approval changes, may necessitate additional FDA review and approval. The labeling, advertising, promotion, marketing and distribution of a drug or biologic product also must be in compliance with FDA requirements which include, among others, standards and regulations for direct-to-consumer advertising, communication of information relating to off-label uses, industry sponsored scientific and educational activities and promotional activities involving the Internet. The FDA has very broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing a company to correct deviations from regulatory standards and enforcement actions that can include seizures, fines, injunctions and criminal prosecution.

Fast track and orphan drug designation

The FDA has developed "fast track" policies, which provide the potential for expedited review of an application. However, there is no assurance that the FDA will, in fact, accelerate the review process for a fast track product candidate. Fast track status is provided only for new and novel therapies that are intended to treat persons with life-threatening and severely debilitating diseases, where there is a defined unmet medical need, especially where no satisfactory alternative therapy exists or the new therapy is significantly superior to alternative therapies. During the development of product candidates that qualify for this status, the FDA may expedite consultations and reviews of these experimental therapies. Furthermore, an accelerated approval process is potentially available to product candidates that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses. The FDA can base approval of a marketing application for a fast track product on an effect on a clinical endpoint, or on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may condition the approval of an application for certain fast track products on additional post-approval studies to validate the surrogate endpoint or confirm the effect on the clinical endpoint. Fast track status also provides the potential for a product candidate to have a "priority review." A priority review allows for portions of the application to be submitted to the FDA for review prior to the completion of the entire application, which could result in a reduction in the length of time it would otherwise take the FDA to complete its review of the application. Fast track status may be revoked by the FDA at any time if the clinical results of a trial fail to continue to support the assertion that the respective product candidate has the potential to address an unmet medical need. A product approved under a "fast track" designation is subject to expedited withdrawal procedures and to enhanced scrutiny by the FDA of promotional materials.

The FDA may grant orphan drug status to drugs intended to treat a "rare disease or condition," which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. If and when the FDA grants orphan drug status, the generic name and trade name of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Aside from guidance concerning the non-clinical laboratory studies and clinical investigations necessary for approval of the application, orphan drug status does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The FDA may grant orphan drug designations to multiple competing product candidates targeting the same uses. A product that has been designated as an orphan drug that subsequently receives the first FDA approval for the designated orphan use is entitled to orphan drug exclusivity, which means the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years from the date of FDA approval. Orphan drug status may also provide certain tax benefits. Finally, the FDA may fund the development of orphan drugs through its grants program for clinical studies.

The FDA has designated defibrotide as an orphan drug to treat VOD and has provided funding for clinical studies for this use. The FDA has approved the Company's application for "fast track" designation for defibrotide to treat VOD with multiple-organ failure occurring after stem cell transplantation by means of injection. The FDA approval process for defibrotide for this use remains dependent upon the successful completion of clinical trials. If our other product candidates meet the criteria, we may also apply for orphan drug status and fast track status for such products.

Market Exclusivity

In addition to orphan drug exclusivity, a product regulated by the FDA as a "new drug" is potentially entitled to non-patent and/or patent exclusivity under the FFDCA against a third party obtaining an abbreviated approval of a generic product during the exclusivity period. Conversely, under current law, a third party cannot obtain an abbreviated approval of a drug regulated as a "biological product" and concomitantly there is no opportunity for non-patent or patent exclusivity under the FFDCA for biological products. An abbreviated approval allows an applicant to obtain FDA approval without generating, or obtaining a right of reference to, the basic safety and effectiveness data necessary to support the initial approval of the drug product or active ingredient. In the case of a new chemical entity (an active ingredient which has not been previously approved with respect to any drug product)

non-patent exclusivity precludes an applicant for abbreviated approval from submitting an abbreviated application until five years after the approval of the new chemical entity. In the case of any drug substance (active ingredient), drug product (formulation and composition) and method of use patents listed with the FDA, patent exclusivity under the FFDCA precludes FDA from granting effective approval of an abbreviated application of an generic product until the relevant patent(s) expire, unless the abbreviated applicant certifies that the relevant listed patents are invalid, not infringed or unenforceable and the NDA/patent holder does not bring an infringement action within 45 days of receipt of notification of the certification or an infringement action is brought within 45 days and a court determines that the relevant patent(s) are invalid, not infringed or un-enforceable or 30 months have elapsed without a court decision of infringement.

