Gentium S.p.A.
Form 20-F
March 31, 2010
As filed with the Securities and Exchange Commission on March 31, 2010

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 20-F

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

OR

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended: December 31, 2009

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

o SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

000-51341
(Commission file number)

GENTIUM S.p.A.
(Exact Name of Registrant as Specified in its Charter)

NOT APPLICABLE
(Translation of Registrant's Name into English)

Italy
(Jurisdiction of incorporation or organization)

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)

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	Name of each exchange on which registered
American Depositary Shares	The Nasdaq Global Market
Ordinary shares, no par value*	The Nasdaq Global Market

(Title of Class)

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

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

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

14,956,317 ordinary shares

- Not for trading, but only in connection with the registration of the American Depositary Shares.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes o No x

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

Yes o No x

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes x No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer o Non-accelerated filer x

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

Item 17 o Item 18 x

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes o No x

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court.

Not applicable.

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PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISORS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

GENTIUM S.P.A.

We are a biopharmaceutical company focused on the development and manufacture of our primary product candidate, defibrotide, an investigational drug based on single-stranded DNA extracted from pig intestines. Our development of defibrotide has been focused on the treatment and prevention of a disease called hepatic veno-occlusive disease, or VOD, a condition in which some of the veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation treatments, that are given prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is associated with multiple-organ failure and high rates of morbidity and mortality. We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. Defibrotide has been given "orphan" status by the U.S. Food and Drug Agency, or FDA, and the European Medicines Agency, or EMEA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide has also been granted "fast-track product" designation by the FDA for the treatment of VOD. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approved basis under a treatment IND protocol in the U.S. and through a named-patient program throughout the rest of the world. We do not know of any FDA or EMEA approved treatments for VOD.

We are currently completing certain preclinical and clinical studies requested by regulatory authorities. As part of our overall strategy, we anticipate filing for regulatory approval for defibrotide in the U.S. and Europe by the end of our second quarter in 2011. We are also working closely on our U.S. regulatory strategy with our commercial partner, Sigma-Tau Finanziaria S.p.A. and its affiliate Sigma-Tau Pharmaceuticals, Inc., to which we have licensed our commercial rights to defibrotide for both the treatment and prevention of VOD in the Americas.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, which are subsequently used to make the finished forms of various drugs. We believe that we are the sole worldwide producer of defibrotide. In addition to defibrotide, we manufacture urokinase and sulglicotide, both of which are sold to third parties. All of the Company's operating assets are located in Italy.

We have accumulated a deficit of approximately €100 million since our inception and expect to continue to incur net operating losses for the foreseeable future. However, absent the need to fund any additional clinical trials, we believe that our cash and cash equivalents, including the upfront payment received from Sigma-Tau Pharmaceuticals, Inc. in connection with the expansion of the license for defibrotide in the Americas, together with revenues generated from our named-patient and cost recovery programs, will be sufficient to meet our obligations for at least the next twelve months.

We are subject to a number of risks, including our ability to successfully obtain regulatory approval for defibrotide, the uncertainty that defibrotide will become a successful commercial product, our ability to generate projected revenue through our named-patient and cost recovery programs, our dependence on corporate partners, our ability to obtain

financing, if necessary, and potential changes in the health care industry.

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 annual report. The selected financial data as of December 31, 2008 and December 31, 2009 and for the three years ended December 31, 2009 are derived from our audited financial statements, which are included in this annual report. The selected financial data as of December 31, 2005, December 31, 2006 and December 31, 2007 and for the years ended December 31, 2005 and December 31, 2006 have been derived from our audited financial statements, which are not included in this annual report. Our historical results are not necessarily indicative of results to be expected in any future period.

The convenience translation into U.S. dollars has been done solely for the benefit of the reader, and does not imply that our results would actually have been these amounts in U.S. dollars had the U.S. dollar been our functional currency.

Statement of Operations Data: (000s omitted except per share data)	For the Years Ended December 31,					
	2005	2006	2007	2008	2009	2009(1)
Revenues:						
Product sales to related party	€ 3,260	€ 3,754	€ 2,704	€ 651	€ 195	$ 279
Product sales to third parties	101	321	2,390	4,792	9,507	13,625
Total product sales	3,361	4,075	5,094	5,443	9,702	13,904
Other revenues	280	109	15	25	129	185
Other revenues from related party	-	140	2,500	1,970	337	483
Total revenues	3,641	4,324	7,609	7,438	10,168	14,572
Operating costs and expenses:						
Cost of goods sold	2,911	3,092	4,584	5,596	4,002	5,736
Charges from related parties	1,047	854	748	537	279	400
Research and development	4,557	8,927	14,497	9,569	3,512	5,033
General and administrative	2,284	5,421	6,279	7,668	6,036	8,651
Depreciation and amortization	118	261	725	998	916	1,313
Write-down of assets	-	-	13,740	3,403	-	-
	10,917	18,555	40,573	27, 771	14,745	21,133
Operating loss	(7,276)	(14,231)	(32,964)	(20,333)	(4,577)	(6,561)
Foreign currency exchange gain (loss), net	(249)	(627)	(4,001)	173	162	232
Interest income (expense), net	(4,148)	490	1,357	256	(110)	(158)
Pre-tax income loss	(11,673)	(14,368)	(35,608)	(19,904)	(4,525)	(6,487)
Income tax expense (benefit):						
Current	-	-	-	-	-	-
Deferred	646	-	-	-	-	-
	646	-	-	-	-	-
Net loss	€ (12,319)	€ (14,368)	€ (35,608)	€ (19,904)	€ (4,525)	$ (6,487)

Net loss per share:						
Basic and Diluted	€ (1.41)	€ (1.78)	€ (1.33)	€ (1.33)	€ (0.30)	$ (0.43)

(1) Euro amounts are translated into U.S. dollars using the Noon Buying Rate for the Euro on December 31, 2009, of U.S. $1.4332 per Euro. No representation is made that the Euro amounts referred to in this annual report could have been or could be converted into U.S. dollars at any particular rate or at all.

The following table summarizes certain of our balance sheet data.

(000s omitted except per share data	2005	2006	2007	2008	2009	2009(1)
Balance Sheet Data:						
Cash and cash equivalent...	€ 12,785	€ 10,205	€ 25,964	€ 11,491	€ 1,392	$ 1,995
Working capital	11,758	13,543	19,002	3,152	1,041	1,492
Property, net	8,631	9,424	11,544	10,751	9,717	13,926
Total assets	26,113	35,393	51,959	26,901	18,167	26,037
Long-term debt, net of current maturities	2,485	5,683	4,421	3,268	3,098	4,440
Shareholders' equity	17,474	21,687	28,359	10,451	7,330	10,505
Capital stock	€ 9,611	€ 11,774	€ 14,946	€ 14,956	€ 106,962	$ 153,298
Number of shares	9,610,630	11,773,613	14,946,317	14,956,317	14,956,317	14,956,317

(1) Euro amounts are translated into U.S. dollars using the Noon Buying Rate for the Euro on December 31, 2009, of U.S. $1.4332 per Euro. No representation is made that the Euro amounts referred to in this annual report could have been or could be converted into U.S. dollars at any particular rate or at all.

Exchange Rate Information

Fluctuations in the exchange rates between the Euro and the U.S. dollar will affect the U.S. 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 U.S. dollar price of the ADSs on the Nasdaq Global Market. The following table sets forth information regarding the exchange rates of U.S. dollars per Euro for the periods indicated, calculated by using the average of the noon buying rates on the last day of each month during the periods presented.

	U.S. Dollar per Euro	
Year	Average	Period End
2005	1.2400	1.1842
2006	1.2661	1.3197
2007	1.3797	1.4603
2008	1.4695	1.3919
2009	1.3935	1.4332

Source: Federal Reserve Statistical Releases H.10 and G.5

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
September 2009	1.4795	1.4235
October 2009	1.5029	1.4532
November 2009	1.5085	1.4828
December 2009	1.5100	1.4243
January 2010	1.4536	1.3870
February 2010	1.3995	1.3476
March 2010 (through March 26, 2010)	1.3758	1.3344

Source: Federal Reserve Statistical Release H.10

On March 26, 2010, the noon buying rate was €1.00 to $1.3398.

