Gentium S.p.A.
Form F-1
December 30, 2005

As filed with the Securities and Exchange Commission on December 30, 2005

Registration No. [_____]

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

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
New York, New York 10177
(212) 351-4500 (Phone) (212) 661-0989 (Fax)

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 (2)	Proposed maximum aggregate offering price (2)	Amount of registration fee
Ordinary shares, par value €1.00 per share (3)	3,101,591 (4)	$7.825	$24,269,949	$2,596.88

(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) 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 $7.825, the average of the high and low prices of the American Depositary Shares on the American Stock Exchange on December 29, 2005.

(3) 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.

(4) Includes 1,100,466 ordinary shares underlying 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 DECEMBER 30, 2005

PRELIMINARY PROSPECTUS

Gentium S.p.A.

3,101,591 American Depositary Shares
Representing 3,101,591 Ordinary Shares

The selling security holders identified in this prospectus are offering up to 3,101,591 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 117 for a list of the selling security holders. See "Plan of Distribution" beginning on page 122 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 11 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.

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.

We have Italian, 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 closing 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
9 months ended September 30, 2005	1.2577	1.206

Source: Bloomberg L.P.

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**
June 2005	1.233	1.204
July 2005	1.220	1.191
August 2005	1.244	1.214
September 2005	1.255	1.200
October 2005	1.214	1.191
November 2005	1.207	1.166
December 2005 (through December 20)	1.203	1.169

Source: Lexis Sungard Historical Quotes

On December 20, 2005, the closing rate was €1.00 to $1.189.

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
				(Unaudited)	
Product sales:					
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