User Fees

A New Drug Application for a prescription drug product that has been designated as an orphan drug is not subject to the payment of user fees to the FDA unless the application includes as indication for other than a orphan indication.

A supplement proposing to include a new indication for a designated orphan disease or condition in an application is also not subject to a user fee, if the drug has been designated an orphan drug with regard to the indication proposed in such supplement.

There is no specific exemption for orphan drug products from annual product and establishment fees. However, sponsors of orphan drugs can request a waiver of such fees on hardship or other grounds.

Other federal legislation may affect our ability to obtain certain health information in conjunction with our research activities. The Health Insurance Portability and Accountability Act of 1996, or HIPAA, mandates, among other things, the adoption of standards designed to safeguard the privacy and security of individually identifiable health information. In relevant part, the U.S. Department of Health and Human Services, or HHS, has released two rules to date mandating the use of new standards with respect to such health information. The first rule imposes new standards relating to the privacy of individually identifiable health information. These standards restrict the manner and circumstances under which covered entities may use and disclose protected health information so as to protect the privacy of that information. The second rule released by HHS establishes minimum standards for the security of electronic health information. While we do not believe we are directly regulated as a covered entity under HIPAA, the HIPAA standards impose requirements on covered entities conducting research activities regarding the use and disclosure of individually identifiable health information collected in the course of conducting the research. As a result, unless they meet these HIPAA requirements, covered entities conducting clinical trials for us may not be able to share with us any results from clinical trials that include such health information.

Foreign Regulatory Approval

Outside of the United States, our ability to market our product candidates will also be contingent upon our receiving marketing authorizations from the appropriate foreign regulatory authorities whether or not FDA approval has been obtained. The foreign regulatory approval process in most industrialized countries generally includes risks that are similar with the FDA approval process we have described herein. The requirements governing conduct of clinical trials and marketing authorizations, and the time required to obtain requisite approvals may vary widely from country to country and differ from that required for FDA approval.

European Union Regulatory Approval

Under the current European Union regulatory system, applications for marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure (which is compulsory for certain categories of drugs) provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization that is obtained in accordance with the procedure and requirements applicable in the member state concerned may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval. The mutual recognition process results in separate national marketing authorizations in the reference member state and each concerned member state.

<u>The centralized procedure</u>

An applicant under the centralized procedure must be a person who is domiciled in the European Union or an entity established in the European Union. The applicant must file a preliminary request containing the information regarding the product candidate, including its description and the location of the production plant, as well as the payment of the application fees. The European Agency for the Evaluation of Medicinal Products (an European Union statutory entity) formally evaluates the preliminary request and indicates either an initial approval to review a full application or a rejection. If the European Agency indicates an initial approval to review a full application, the applicant must submit the application to the European Agency. This application must indicate certain specific information regarding the product candidate, including the composition (quality and quantity) of all the substances contained in the product, therapeutic indications and adverse events, modalities of use, the results of physical, chemical, biological and microbiological tests, pharmacological and toxicity tests, clinical tests, a description of production and related control procedures, a summary of the characteristics of the product as required by the European legislation and samples of labels and information to consumers. The applicant must also file copies of marketing authorizations obtained, applications filed and denials received for the same product in other countries, and must prove that the manufacturer of the product candidate is duly authorized to produce it in its country.

The European Agency (through its internal Committee for Proprietary Medicinal Products) examines the documents and information filed and may carry out technical tests regarding the product, request information from the member state concerned with regard to the manufacturer of the product candidate and, when it deems necessary, inspect the manufacturing facility in order to verify that the manufacturing facility is consistent with the specifications of the product candidate, as indicated in the application.

The Committee generates and submits its final opinion to the European Commission, the member states and the applicant. The Commission then issues its decision, which is binding on all member states. However, if the Commission approves the application, member states still have authority to determine the pricing of the product in their territories before it can be actually marketed.

The European Agency may reject the application if the Agency decides that the quality, safety and effectiveness of the product candidate have not been adequately and sufficiently proved by the applicant, or if the information and documents filed are incomplete, or where the labeling and packaging information proposed by the applicant do not comply with the relevant European rules.