We use the Euro as our functional currency for financial reporting. This annual report 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 annual report could have been or could be converted into U.S. dollars at any particular rate or at all.

CAPITALIZATION AND INDEBTEDNESS

Not applicable.

REASONS FOR THE OFFER AND USE OF PROCEEDS

Not applicable.

RISK FACTORS

You should carefully consider the risks described below, in conjunction with the other information and financial statements and related notes included elsewhere in this annual report, 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 ADSs could decline and you could lose all or part of your investment.

Risks Relating to Our Business

We may not be able to meet our future cash requirements without obtaining additional capital from external sources.

As of December 31, 2009, we had €1,392 million in cash and cash equivalents. We have generated net losses since our inception. Our net losses for the year ended December 31, 2009 and for the year ended December 31, 2008 were €4.53 million and €19.90 million, respectively. We expect to incur significant losses over the next several years as we pursue regulatory approval for defibrotide, which may require additional clinical trials, testing and regulatory compliance activities, and commercialization efforts and related activities. In addition, our long-term ability to generate cash from operations is dependent in part on the success of our current strategic partner, Sigma-Tau Pharmaceuticals, Inc., as well as the likelihood and timing of new strategic licensing and partnering relationships and/or the successful commercialization of defibrotide. If we incur operating losses for longer than we expect and/or we are unable to raise additional capital, we may become insolvent and unable to continue our operations.

Since our inception, we have financed our operations primarily through the sale of equity and convertible notes, interest income earned on cash and cash equivalents, and debt provided through secured lines of credit. If we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly-issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations.

Absent the need to fund any additional clinical trials, we believe that our cash and cash equivalents, including the upfront payment received from Sigma-Tau Pharmaceuticals, Inc. in connection with the expansion of the license for defibrotide in the Americas, together with revenues generated from our named-patient and cost recovery programs, will be sufficient to meet our obligations for at least the next twelve months. However, if we elect to increase our spending above current plans or perform additional clinical trials, we may need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all.

Our failure to raise additional funds in the future may delay the development of defibrotide.

The development of defibrotide will require a commitment of substantial funds in order to obtain regulatory approval. For the year ended December 31, 2009, our cash used in operating activities was €5.16 million. Capital expenditures for year ended December 31, 2009 was €0.25 million. You should review the additional information about our liquidity and capital resources in the Operating and Financial Review and Prospects section of this annual report.

Our future capital requirements are dependent upon many factors, some of which are beyond our control, including:

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the successful and continued development of defibrotide in preclinical and clinical testing in our existing and any future clinical trials;

- 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 costs associated with building a future commercial infrastructure;
- the costs associated with implementing any upgrades to our manufacturing facility required by the United States Food and Drug Administration, or FDA, European Medicines Agency, or EMEA, or other regulators;
- the timing of regulatory approvals needed to market defibrotide;
- success of our named-patient and cost recovery programs; and
- market acceptance of defibrotide.

We may need additional funds before we have obtained regulatory approval for defibrotide. 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 defibrotide. We may also be forced to curtail, cease or restructure our operations, obtain funds by entering into arrangements with collaborators on unattractive terms or relinquish rights to defibrotide that we would not otherwise relinquish in order to continue independent operations.

We have started to generate limited revenues from sales of defibrotide and have had significant losses to date, and we do not know whether we will ever generate significant revenues or achieve profitability.

We have generated limited revenues through commercial sales of our active pharmaceutical ingredients and, recently, pre-approval sales of defibrotide through our named-patient and cost recovery programs. We had total net product sales of €5.09 million, €5.44 million and €9.70 million in 2007, 2008 and 2009, respectively. Even if we are successful in obtaining regulatory approval to market defibrotide, we may have very limited markets and may not generate enough revenues from defibrotide to fund our business. In addition, the FDA and EMEA have designated defibrotide to treat severe VOD and defibrotide to prevent VOD, as "orphan drugs," which generally means that fewer than 200,000 people are affected by the disease or condition.

Our ability to continue as a going concern is largely dependent on the revenues being generated from the distribution of defibrotide on a pre-approved compassionate use basis through our named-patient and cost recovery programs. If we fail to generate projected revenues from such compassionate use programs, we may need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all, in order to fund our operations over the next twelve months.

We expect to continue to incur significant expenses as we develop and seek regulatory approval for defibrotide. We incurred a net loss of €35.61 million, €19.90 million and €4.53 million in 2007, 2008 and 2009, respectively. 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 American Depositary Shares, or ADSs, may decline.

We currently do not have any regulatory approvals to sell defibrotide to treat or prevent VOD, and we cannot guarantee that we will ever be able to sell defibrotide to treat or prevent VOD anywhere in the world.

We must demonstrate that defibrotide satisfies rigorous standards of safety and effectiveness before the FDA, EMEA and other regulatory authorities will approve defibrotide for commercial marketing. While we have completed two clinical trials for defibrotide to treat and prevent VOD, the data obtained from these trials may not be sufficient to obtain regulatory approval and we may be required to conduct additional clinical trials. We do not currently have the funds to run an additional clinical trial and we would likely need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all. As a result, we may not be able to commercialize defibrotide for sale anywhere in the world.

The FDA and other regulatory authorities may require us to conduct other clinical trials of defibrotide to treat severe VOD or prevent VOD, which may delay or prevent approval and commercialization of our product candidate.

On December 7, 2009, we announced final clinical trial results for our current Phase III clinical trial of defibrotide to treat severe VOD and our Phase II/III pediatric prevention trial in Europe to prevent VOD, both of which were presented at the American Society of Hematology Conference in New Orleans. While data from these two trials are encouraging, we may have to conduct a new clinical trial of defibrotide to treat VOD using a concurrent control group of untreated patients before obtaining regulatory approval in the U.S. or Europe for either the treatment or prevention indications. We currently do not, and we may never, have enough capital to commence and complete a new clinical trial of defibrotide to treat VOD. In addition, even if we are able to commence a new clinical trial, one or more

clinical centers where the clinical trial is to be conducted may not be willing to conduct such a clinical trial 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 concurrent control group of untreated patients, 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. Therefore, we may never be able to obtain regulatory approval of defibrotide to treat VOD.

We may be required to suspend or discontinue any future clinical trials, if necessary, due to adverse events or other safety issues that could preclude approval of defibrotide and negatively affect our business model and stock price.

If we are required to conduct any future clinical trials for defibrotide, such trials may be suspended at any time for a number of safety-related reasons. For example, we may voluntarily suspend or terminate such clinical trials if at any time we believe that defibrotide prevents an unacceptable risk to the clinical trial patients. In addition, institutional review boards 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 is a complication 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 severe VOD. 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 the FDA and other regulatory authorities in determining whether defibrotide can, from a risk-benefit perspective, be considered to be safe and effective to treat severe VOD and prevent VOD, to prevent deep vein thrombosis, or any other indication for which approval is sought.

It is possible that additional adverse events or safety issues could emerge from future data, which could impact conclusions relating to the safety of defibrotide. Any problems that arise from the use of defibrotide would severely harm our business operations.

We expect to rely upon our affiliate, Sirton Pharmaceuticals S.p.A., for various services, and we may not be able to quickly replace these services if it becomes bankrupt or otherwise unavailable.

We depend on a number of services from Sirton Pharmaceuticals S.p.A., including steam related to our manufacturing plant, lab space, and filling and packaging services for defibrotide for use in our compassionate use programs and any future clinical trials. If Sirton were to become bankrupt or otherwise cease providing these services, we may not be able to replace these services in a timely manner. Such a delay would impact our compassionate use programs and any future clinical trials.

Sirton, who is our affiliate, owes us a receivable that we may not be able to collect.

At December 31, 2009, Sirton owed us a receivable of €1.38 million and we owed Sirton a payable of €0.28 million. Sirton has been unable to make timely payments on the outstanding receivables. Currently, Sirton is evaluating its strategic options in order to avoid bankruptcy, which raises additional concerns on our ability to collect the outstanding receivables. In 2009, the Company and Sirton formally offset €0.74 million of payables due to Sirton against the same amount of receivables due from Sirton. We may never be able to collect the net receivable due to us from Sirton.

Defibrotide 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 defibrotide is 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 defibrotide or its manufacture, or failure to comply with regulatory requirements, may result in:

- restrictions on defibrotide or manufacturing processes;
- withdrawal of defibrotide 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 defibrotide when and if defibrotide is approved.

Our manufacturing facility and the manufacturing facility of Patheon S.p.A., who we have contracted to fill and finish defibrotide, are subject to continuing regulation by Italian authorities and are subject to inspection and regulation by the FDA and EMEA. These authorities could force us to stop manufacturing our products if they determine that we or Patheon are not complying with applicable regulations or require us to complete further costly alterations to our facilities.

We manufacture active pharmaceutical ingredients at our manufacturing facility in Italy. We have hired Patheon S.p.A. to process our lead active pharmaceutical ingredient, defibrotide, into the finished drug at Patheon's manufacturing facility. These facilities are subject to continuing regulation by the Italian Health Authority and other Italian regulatory authorities with respect to manufacturing defibrotide. The facilities are also subject to inspection and regulation by the FDA and EMEA with respect to manufacturing our product candidates for investigational use. Also, part of the process for obtaining approval from the FDA and EMEA for defibrotide is approval by those authorities of these manufacturing facilities in compliance with current good manufacturing practices. After receiving initial approval, if any, the FDA or EMEA will continue to inspect our manufacturing facilities, including inspecting them unannounced, to confirm whether we and Patheon are complying with good manufacturing practices.

These regulators may require us to stop manufacturing our products and may deny us approval to manufacture our product candidates if they determine that we or Patheon are not complying with applicable regulations. In addition, these regulators may require us to complete costly alterations to our facilities.

We expect to rely upon a sole processor, Patheon Italia, to fill and finish defibrotide into marketable formulations, and we may not be able to quickly replace Patheon if it fails in its duties.

If Patheon does not or is not able to perform these services for any reason, it may take us time to find a replacement processor. Such a delay could potentially put us in breach of our contractual obligations into which we may enter, violate local laws requiring us to deliver the product to those in need, and impact our revenues.

We may have difficulty obtaining raw material for defibrotide.

Defibrotide is based on pig intestines. If our current sources of pig intestines develop safety problems or other issues that impact our supply of pig intestines, we may not be able to find alternative suppliers in a timely fashion. In that case, we would have to slow or cease our manufacture of defibrotide.

If our third-party clinical trial vendors fail to comply with strict regulations, the clinical trials for defibrotide 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 defibrotide. We rely on third parties to assist us in managing, monitoring and conducting our clinical trials. We have entered into and expect to continue to enter into clinical trial agreements with numerous centers throughout the world in order to continue the development of defibrotide. In addition, we have entered into an agreement with MDS Pharma Services (U.S.) Inc. (now INC Research Inc.) to perform clinical research services in connection with clinical trials conducted in the United States and agreements with KKS-UKT, GmbH (now CenTrial, GmbH) and MDS Pharma Services S.p.A. (now Inc Research S.r.l.) 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 defibrotide 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 good clinical practices. If the FDA determines that these clinical sites or 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.

We are currently dependent on third parties to market and distribute defibrotide in finished dosage form, and we may continue to be dependent on third parties to market and distribute defibrotide.

Our internal ability to handle the marketing and distribution functions for defibrotide is limited and we do not expect to develop the capability to provide marketing and distribution for defibrotide. Our long-term strategy includes either developing marketing and distribution capacity internally or entering into 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 and prevent VOD in North America, Central America and South America and we may need to develop these capabilities internally or enter into similar agreements to market and distribute defibrotide to prevent VOD outside the Americas. 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 qualified personnel and key relationships, we may be unable to successfully develop and commercialize defibrotide or otherwise manage our business effectively.

We are highly dependent on our senior management, whose services are critical to the successful implementation of research and development, manufacturing and regulatory strategies and develop and maintain relationships with qualified researchers. If we lose their services or the services of one or more of the other members of our senior management or other key researcher, our ability to successfully commercialize defibrotide or otherwise manage our business effectively could be seriously harmed.

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 defibrotide 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 cannot incentivize such key employees with certain forms of equity grants, such as restricted stock awards, or grant stock options with an exercise price at or near the recent trading prices of our ADSs, both of which could further limit our ability to retain and hire key personnel.

On March 1, 2010, we announced our decision to close our New York office and began transitioning the New York activities to our headquarters in Como, Italy. If we are unsuccessful in transitioning these activities, our business and results of operations could be negatively impacted. In addition, we may 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.

All 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 all 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 €15 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 have sold Prociclide and Noravid (two formulations of defibrotide) in Italy to treat vascular disease with risk of thrombosis, which may affect the pricing of defibrotide in Europe for the prevention or treatment of VOD.

Until December 31, 2008, through our distribution agreement with Crinos S.p.A., we sold Prociclide and Noravid (both forms of defibrotide) in Italy to treat vascular disease with risk of thrombosis. While we have stopped selling Prociclide and Noravid for this treatment in Italy, if defibrotide is approved for sale in Europe or Italy to treat and prevent VOD, or both, we may need to also obtain approval from regulators as to what price we can charge for these uses of defibrotide. The regulators may impose an artificially low cap on defibrotide based on the relatively low price-point of Prociclide and Noravid previously sold in Italy for the treatment of vascular disease with risk of thrombosis.

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. Incidence of VOD may decrease with new technologies and conditioning regimens, which will negatively impact our sales opportunities. While we are unaware of any other products or product candidates that treat or prevent VOD, we believe that other companies have products or are currently developing products to treat some of the same disorders and diseases that defibrotide is designed to treat. These companies include Genzyme Corp., Millennium Pharmaceuticals, Inc., Otsuka Pharmaceutical Co., Ltd., Eisai Co., Ltd., and Celgene Corp.

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 or develop a generic form of defibrotide. Their products may also prove to be more effective, safer or less costly than defibrotide, which could hurt our ability to recognize any significant revenues.

In May 2003, the FDA designated defibrotide as an orphan drug to treat severe VOD. In January 2007, the FDA designated defibrotide as an orphan drug to prevent VOD as well. If the FDA approves the New Drug Applications that we intend to file before approving a New Drug Application filed by anyone else for these uses 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 to another applicant may be granted for the same 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 its product is safer, more effective or otherwise clinically superior to our product. In that case, our product would not have market exclusivity. Additionally, while we are not aware of any other company researching defibrotide for these uses, if another company does develop defibrotide for these uses, there is no guarantee that the FDA will approve our New Drug Application before approving the other company's defibrotide product for these uses, in which case the first product approved would have market exclusivity and our products would not be eligible for approval until that exclusivity expires.

In July 2004, EMEA 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 to another applicant for the same 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 its product is safer, more effective or otherwise clinically superior to our product. 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 defibrotide can be approved for sale and commercialized, our relevant patent rights may expire or remain in force for only a short period following commercialization. We have been issued a patent in the U.S. and several other countries which covers the method for determining the biological activity of defibrotide. This patent expires in 2022 in most countries. We believe this to be an important patent because the analytical release of a biological product like defibrotide is a key step in confirming the purity and biological activity of the final product. There may be no opportunities to extend this patent and thereby extend exclusivity related to FDA and EMEA, in which case we could face increased competition for defibrotide. Patent expiration could adversely affect our ability to protect future product development and, consequently, our operating results and financial position. In addition, generic innovators may be able to circumvent this patent and design a novel analytical method for determining the biological activity of defibrotide. In this case, a generic defibrotide could potentially be on the market once the relevant protections offered by our orphan designations end.

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, South Korea and other countries which do not have the same level of protection of intellectual property rights that 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 American Depositary Shares

Our ADSs have generally had low trading volume, and its public trading price has been volatile.

Between our initial public offering on June 21, 2005 and December 31, 2009, the closing price of our American Depositary Shares, or ADSs, have fluctuated between $.33 and $24.40 per share, with an average daily trading volume for the twelve months ended December 31, 2009 of approximately 54,736 ADSs. The market may experience significant price and volume fluctuations that are often unrelated to the operating performance of individual companies.