The European Agency has also established an accelerated evaluation procedure applying to product candidates aimed at serious diseases or conditions for which no suitable therapy exists, if it is possible to predict a substantial beneficial effect for patients.

The marketing authorization is valid for five years and may be renewed, upon application, for further five year terms. After the issue of the authorization the holder must constantly take into consideration scientific and technical progress so that the product is manufactured and controlled in accordance with scientific methods generally accepted.

We plan to apply for approvals for our product candidates under the centralized procedure. We believe that the centralized procedure will result in a quicker approval of our product candidates than the decentralized procedure due to the fact that we intend to market our product candidates in many European Union member states, rather than just one.

The decentralized procedure

The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization—obtained in accordance with the procedure and requirements applicable in the member state concerned (see the description below for Italy)—may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval. The mutual recognition process results in separate national marketing authorizations in the reference member state and each concerned member state.

An application under the decentralized procedure begins with the applicant obtaining a national marketing authorization. An example of the process for obtaining a national marketing authorization in Italy is set forth below. The applicant then submits an application for authorization in other member states and the European Agency. If any of the member states refuses to recognize the authorization by the original member state, the matter is deferred to arbitration proceedings, unless the applicant withdraws its request in the member state refusing recognition. The characteristics of the product in the new applications must be identical to those approved in the original member state.

The competent Health Authority of a member state is bound to recognize the decision of another member state if it ascertains that the same application has been filed also in the other member state or that the approval has already been granted in the other member state. This requirement in intended to ensure the wide and effective application of mutual recognition within the European Union.

Italian Regulatory Approval

An application for marketing authorization in Italy must be filed with the competent office of the Italian Ministry of Health and must contain certain specific information, including the composition (quality and quantity) of all the substances contained in the product, therapeutic indications and adverse events, modalities of use, the results of physical, chemical, biological and microbiological tests, pharmacological and toxicity tests, clinical tests, a description of production and related control procedures and samples of labels and information to consumers. Italian legislation (in accordance with European laws) regulates in great detail the information to be indicated on the packaging. Marketing authorization includes a 10-year protection period during which no one else may use the results of the clinical trials included in the application to apply for a substantially similar drug. This period may be extended where there are new therapeutic indications for the same product, which require new complete clinical studies and justify the same protection as that granted to a new drug.

The Ministry may grant or deny the national authorization after a review of the contents of the application, both from a formal and substantial viewpoint. If an authorization is granted, it is valid for an initial period of five years and, upon application, may be renewed for subsequent five year terms. In particular, Ministry examines the quality, effectiveness and safety of the product and the Italian Drugs' Committee (*Commissione Unica del Farmaco*), a statutory agency supporting the Ministry in the authorization process, prepares an evaluation report on the test results. The Ministry may also order further tests prior to granting or denying the authorization regarding the suitability of the production and control methods described in the application. The Ministry may reject the authorization if the ordinary use of the drug has adverse events, the quality and quantity of the ingredients of the drugs do not correspond to the data indicated in the application, there is a lack, either total or partial, of beneficial therapeutic effects or the information and the documents included in the application do not comply with the requirements provided by law. After the Ministry grants a national authorization, the Ministry may temporarily suspend or revoke the authorization if the information disclosed in the relevant application turns out to be incorrect, the drug no longer meets the necessary quality, effectiveness or safety requirements, or adequate production controls have not been carried out.

Clinical Trials

Italy has recently implemented European legislation regarding good practices in drug clinical trials. As a result, clinical trials are now governed in great detail and failure to comply with these rules means that the results of the trials will not be taken into consideration in evaluating an application for a marketing authorization.

Prior to starting any clinical trial, the organizing and/or financing entity must obtain the approval of the competent health authorities (which vary depending on the type of drug concerned) and obtain the favorable opinion of the Ethical Committee, an independent body. Good practice rules include the following principles:

· the predictable risks and inconveniences shall not outweigh the beneficial effects for the person subject to the trials and for the other current and future patients;

· the person participating in the trials must have been duly informed of all the relevant circumstances and in particular of the right to interrupt the experimentation at any time without any prejudicial consequence, and must have given consent after having been properly informed;

· the right of the participants to their physical and mental integrity, as well as their right to privacy, shall be respected;

· the entity organizing the trial must have obtained adequate insurance coverage for any damage that may derive to the participants because of the trial;

· the name of a person to be contacted for any information must be communicated to the participant; and

· the trial must be conducted by suitably qualified medical personnel.

The trial must be constantly monitored, in particular with regard to serious adverse events which are not envisaged in the approved clinical protocol. Whenever the safety of the participants is in danger due to unexpected serious adverse events, the Ministry of Health must be promptly informed by the entity organizing the trials. Italian legislation provides sanctions (criminal sanctions and administrative fines) in case of violation of specific good practice rules.

Post-approval issues

There are many national legislative instruments (implementing European Union rules) governing controls on drugs in the post-authorization phase. For instance, the holder of the national marketing authorization must promptly record in detail and notify any adverse reaction to the drug of which it becomes aware, regardless of the country where the reaction occurs, also preparing periodic update reports on these adverse events. For these and other purposes, the holder of the authorization must hire and maintain in its organization a person expert in the field and responsible for all drug controlling and reporting activities.

Moreover, any form of information and advertising aimed at promoting the sale of drugs is governed by specific national legislation (also implementing European Union rules), which provides for the requirements and limitations of advertising messages in general, as well as of other particular promotional activities, such as the organization of conferences regarding certain drugs and the distribution of free samples.

The export of drugs from Italy is not subject to authorization (except for plasma and blood-related products), but the import into Italy from non-European Union countries must be authorized by the Ministry of Health, on the basis of the adequacy of the quality controls to be carried out on the imported drugs.

European orphan drug status

European legislation lays down a particular procedure for the designation of medicinal products as orphan drugs. Such designation may include incentives for the research, development and marketing of these orphan drugs and, in case of a subsequent successful application for a marketing authorization regarding the same therapeutic indications, grants a substantial period of market exclusivity.

A medicinal product - at any stage of its development but in any case prior to the filing of any application for the marketing authorization - may be designated as an orphan drug if the person/entity that has applied for the designation can establish that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five persons out of every ten thousand persons in the European Union, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the medicinal product would generate sufficient income to cover the necessary investments. Moreover, the sponsor must prove that there is no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.

In order to obtain the designation of a medicinal product as an orphan drug, the sponsor shall submit an application to the European Agency for the Evaluation of Medical Products, which must describe the indication of the active ingredients of the medicinal product, the proposed therapeutic indications and proof that the criteria established by the relevant European legislation are met.

The European Agency reviews the application and prepares a summary report to a special Committee for Orphan Medicinal Products, which issues an opinion within 90 days of the receipt of the application. The European Commission must adopt a decision within 30 days of the receipt of the committee’s opinion. If the European Commission approves the application, the designated medicinal product is entered in the European Register of Orphan Medicinal Products and the product is eligible for incentives made available by the European Union and by member states to support research into, and development and availability of, orphan drugs.

After the registration, the sponsor must submit to the European Agency an annual report on the state of development of the designated orphan drug. A designated orphan drug may be removed from the Register of Orphan Medicinal

Products in three cases:

· at the request of the sponsor;

· if it is established, before the market authorization is granted, that the requirements laid down in the European orphan drug legislation are no longer met; or

· at the end of the period of market exclusivity (as explained below).

Orphan drug market exclusivity means that the European Union shall not, for a period of 10 years from the grant of the marketing authorization for an orphan drug, accept any other application for a marketing authorization, grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indications in respect of a similar medicinal product. This period, however, may be reduced to six years if at the end of the fifth year it is established that the criteria laid down in the legislation are no longer met by the orphan drug, or where the available evidence shows that the orphan drug is sufficiently profitable, so that market exclusivity is no longer justified.

However, as an exception to orphan drug market exclusivity, a marketing authorization may be granted for the same therapeutic indications to a similar medicinal product if:

· the holder of the marketing authorization for the orphan drug has given his consent to the second applicant;

· the holder of the marketing authorization for the orphan drug is unable to supply sufficient quantities of the latter; or

· the second applicant can establish in its application that the second medicinal product, although similar to the authorized orphan drug, is safer, more effective or otherwise clinically superior.