In addition to general market volatility, many factors may have a significant adverse effect on the market price of our ADSs, including:

- continuing operating losses, which we expect over the next several years as we continue our development activities;
- announcements of decisions made by regulators;
- results of our preclinical studies and clinical trials;
- announcements of improvements, new commercial products, failures of products, or progress toward commercialization by our competitors or peers;
- influence and control by our commercial partner and significant shareholder, Sigma-Tau Finanziaria S.p.A.;
- developments concerning proprietary rights, including patent and litigation matters;
- publicity regarding actual or potential results with respect to product candidates under development by us or by our competitors;
- regulatory developments; and
- quarterly fluctuations in our financial results.

We may not remain listed on the Nasdaq Global Market.

Between our public offering and May 2006, our ADSs were listed on the American Stock Exchange. Since May 2006, our ADSs have been listed on the Nasdaq Global Market. The Nasdaq Global Market sets forth various requirements that we must meet in order for our ADSs to continue to be listed on the Nasdaq Global Market. Violations of the continued listing requirements include:

- if the closing bid price of our ADSs drops below $1.00 for a period of 30 consecutive trading days;
- if our stockholders' equity falls below $10 million; or
- if we fail to maintain a market value of publicly held securities of at least $5 million for 30 consecutive trading days.

If we violate any of these continued listing requirements, our ADSs could be delisted from the Nasdaq Global Market. The delisting of our ADSs could have negative results, including the potential loss of confidence by suppliers and employees, the loss of institutional investor interest, and fewer business development opportunities.

As of December 31, 2009, our stockholders' equity was $10.5 million (€7.33 million). If we fail to meet the stockholders' equity or fail to meet the minimum bid price and minimum market value requirements, we may be delisted from the Nasdaq Global Market.

Our largest shareholders exercise 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, including obtaining potential financing.

Our largest shareholder, FinSirton S.p.A., will own approximately 25% of our outstanding ordinary shares at March 31, 2010. Dr. Laura Ferro, who is our former Chief Executive Officer and President and a current member on our board of directors, together with members of her family controls FinSirton. In addition, Sigma-Tau Finanziaria S.p.A., along with its affiliates, will own approximately 18% of our outstanding ordinary shares at March 31, 2010. Marco Codella, who is the chief financial officer of Sigma-Tau Finanziaria, serves as a member of our board of directors. Moreover, we have licensed our rights in defibrotide to treat and prevent VOD to Sigma-Tau Pharmaceuticals, Inc., a wholly owned subsidiary of Sigma-Tau Finanziaria.

Both FinSirton and Sigma-Tau Finanziaria may 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. 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.

As discussed in our risk factor entitled "Our shareholders can prevent us from executing a financing by alleging that our board of directors acted with serious irregularities when approving such financing, because the terms of such financing could harm our company," both FinSirton and Sigma-Tau Finanziaria own enough of our ordinary shares to bring legal action against our board of directors and may be able to prevent us from completing an important corporate event, such as a financing. In addition, under Italian law, directors are not required to recuse themselves from any discussion even if a conflict of interest exists. Accordingly, directors that are affiliated with our shareholders may be present for certain discussions that involve or impact the shareholders to which such directors are affiliated.

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 outstanding ordinary shares, ordinary shares issuable upon exercise of warrants and ordinary shares issuable upon exercise of options are not subject to lock-up agreements. We have filed registration statements registering the resale of most of our outstanding ordinary shares and related ADSs and all of our ordinary shares and related ADSs issuable upon exercise of our outstanding warrants and options. Such registration and ultimate sale of the securities in the markets may adversely affect the market for the ADSs.

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 annual report 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.

Risks Relating to Being an Italian Corporation

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

We are 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. 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 of directors 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 an extraordinary meeting duly called, upon the favorable vote of the required majority, which may change depending on whether the meeting is held on a first or second call. These meetings take time to call. In addition, an Italian notary public must verify the compliance of the capital increase with our bylaws and applicable Italian law. Further, in general, under Italian law, our existing shareholders and any holders of convertible securities (except in specific cases) have preemptive rights to acquire any such shares pro rated on their percentage interest in our company and on the same terms as approved for such capital increase. 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 by the board 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 provides, with respect to shareholders' resolutions approving capital increase, that, in the event of absence of the minutes of the meeting, impossibility or illegality of the resolution, any interested person may, for a period of 180 days following the filing of the shareholders' resolution with the Register of Companies, challenge such resolution. If a shareholders' meeting was not called to approve the capital increase, the relevant resolution should be considered invalid and, any interested person may challenge the capital increase for a period of 90 days following the approval of the financial statements referring to the year during which the shareholders' resolution has been, also partially, executed. In addition, once our shareholders authorize a capital increase, all those authorized shares that have been subscribed need to be entirely paid-up before the shareholders may authorize a new capital increase. These restrictions could limit our ability to issue new equity or convertible debt securities on a timely basis.

Our shareholders can prevent us from executing a financing by alleging that our board of directors acted with serious irregularities when approving such financing, because the terms of such financing could harm our company.

On August 12, 2008, Sigma-Tau Finanziaria S.p.A., together with one of its affiliates, filed a claim in the Court of Como claiming that our board of directors acted with serious irregularities in violation of their duties as directors when approving a potential financing, because such financing could harm the company. On August 18, 2008, the Court of Como issued a temporary order preventing us from moving forward with a potential financing. While this claim was later dismissed for lack of damages, it did, nonetheless, prevent the directors from implementing the potential financing. Any group of shareholders constituting at least 10% of our outstanding ordinary shares could bring a similar action on a future board resolution regarding a financing or other important corporate action, and an Italian court could prevent the transaction from moving forward by issuing an order to that effect.

We are restricted under Italian law as to the amount of debt securities that we may issue relative to our equity.

Italian law provides that we may not issue debt securities for an amount exceeding twice the amount of our capital, of our legal reserve and of 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 Italian GAAP 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 amount of such ordinary shares that

is allocated to the capital. At December 31, 2009, the sum of our capital, legal reserves and other reserves on our unaudited Italian GAAP balance sheet was €28.6 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 allocate 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.

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 to reflect on-going losses, in certain cases of losses exceeding 1/3 of the capital of the Company. We are also required to maintain a minimum capital of €120 thousand. At December 31, 2009, our Italian GAAP capital was approximately €14.9 million. If we suffer losses from operations that 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) to at least €120 thousand 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, our company could be liquidated.

We apply our losses from operations against our legal reserves and capital. If our capital is reduced for more than one-third as a result of losses, our board of directors must call a shareholders' meeting as soon as possible. The shareholders should take appropriate measures, which may include, inter alia, either the reduction of the legal reserves and capital by the amount of the remaining losses, or the carrying out of the losses forward for up to one year. If the shareholders vote to elect to carry the losses forward up to one year, and at the end of the year, the losses are still more than one-third of the amount of the capital, then we must reduce our capital by the amount of the losses.

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 "Item 10, Additional Information, 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. In particular, the following laws are worth mentioning: (i) Law no. 604/1966, regulating the individual dismissals; (ii) Law no. 223/1991, concerning the collective dismissal procedure; (iii) Law no. 428/1990, providing for the information and consultation procedure in case of transfer of the undertaking or part thereof and (iv) Legislative decree no. 25/2007, introducing a general right to information and consultation for employees. 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 annual report may contain forward-looking statements that involve substantial risks and uncertainties regarding future events or our future performance. When used in this annual report, the words "anticipate," "believe," "estimate," "may," "intent," "continue," "will," "plan," "intend," and "expect" and similar expressions identify forward-looking statements. 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 annual report 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 or ADSs, you should be aware that the occurrence of the events described in the "Risk Factors" section and elsewhere in this annual report 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 annual report. 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 annual report. We have not authorized anyone to provide you with information different from that contained in this annual report. The information contained in this annual

report is accurate only as of the date of this annual report.

ITEM 4. INFORMATION ON THE COMPANY

HISTORY AND DEVELOPMENT OF THE COMPANY

We were originally formed in 1993 as Pharma Research S.r.L., an Italian private limited company. In December 2000, we changed from a private limited company to an Italian corporation. 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 governed by the Italian Civil Code.