RAW MATERIALS

We extract many of our products and product candidates from the DNA of pig intestines through well-established processes used by others to manufacture many other drugs. In particular, we extract defibrotide and calcium heparin from swine intestinal mucosa and sulglicotide from swine duodenum. In 2004, we entered into supply agreements with La.bu.nat. S.r.l. for La.bu.nat. to supply us with the swine intestinal mucosa and swine duodenum we need to produce defibrotide, calcium heparin and sulglicotide. We believe La.bu.nat can meet our current and near-term supply needs.

The initial contract term of the swine intestinal mucosa supply agreement expires on December 31, 2007, with automatically renewable three year periods, unless either party notifies the other party in writing six months prior to the annual date of termination. We must give written purchase orders to La.bu.nat at least two months in advance of the date of delivery. The purchase price is fixed at €0.1677 per kilogram until April 10, 2005 (plus an additional €0.0135 for the first 2,400,000 kilograms), at which time the price will increase 5% until December 31, 2006. After December 31, 2006, both parties may request renegotiation of the price with reference to market trends and manufacturing costs. In the event that the parties cannot agree on a renegotiated price, an arbitrator will determine the new price.

The initial contract term of the swine duodenum supply agreement expires on December 31, 2007, with automatically renewable three year periods, unless either party notifies the other party in writing six months prior to the annual date of termination. We must give written purchase orders to La.bu.nat at least four months in advance of the date of delivery. The purchase price is fixed at €1.1286 per kilogram until December 31, 2005. After that date, both parties may request renegotiation of the price with reference to market trends and manufacturing costs. If the parties cannot agree on a renegotiated price, an arbitrator will determine the new price.

While we have no current arrangements with any other supplier of our critical raw material, we believe there are suitable alternative sources of pig intestine. The FDA and other regulatory bodies may evaluate La.bu.nat.’s or any other supplier’s processing centers as part of approving our product candidates and our ongoing production of our products.

Our other product, urokinase, is derived from human urine, which is subject to similar regulatory review. While we currently purchase the urine from only one supplier of urine and do not have a fixed supply agreement with that supplier, we believe there are suitable alternative sources of the material.

Historically, there has been no significant price volatility for any of our raw materials. It is possible that widespread illness or destruction of pigs could result in volatility of the price of pig intestines.

MANUFACTURING AND FACILITIES

We own a manufacturing facility near Como, Italy which, at September 30, 2005, is subject to three mortgages securing repayment of an aggregate of approximately €2.32 million of debt owed to Banca Nazionale del Lavoro. In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets their current good manufacturing practices, or GMP, including requirements for equipment verification and validation of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but in 2004 we completed an approximately €7.2 million major overhaul and upgrade in anticipation of such an inspection. We have also upgraded our quality control laboratory equipment and upgrade equipment for our molecular biology and cell culture laboratories in 2005 in further anticipation of an FDA inspection at a cost of approximately €513 thousand.

We incurred costs of €207 thousand to purchase an electrical meter and back-up electrical power generator, including an advance payment to the utility company. We currently use Sirton's electrical meter, but Italian law requires us to have separate equipment. We are installing the back-up generator to avoid interruption of our operations during power outages. We are planning to replace a storage tank for certain solvents. We anticipate that the replacement of the storage tank will be necessary to satisfy the FDA that the facility meets their good manufacturing practices. We expect to complete these upgrades in 2007. We raised the money to fund these improvements from our sale of our Series A notes and our initial public offing and may also use some of the net proceeds of our initial public offering and our October 2005 private placement to pay for the future improvements. These improvements will not increase the manufacturing capacity of our facility.

We produce defibrotide, sulglicotide and calcium heparin at this facility. Defibrotide and calcium heparin are produced simultaneously. However, since the first steps of the manufacturing processes for defibrotide and sulglicotide utilize the same equipment, we do not run the manufacturing facility to produce defibrotide and sulglicotide simultaneously. We typically produce one of these products for a few weeks and then produce the other for a few weeks. Without adding additional shifts, we can increase our production of defibrotide and calcium heparin by reducing our production of sulglicotide. Similarly, we can increase our production of sulglicotide by decreasing our production of defibrotide and calcium heparin. We produce urokinase in a separate facility that is owned by Sirton and leased to us under a written lease agreement.