We were 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 1970s. In 1986, our founding company received approval to sell Prociclide and Noravid (both forms of defibrotide) in Italy to treat deep vein thrombosis, and, in 1993, our founding company received approval to manufacture and sell a form of defibrotide in Italy to both treat and prevent all vascular disease with risk of thrombosis. We are currently focused on the development of defibrotide to treat and prevent VOD in the United States and Europe.

In June 2005, we consummated an initial public offering of our ADSs, which began trading on the American Stock Exchange. In May 2006, we transitioned the trading of our ADSs from the American Stock Exchange to the Nasdaq Global Market.

We have Italian, United States and international trademark rights in "Gentium." We also have a number of patent registrations issued and pending in Italy, the United States and other countries. This annual report 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 annual report contains market data and industry forecasts that were obtained from industry publications and third parties.

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 annual report. Our registered agent for service of process in New York is CT Corporation System, located at 111 Eighth Avenue, 13th Floor, New York, New York 10011, telephone number (212) 894-8940.

CAPITAL EXPENDITURES

The following table sets forth our capital expenditures for each year in the three-year period ended December 31, 2009.

	For the Year Ended December 31,		
(in thousands)	2007	2008	2009
Land and buildings	€ 162	€ 4	€ -
Plant and machinery	1,839	544	206
Industrial equipment	582	179	5
Other	90	13	23
Leasehold improvements	249	27	3
Computer Software	69	224	12
Construction in progress	250	172	28
Total	€ 3,241	€ 1,163	€ 277

All of these capital expenditures are in Italy. We are financing these expenditures from offerings of our ordinary shares and loans from third parties.

BUSINESS OVERVIEW

We are building upon our extensive experience with defibrotide, an investigational drug based on DNA derived from pig intestines, which our founding company discovered over 20 years ago. We are focused on development and manufacture of defibrotide to treat and prevent VOD, a condition in which some of the veins in the liver are blocked as a result of cancer treatments such as chemotherapy or radiation treatments that are given prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is associated with multiple-organ failure and results in high morbidity and mortality. Defibrotide has been studied in a number of clinical trials and more recently we have concluded a Phase III clinical trial of defibrotide to treat severe VOD in the United States, Canada and Israel. In addition, we have concluded a Phase II/III clinical trial of defibrotide in Europe to prevent VOD in children. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approved basis under a treatment IND protocol in the U.S. and through a named-patient program throughout the rest of the world.

Due to the historically low complete response and survival rates and lack of treatments for VOD, we believe there is an immediate need for a drug to treat and prevent VOD. The FDA has a "fast track" designation program which is designed to facilitate the development and expedite their review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. The FDA has designated defibrotide to treat severe VOD as a fast track product. The FDA approval process for defibrotide for this use remains dependent upon sufficient data in connection with a clinical trial to treat severe VOD.

On December 7, 2009, we announced final clinical trial results for our current Phase III clinical trial of defibrotide to treat severe VOD and our Phase II/III pediatric prevention trial in Europe to prevent VOD. We are currently completing certain preclinical and clinical studies requested by regulatory authorities. As part of our overall strategy, we anticipate filing for regulatory approval for defibrotide in the U.S. and Europe by the end of second quarter 2011. We expect to utilize the data from the two studies, together with data obtained from our compassionate use programs, whereby we have been authorized to distribute defibrotide on a pre-approval basis, to support our regulatory submissions and any future clinical trials that may be necessary. We are also working closely on our U.S. regulatory strategy with our commercial partner, Sigma-Tau Finanziaria S.p.A. and its affiliate Sigma-Tau Pharmaceuticals, Inc., to which we have licensed our commercial rights to defibrotide for both the treatment and prevention of VOD in the Americas.

We also manufacture defibrotide and sulglicotide at our manufacturing facility near Como, Italy, and we lease a facility from one of our affiliates, Sirton, to manufacture urokinase. These products are active pharmaceutical ingredients used to make other drugs. Our revenues from the sales of these products to date have amounted to €5.1 million, €5.4 million and €9.7 million in 2007, 2008 and 2009, respectively. In 2009, we launched a named-patient program and cost recovery program, which have generated approximately €4.9 million in net sales for the year ended December 31, 2009.

Our strategy is to obtain regulatory approval for defibrotide to treat and prevent veno-occlusive disease. Since 2004, we have spent more than €10 million on upgrades to our facilities that we believe will facilitate the FDA and European regulatory approval process for defibrotide and enable our future production. We plan to work with our existing license partner, Sigma-Tau Pharmaceuticals, Inc., and are seeking additional license partners to help with the development and commercialization of defibrotide. We also are attempting to grow our active pharmaceutical ingredient, or API, business through volume and price increases of sulglicotide and urokinase.

Market Overview

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

One of the disorders of the vascular system that can result from chemotherapy, radiation therapy, hormone therapy and stem cell and bone marrow transplants is VOD. These therapies can cause extensive damage to the cells that line the walls of small veins in the liver. The body's natural response is to swell or clot the sites of injury, but this blocks or "occludes" the vein. This blockage of the veins is called "Hepatic Veno-Occlusive Disease," or VOD. VOD can cause damage to the liver and, in its severe form, leads to failure of the liver and other organs (multiple-organ failure), which usually results in death. According to 2003 data from the International Bone Marrow Transplant Registry and the European Bone Marrow Transplant Registry, approximately 21,000 people receive bone marrow transplants, which are types of stem cell transplants, each year in the United States. Based on our review of more than 200 articles in the medical literature, we believe that approximately 12% of patients who undergo stem cell transplants develop VOD. According to an article in the November 15, 1998 edition of Blood, the Journal of the American Society of Hematology, by Enric Carreras et. al., approximately 28% of patients who develop VOD progress to severe VOD. Based upon a historical study conducted by Dana-Farber at three centers consisting of 38 patients, we believe that of the patients who develop severe VOD, only approximately 11% achieve a complete response within 100 days after a stem cell transplantation and only approximately 20% survive more than 100 days. VOD poses a severe risk to the victim's health. We believe that there are no FDA or EMEA approved treatments at this time for VOD.

Strategy

Our strategic objective is to obtain regulatory approval for defibrotide to treat and prevent VOD. We plan to continue to work with our existing license partner, Sigma-Tau Pharmaceuticals, Inc., for the development of defibrotide and commercialization of defibrotide in the Americas. Outside of the Americas, we are seeking additional license partners to help with the development and commercialization of defibrotide. We also are attempting to grow our active pharmaceutical ingredient, or API, business through volume and price increases of sulglicotide and urokinase.

- Obtain regulatory approval to use defibrotide to treat and prevent VOD. Gentium, as well as independent investigators, have run several studies showing the potential efficacy and safety of defibrotide in the treatment and prevention of VOD (see detail under "Product Candidate" section below). We have received orphan status from both the FDA and EMEA for defibrotide. In addition, we have received fast track designation for the use of defibrotide for the treatment of severe VOD prior to stem cell transplantation. The approval of defibrotide for either the treatment or prevention of VOD may be dependent on one or more future clinical trials. It is possible that both the FDA and EMEA will view the results of treatment and prevention trials as supportive of one another, although the exact regulatory approval may include only an indication of prevention, treatment, or both.

- Increase our marketing capacity, including the use of strategic partnerships. We have a strategic license agreement with Sigma-Tau Pharmaceuticals, Inc. to market defibrotide to treat and prevent VOD in North America, Central America and South America upon regulatory approval and have granted Sigma-Tau Pharmaceuticals, Inc. a right of first refusal in those territories with respect to offers made by third parties to market defibrotide to prevent VOD. We intend to develop the capacity to market defibrotide in other jurisdictions and/or pursue similar marketing agreements with other strategic partners for Europe and Asia Pacific.

- Compassionate use programs to maximize pre-approval data. We distribute defibrotide on a pre-approved compassionate use basis through our named-patient and treatment IND programs. We obtain data on the efficacy and safety of defibrotide through these programs. We expect to utilize this data to supplement the data obtained from our completed clinical trials and any future clinical trials that may be necessary. As of February 28, 2010, over 475 patients have received defibrotide through this program.

- Growth of API Business. We currently sell sulglicotide to Samil for use in the South Korean market, and to Crinos for use in the Italian market and urokinase to Crinos, for the Italian market, and UCB for the Spanish market, and, to a small extent, sodium heparin for use in the Italian market. Our goal is to maximize the utilization of our manufacturing facility and we are exploring ways to increase capacity of urokinase and sulglicotide. We are also looking at re-negotiating our existing supply agreements to achieve greater profitability and longer-term commitments.

Product Candidate

Defibrotide is an investigational drug based on single-stranded DNA extracted from pig intestines which is under development for the treatment and prevention of VOD, a consequence of cancer treatments, such as chemotherapy or radiation treatments, that are given prior to stem cell transplantation. Currently, and to the best of our knowledge, there are no FDA or EMEA approved treatments for this life-threatening disease. Defibrotide was granted orphan status in 2003 for the treatment of severe VOD and in 2007 for the prevention of VOD, and similar status by EMEA in 2004 for both the treatment and prevention of VOD. Orphan status provides us with limited market exclusivity upon regulatory approval. Defibrotide has also been granted fast-track product designation by the FDA for the treatment of VOD. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approved basis under a treatment IND protocol in the U.S. and through a named-patient program throughout the rest of the world.

Defibrotide to treat severe VOD

The December 2000 edition of the British Journal of Hematology published the results of a 40 patient "compassionate use" study of defibrotide to treat VOD conducted in 19 centers in Europe from December 1997 to June 1999. Twenty-two patients, or 55%, showed a complete response. Nineteen patients, or 47%, survived more than 100 days after stem cell transplantation. The study found that four patients of the 19 patients who survived more than 100 days subsequently died. Twenty-eight patients were judged likely to die or had evidence of multiple-organ failure. Ten of the 28 "poor risk" patients, or 36%, showed a complete response within 100 days after stem cell transplantation, all of whom also survived for at least 100 days. The study found that defibrotide was generally safely administered with no significant side-effects.

The December 15, 2002 edition of Blood published results from 88 patients with severe VOD following stem cell transplants who were treated with defibrotide from March 1995 to May 2001. This study reported data on 19 patients treated under individual Investigational New Drug Applications and on a subsequent 69 patient multi-center Phase I/II clinical trial that was conducted under an Investigational New Drug Application held by a Dana-Farber investigator. The primary goal of the trial was the assessment of the potential effectiveness of the drug and its side effects, if any. All patients in the clinical trial received defibrotide on an emergency basis. This study found that 32 patients, or 36%, showed a complete response within 100 days after stem cell transplantation, and 31 patients, or 35%, of those patients survived at least 100 days after stem cell transplantation with minimal adverse effects, primarily transient mild hypotension. Thirteen of those 31 patients who had survived more than 100 days had died by October 2001, the last date for which survival information was available. No mortality from VOD or other toxicity related to the cancer treatment was seen more than 134 days after treatment with defibrotide, with the most common cause of later death being relapse.

The Dana-Farber investigator also sponsored, under his Investigational New Drug Application, a Phase II clinical trial in the United States of defibrotide which enrolled 150 stem cell transplant patients with severe VOD, of whom 141 were evaluable, at nine cancer centers. This trial was partially funded by a $525 thousand grant from the orphan drug division of the FDA. The purpose of this trial was to evaluate the effectiveness of this drug, including the effect of the drug on the survival rate of patients with severe VOD, the effective dosage and potential adverse side effects. The primary endpoint was complete response, with survival after 100 days as a secondary endpoint. The Dana-Farber investigator presented the results from this Phase II clinical trial at the 47th Annual Meeting of the American Society of Hematology on December 12, 2005. Results show that of 141 patients evaluable for response, 65 patients, or 46%, showed a complete response within 100 days after stem cell transplantation and 62 patients, or 41%, survived at least 100 days after stem cell transplantation, with minimal adverse events.

The January 2004 edition of Bone Marrow Transplantation published results from 45 children and adolescents with VOD following stem cell transplants who were treated with defibrotide. Twenty-two of the 45 patients had severe

VOD. Thirty-four of the 45 patients, or 76%, had a complete response within 100 days after stem cell transplantation and 29 patients, or 64%, survived at least 100 days after stem cell transplantation. Of the 22 patients with severe VOD, 11 patients, or 50%, had a complete response and 8 patients, or 36%, survived at least 100 days after stem cell transplantation. The study found that defibrotide was well tolerated; about one-third of the patients had a form of coagulopathy, and treatment was discontinued in two cases where a severe bleeding disorder was observed, although the events could not be clearly attributed to defibrotide.

We started a historically controlled Phase III clinical trial in the United States, Canada and Israel for this use in December 2005 in patients with severe VOD. The primary endpoint is complete response within 100 days after stem cell transplantation and the secondary endpoint is survival after 100 days.

On December 7, 2009, we announced final clinical trial results for our current Phase III clinical trial of defibrotide to treat severe VOD at the American Society of Hematology Conference in New Orleans. On an intent to treat basis (ITT), 24% of patients in the Defibrotide arm compared to 9% of patients in the historical control arm achieved complete response at 100 days (p=0.0148). For the secondary efficacy analysis on an ITT basis, the mortality rate at day 100 was 75% for patients in the historical control arm compared to 62% for patients in the Defibrotide arm (p=0.0508). The ITT analysis included 123 patients with symptoms consistent with VOD that were identified and then reviewed for eligibility in the historical control arm by an independent medical review committee. 32 cases were selected as having an unequivocal diagnosis of severe VOD and multi-organ failure (graft versus host disease was ruled out) and met all protocol-required entry criteria. 102 patients were enrolled in the defibrotide treatment group and baseline characteristics were balanced between the two arms.

Defibrotide to prevent VOD

We believe there is a significant market opportunity for defibrotide to prevent VOD for patients at risk of developing VOD. Based on our experience researching VOD, we believe that many recipients of high doses of chemotherapy, radiation therapy or hormone therapy or of therapies that prepare for stem cell transplants have an elevated risk of developing VOD. The European Group for Blood and Marrow Transplantation, a not-for-profit scientific society, conducted a Phase II/III clinical trial in Europe and Israel of defibrotide to prevent VOD in children. Unlike our Phase III treatment trial in the United States, we had a randomized control group of patients who received no treatment unless they developed VOD, at which time they received defibrotide treatment.

The results of a study on defibrotide in patients at high risk of VOD were presented at the 2002 annual meeting of the American Society of Hematology. One of 57 patients who received defibrotide as a preventative agent developed VOD. No patients experienced significant bleeding.

At the 2005 annual meeting of the European Group for Blood and Marrow Transplantation, the results of a study on defibrotide in patients who received chemotherapy and stem cell transplants were announced. Eight of 44 patients, or 18%, who received defibrotide developed VOD, of which three patients, or 7%, developed severe VOD. By comparison, four of 16 control group patients, or 25%, who received heparin instead of defibrotide, developed VOD, of which two, or 12.5%, developed severe VOD. There were no serious adverse events attributed to the use of defibrotide.

At the 2006 annual meeting of the American Society of Hematology conference, the results from a preliminary pilot clinical study in Switzerland by the University Hospital of Geneva on defibrotide in patients at high risk of VOD were announced. The results suggested that defibrotide may provide effective and safe prevention against VOD. The study tested patients who received stem cell transplants. None of the 157 successive transplant patients who received defibrotide as a preventative agent developed VOD. By comparison, 10 of 52 patients who underwent transplants in the same center before the study developed VOD, which was fatal in three cases. The study report indicated that mild to moderate toxicity such as mild nausea, fever and abdominal cramps was documented, although the report stated that it was difficult to determine whether the toxicity was directly attributable to the defibrotide, the chemotherapy that preceded the stem cell transplants or other drugs used during the stem cell transplants. The study report did not indicate the number of patients who experienced this toxicity.

The July 2007 edition of Bone Marrow Transplant published the results of a study on defibrotide in patients who received stem cell transplants. While a majority of these patients received reduced intensity cancer treatments, they still had other risk factors for VOD. None of the 58 patients who received defibrotide as a preventative agent developed VOD. No serious adverse events were reported.