We typically operate our manufacturing facility on a single eight hour shift per day basis. Our estimated current production, our production capacity (assuming we do not produce any sulglicotide) and percentage of utilization for defibrotide and calcium heparin for the fiscal year 2006 are set forth below:

Product	Estimated Current Production Levels (kilograms/year)	Maximum Production Capacity With One Eight Hour Shift (kilograms/year)	Percentage of Utilization
Defibrotide	3,000	4,400	68%

Product	Estimated Current Production Levels (millions of units/year)	Maximum Production Capacity With One Eight Hour Shift (millions of units/year)	Percentage of Utilization
calcium heparin	28,000	41,000	68%

We currently manufacture defibrotide to treat and prevent venous thrombosis in Italy. Compared to the dosage necessary to treat and prevent VOD and to treat multiple myeloma, the treatment for this current use is significantly longer and therefore the overall amount of defibrotide is much larger than would be used to treat or prevent VOD or to treat multiple myeloma. Accordingly, if we obtain FDA or European regulatory approvals for those new uses, a smaller portion of our maximum capacity would be required for the manufacture of defibrotide for those additional uses.

Our estimated current production, production capacity (assuming we do not produce any defibrotide or calcium heparin) and percentage of utilization for sulglicotide for the fiscal year 2006 are set forth below:

Product	Estimated Current Production Level (kilograms/year)	Maximum Production Capacity With One Eight Hour Shift (kilograms/year)	Percentage of Utilization
Sulglicotide	1,050	2,750	38%

Our estimated current production, production capacity and percentage of utilization for urokinase for the fiscal year 2006 are set forth below:

Product	Estimated Current Production Level (millions of units/year)	Maximum Production Capacity With One Eight Hour Shift (millions of units/year)	Percentage of Utilization
Urokinase	17.4	37	47%

Our business plan does not include increasing our current levels of production of urokinase, although our contract with Samil requires us to increase our production of sulglicotide to 2,600 kilograms in the period from January 20, 2005 to January 20, 2006 and to 3,400 kilograms in the period from January 20, 2006 to January 20, 2007. However, we believe it would be possible to increase the production of our products and to manufacture defibrotide and sulglicotide simultaneously by adding additional shifts of employees. This would also involve additional expenses.

Our facility is subject to customary regulation by regional agencies regarding worker health and safety, fire department, water, air, noise and environmental pollution and protection by Azienda Sanitaria Locale and Agenzia Regionale Prevenzione e Ambiente. We have engaged Lariana Depur, a consortium that specializes in the treatment of waste water, to treat our waste water. We monitor our waste water to control the levels of nitrogen, chlorides and chemical oxygen before delivering the waste water to Lariana Depur for additional treatment. We do not expect any difficulties in complying with these regulations. Also, we installed two scrubbers to reduce the odors and chemicals released into the air by the facility to comply with Italian regulations.

CAPITAL EXPENDITURES

The following table sets forth our capital expenditures, before retirements, for each year in the four-year period ended December 31, 2004 and the nine months ended September 30, 2005. Most of our 2003 and 2004 expenditures relate to the major upgrade of our facility we completed in 2004.

(thousands)	For The Years Ended December 31, 2002	2003	2004	For The Nine Months Ended September 30, 2005 *(Unaudited)*
Land and buildings	€ 54	€ 10	€ 1,244	€ 107

Plant and machinery	191	26	3,690	398
Industrial equipment	5	23	169	27
Other	—	—	75	33
Construction in progress	126	2,509	—	459
Total	€ 376	€ 2,568	€ 5,178	€ 1,024

EMPLOYEES

The table below shows the number, activity and geographic location of our employees as of December 31, 2001, 2002, 2003 and 2004 and as of September 30, 2005. All of our employees are in Italy, although Cary Grossman, our Chief Financial Officer, who was hired as an independent contractor in August 2004, is based in the United States. Most of our administrative, accounting, finance and business development services are performed by employees of FinSirton and Sirton.