The results of a study on defibrotide in patients who received stem cell transplants and had elevated risks for VOD were reported in the November 16, 2007 edition of Blood. One of 41 evaluable patients who received defibrotide as a preventative agent developed VOD. No serious adverse events were reported.

On December 7, 2009, we announced final clinical trial results from our Phase II/III pediatric prevention study to prevent VOD at the American Society of Hematology conference. Defibrotide demonstrated a 40% reduction in the incidence of VOD within 30 days after stem cell transplantation. The analysis included 356 patients; 180 patients in the prophylaxis arm and 176 patients in the control arm. Although the study was not powered to assess mortality, a composite score was measured as a secondary endpoint, incorporating VOD-associated morbidity (including respiratory failure, renal failure, encephalopathy) and mortality; this score significantly favored defibrotide prophylaxis ($p=0.0340$). The study confirmed that the mortality in patients with VOD, independent of severity, is four times higher than in patients without VOD. Additionally, the incidence and severity of acute graft versus host disease (GvHD) by day 100 in the allogeneic SCT recipients (246 patients) was significantly reduced from 63% for the

control arm to 45% for the prophylaxis arm (p=0.0044 for incidence of GvHD and p=0.0032 for severity). Defibrotide was well tolerated and no difference in adverse events was observed between the two study arms.

Defibrotide Pre-Approval

Historically, we sold defibrotide as an active pharmaceutical ingredient to our affiliate, Sirton, who then used the active pharmaceutical ingredient for defibrotide to fill and finish the product into ampoule and capsule forms. Sirton then sold these forms of defibrotide to Crinos S.p.A., a subsidiary of Stada Arzneimittel AG. Crinos, pursuant to a distribution agreement entered into with us, sold these products throughout Italy, under the trademarks Prociclide and Noravid, to treat and prevent vascular disease with risk of thrombosis.

In 2007, we changed our relationship with Sirton, from customer to a contract manufacturer, and sold the finished forms of Prociclide and Noravid to Crinos directly. On December 31, 2008, the distribution agreement with Crinos expired and, consistent with our overall strategy, we chose not to renew this agreement and discontinued the manufacture of defibrotide to be finished into Prociclide and Noravid. We have not pursued any sales of Prociclide and Noravid in the Italian market in 2009. On August 19, 2009, the Italian Health Agency accepted the Company's request to withdraw the marketing authorization for Prociclide and Noravid; however, these products will be sold in Italy through May 2010. The Company had made the request to withdraw the marketing authorization of these forms of defibrotide as part of the Company's overall strategy regarding the development of defibrotide to treat and prevent VOD.

On March 6, 2009, we entered into a supply and distribution agreement with IDIS Limited, whereby IDIS was contracted to be the exclusive supplier of defibrotide on a named-patient supply basis in all countries other than countries in Europe and the Americas. This agreement was amended on April 15, 2009 to include all countries other than Italy and countries in the Americas, and further amended on May 22, 2009 to include all countries other than Italy and the United States of America. Gentium supplies the finished and labeled product to IDIS who in turn provides the product directly to hospitals in all countries except Italy and the United States.

We have also instituted an expanded access program, which gives patients diagnosed with VOD in the United States access to defibrotide under a treatment IND. Under an expanded access program, the FDA allows early access to investigational drugs that are being developed to treat serious or life-threatening diseases for which there is no satisfactory alternative therapy. We decided to undertake this expanded access program due to the large numbers of requests for compassionate use of defibrotide, and the corresponding burden that sites and investigators have been undergoing to obtain institutional review board and FDA approval for such compassionate use requests. On September 29, 2009, we entered into an agreement with US Oncology Clinical Development, whereby US Oncology was contracted as a clinical research organization to administer and recover costs on behalf of us in connection with this program. We expect to collect additional usage tolerability and safety data from patients of this program to support our planned New Drug Application for the treatment of Severe VOD and/or the prevention of VOD.

Our revenues from sales of defibrotide, including Prociclide and Noravid, were €2.76 million, €1.73 million, and €4.90 for 2007, 2008 and 2009, respectively.

Other Products

Sulglicotide

Sulglicotide is developed from swine duodenum and appears to have ulcer healing and gastrointestinal protective properties. We sell sulglicotide primarily to Samil, a South Korean company, for use in manufacturing a product of Samil's in South Korea, and to Crinos S.p.A. to be sold in the Italian market.

Urokinase

Urokinase is made from human urine and has the potential to dissolve fibrin clots and, as such, is used to treat various vascular disorders such as deep vein thrombosis and pulmonary embolisms. We sell urokinase to a number of companies, including Crinos and UCB.

Seasonality

Seasonality does not affect our business, although the timing of manufacturer orders can cause variability in sales.

Regulatory Matters

Overview

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

Non-compliance with applicable regulatory requirements can result in, among other things, injunctions, seizure of products, total or partial suspension of product manufacturing and marketing, failure of the government to grant

approval, withdrawal of marketing approvals, civil penalty actions and criminal prosecution. Except as discussed below, we believe that we are in substantial compliance in all material respects with each of the currently applicable laws, rules and regulations mentioned in this section. During the most recent biannual inspection of our manufacturing facility by the Italian Health Authority in February 2007, the Italian Health Authority noted by way of observations certain deficiencies in regard to the operation of our facility. We have corrected all of the deficiencies. Also, a regional Italian regulatory inspector, during an April 2005 inspection of our manufacturing facility, requested that we install an exhaust vent on one of our machines. We have installed this device. In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets their current good manufacturing practices, or GMP, including requirements for equipment verification and validation of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but since 2004 we spent over €10 million in upgrades to our facility in anticipation of such an inspection. We are not aware of any other situation that could be characterized as an incidence of non-compliance in the last three years.

United States Regulatory Approval

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

- our performance of satisfactory preclinical laboratory and animal studies under the FDA's good laboratory practices regulations;
- our submission to and acceptance by the FDA of an IND which must become effective before human clinical trials may begin in the United States;
- our successful completion of a series of adequate and well-controlled human clinical trials to establish the safety, purity, potency and effectiveness of any product candidate for its intended use under the FDA's good clinical practices regulations;
- our submission to, and review and approval by, the FDA of a marketing application prior to any commercial sale or shipment of a product; and
- our development and demonstration of manufacturing processes which conform to FDA-mandated current good manufacturing practices.

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

Preclinical Testing

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

Clinical Trials

In addition to FDA review of an Investigational New Drug Application, each clinical institution that desires to participate in a proposed clinical trial must have the clinical protocol reviewed and approved by an Institutional Review Board. The Institutional Review Boards consider, among other things, ethical factors, informed consent and the selection and safety of human subjects. Clinical trials must also be conducted in accordance with the FDA's good clinical practices requirements. The FDA, and/or the Institutional Review Board at each institution at which a clinical trial is being performed, may order the temporary or permanent discontinuation of a clinical trial at any time if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients.

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

Phase I

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

Phase II

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

- further identify any possible adverse side effects and safety risks;
- assess the preliminary or potential effectiveness of the product candidate for the specific targeted disease or medical condition; and
- assess dosage tolerance and determine the optimal dose for a Phase III trial.

Phase III

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

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

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

Post-Approval Regulations

If a product candidate receives regulatory approval, the approval is limited to specific clinical uses. Subsequent discovery of previously unknown problems with a product may result in restrictions on its use or even complete withdrawal of the product from the market. Any FDA-approved products manufactured or distributed by us are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse events or experiences. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies, and are subject to periodic inspections by the FDA and state agencies for compliance with current good manufacturing practices, or GMPs, which impose rigorous procedural and documentation requirements upon us and our contract manufacturers. Failure to comply with these requirements may result in, among other things, total or partial suspension of production activities, failure of the FDA to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals.