	December 31,				September 30,
	2001	2002	2003	2004	2005
					(unaudited)
Administration, accounting, finance, business development	0	1	1	1	6
R&D, clinical, regulatory, quality assurance & control	7	6	11	17	16
Production	7	14	14	17	24
Total	14	21	26	35	46

Italian law imposes certain confidentiality obligations on our employees and provides that either any intellectual property created by them while in our employ belong to us or we have a right of option on it, although we must compensate them for such intellectual property creation. Our employees in Italy are subject to national collective bargaining agreements. National agreements are negotiated collectively between the national associations of companies within a given industry and the respective national unions. National agreements provide a basic framework on working conditions, including, among other things, pay, security and other provisions. Our employees other than executive officers in Italy are subject to a collective bargaining agreement that was renewed on December 17, 2003 and expires on December 31, 2005. Our executive officers in Italy are subject to a collective bargaining agreement that was renewed on November 20, 2004 and expires on December 31, 2008. We believe that we maintain satisfactory relations with our employees.

Under Italian law, employees are entitled to amounts based on salary and years of service upon leaving their employment, even if we terminate them for cause or they resign. We had a liability for these termination indemnities of €693 thousand at September 30, 2005. Under Italian law, we make social security and national healthcare contributions for our employees to the Italian government, which provides pension and healthcare insurance benefits.

COMPETITION

Our industry is highly competitive and characterized by rapid technological change. Significant competitive factors in our industry include:

· controlling the manufacturing costs;

· the effectiveness and safety of products;

· the timing and scope of regulatory approvals;

· the willingness of private insurance companies and government sponsored health care programs to reimburse patients or otherwise pay for the drugs and the related treatments;

· the availability of alternative treatments for the disorders as well as the availability of alternatives to the treatments which cause or contribute to these disorders (such as chemotherapy, radiation therapy, stem cell transplants, etc.);

· the ability to perform clinical trials, independently or with others;

· intellectual property and patent rights and their protection; and

· sales and marketing capabilities.

We face competition in both the development and marketing of our product candidates. During development alternative treatments for similar or completely different disorders may limit our ability to get participants or co-sponsors for clinical trials with our product candidates. Any product candidates that we successfully develop that are approved for sale by the FDA or similar regulatory authorities in other countries may compete with products currently being used or that may become available in the future. Many organizations, including large pharmaceutical and biopharmaceutical companies, as well as academic and research organizations and government agencies, may be interested in pursuing the research and development of drug therapies that target the blood vessel wall. Many of these organizations have substantially greater capital resources than we have, and greater capabilities and resources for basic research, conducting preclinical studies and clinical trials, regulatory affairs, manufacturing, marketing and sales. As a result, our competitors may develop or license products or other novel technologies that are more effective, safer or less costly than our existing products or products that are being developed by us, or may obtain regulatory approval for products before we do. Clinical development by others may render our products or product candidates noncompetitive.

While we are unaware of any other products or product candidates that treat or prevent VOD or the apoptosis that our product candidate oligotide is designed to treat, we believe that other companies have products or are currently developing products to treat some of the same disorders and diseases that our other product candidates are designed to treat.

Our statements above are based on our general knowledge of and familiarity with our competitors.

LEGAL PROCEEDINGS

Currently, we are not a party to or engaged in any material legal proceedings.

MANAGEMENT

Executive Officers, Significant Employees and Directors

Set forth below is the name, age, position and a brief account of the business experience of each of our executive officers, significant employees, directors and director nominees as of December 31, 2005. The business address of each of the individuals listed below, except for Cary Grossman, is Piazza XX Settembre 2, 22079 Villa Guardia (Como), Italy. Cary Grossman's business address is 9821 Katy Freeway, Suite 500, Houston, Texas, 77024.

Name	Age	Position
Dr. Laura Ferro	54	President and Chief Executive Officer, Director
Cary Grossman	51	Executive Vice-President and Chief Financial Officer
Sauro Carsana	52	Director
Dr. Massimo Iacobelli	46	Senior Vice-President, Scientific Director
Dr. Guenther Eissner	41	Senior Vice-President, Chief of Biology Research Laboratory