If the FDA approves one or more of our product candidates, we and our contract manufacturers must provide certain safety and effectiveness information while the drug is marketed. Product changes, as well as changes in the manufacturing process or facilities where the manufacturing occurs or other post-approval changes, may necessitate additional FDA review and approval. The labeling, advertising, promotion, marketing and distribution of a drug or biologic product also must be in compliance with FDA requirements which include, among others, standards and regulations for direct-to-consumer advertising, communication of information relating to off-label uses, industry sponsored scientific and educational activities and promotional activities involving the Internet. The FDA has very

broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing a company to correct deviations from regulatory standards and enforcement actions that can include seizures, fines, injunctions and criminal prosecution.

Fast track and orphan drug designation

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

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

The FDA has designated defibrotide as an orphan drug for the treatment of severe VOD and the prevention of VOD and has provided funding for clinical studies for defibrotide to treat VOD. The FDA has approved the Company's application for "fast track" designation for defibrotide to treat severe VOD occurring after stem cell transplantation by means of injection. If our other product candidates meet the criteria, we may also apply for orphan drug status and fast track status for such products.

Market Exclusivity

In addition to orphan drug exclusivity, a product regulated by the FDA as a "new drug" is potentially entitled to non-patent and/or patent exclusivity under the Federal Food, Drug and Cosmetic Act, or FFDCA, against a third party obtaining an abbreviated approval of a generic product during the exclusivity period. An abbreviated approval allows an applicant to obtain FDA approval without generating, or obtaining a right of reference to, the basic safety and effectiveness data necessary to support the initial approval of the drug product or active ingredient. In the case of a new chemical entity (an active ingredient which has not been previously approved with respect to any drug product) non-patent exclusivity precludes an applicant for abbreviated approval from submitting an abbreviated application until five years after the approval of the new chemical entity. In the case of any drug substance (active ingredient), drug product (formulation and composition) and method of use patents listed with the FDA, patent exclusivity under the FFDCA precludes FDA from granting effective approval of an abbreviated application of a generic product until the relevant patent(s) expire, unless the abbreviated applicant certifies that the relevant listed patents are invalid, not infringed or unenforceable and the NDA/patent holder does not bring an infringement action within 45 days of receipt of notification of the certification or an infringement action is brought within 45 days and a court determines that the relevant patent(s) are invalid, not infringed or unenforceable or 30 months have elapsed without a court decision of infringement.

User Fees

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

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

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

HIPAA

Other federal legislation may affect our ability to obtain certain health information in conjunction with our research activities. The Health Insurance Portability and Accountability Act of 1996, or HIPAA, mandates, among other things, the adoption of standards designed to safeguard the privacy and security of individually identifiable health information. In relevant part, the U.S. Department of Health and Human Services, or HHS, has released two rules to date mandating the use of new standards with respect to such health information. The Privacy Rule imposes new standards relating to the privacy of individually identifiable health information. These standards restrict the manner and circumstances under which covered entities may use and disclose protected health information so as to protect the privacy of that information. The second rule released by HHS establishes minimum standards for the security of electronic health information. In addition, the American Recovery and Reinvestment Act of 2009, or ARRA, imposed additional requirements for covered entities to protect individually identifiable health information. While we do not believe we are directly regulated as a covered entity under HIPAA, the HIPAA standards and requirements under ARRA impose requirements on covered entities conducting research activities regarding the use and disclosure of individually identifiable health information collected in the course of conducting the research. As a result, unless they meet these HIPAA and ARRA requirements, covered entities conducting clinical trials for us may not be able to share with us any results from clinical trials that include such health information.

Foreign Regulatory Approval

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

European Union Regulatory Approval

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

The centralized procedure

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

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

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

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

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

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

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

The decentralized procedure

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

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

Post-approval issues

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

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

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

Pediatric Investigation Plan

The pediatric investigation plan, or PIP, is a key element in the European pediatric regulations and came into effect in January 2007. The PIP is a plan for defining the use of a medicinal product across all age groups of the pediatric population and across all indications. The pediatric committee, or PDCO, is a body within EMEA responsible for overseeing the requirements of the pediatric regulation. The PDCO may grant a waiver from using a medicinal product in certain (or all) indications and/or certain (or all) pediatric age groups, and/or a deferral of the start or completion of all or some of the studies in the PIP. If a sponsor complies with a PIP agreed by PDCO, the sponsor may receive a six-month extension on patents covering the product described in the plan, or if the product has been designated an orphan drug by EMEA, an additional two years of market exclusivity, even if a pediatric indication is not approved.

European orphan drug status

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

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

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

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

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

- at the request of the sponsor;
- if it is established, before the market authorization is granted, that the requirements provided for in the European orphan drug legislation are no longer met; or
- at the end of the period of market exclusivity (as explained below).

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

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

- the holder of the marketing authorization for the orphan drug has given his consent to the second applicant;
- the holder of the marketing authorization for the orphan drug is unable to supply sufficient quantities of the latter; or
- the second applicant can establish in its application that the second medicinal product, although similar to the authorized orphan drug, is safer, more effective or otherwise clinically superior.

Raw Materials

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

The contract term of the swine intestinal mucosa supply agreement expires on December 31, 2010, with automatically renewable three year periods, unless either party notifies the other party in writing six months prior to the annual date

of termination.

The contract term of the swine duodenum supply agreement expires on December 31, 2010, with automatically renewable three year periods, unless either party notifies the other party in writing six months prior to the annual date of termination.

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

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

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

Competition

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

- controlling the manufacturing costs;
- the effectiveness and safety of products;
- the timing and scope of regulatory approvals;
- the willingness of private insurance companies and government sponsored health care programs to reimburse patients or otherwise pay for the drugs and the related treatments;
- the availability of alternative treatments for the disorders as well as the availability of alternatives to the treatments which cause or contribute to these disorders (such as chemotherapy, radiation therapy, stem cell transplants, etc.);
- the ability to perform clinical trials, independently or with others;
- intellectual property and patent rights and their protection; and
- sales and marketing capabilities.

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

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

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

Legal Proceedings

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

ORGANIZATIONAL STRUCTURE

We were 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. In 1993, FinSirton formed our company as Pharma Research S.r.L., an Italian private limited company, to pursue research and development activities of prospective pharmaceutical specialty products. FinSirton is our largest shareholder, and is controlled by Dr. Laura Ferro, our former Chief Executive Officer and President and a current member of our board of directors, together with her family. In December 2000, we changed from a private limited company to a corporation and 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 have no subsidiaries.

PROPERTY, PLANT AND EQUIPMENT

Manufacturing and Facilities

We own a manufacturing facility near Como, Italy which, at December 31, 2009, is subject to a mortgage securing repayment of an aggregate of €2.0 million of debt owed to Banca Nazionale del Lavoro. The manufacturing facility is 2,350 square meters in size. In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets their current good manufacturing practices, or GMPs, including requirements for equipment verification and validation of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but since 2004 we have spent more than €10 million for upgrades to our facility in anticipation of such an inspection.

We produce defibrotide and sulglicotide at this facility and have capability to produce sodium and calcium heparin. In 2006, we replaced a principal reactor in the defibrotide production line and separated the defibrotide production line from the sulglicotide line by installing an additional reactor. These improvements allow us to produce both defibrotide or calcium and sodium heparin and sulglicotide simultaneously and to double our potential capacity to manufacture defibrotide and sulglicotide.

We typically operate our manufacturing facility on two eight hour shifts per day. Our estimated current production, our production capacity, and percentage of utilization for defibrotide for the fiscal year 2010 are set forth below:

Product	Estimated Current Production Levels (kilograms/year)	Maximum Production Capacity With Two Eight Hour Shifts (kilograms/year)	Percentage of Utilization
Defibrotide	180	4,400	4%

Until December 31, 2008, we manufactured defibrotide to be filled and finished and sold under the trademarks Prociclide and Noravid to treat and prevent vascular disease with risk of thrombosis in Italy. We have discontinued the manufacture of defibrotide for this use; however, we will continue to manufacture defibrotide to meet future demands and for clinical trials and compassionate use purposes.

Our estimated current production, production capacity, and percentage of utilization for sulglicotide for the fiscal year 2010 are set forth below:

Product	Estimated Current Production Level (kilograms/year)	Maximum Production Capacity With Two Eight Hour Shifts (kilograms/year)	Percentage of Utilization
Sulglicotide	7,015	7,015	100%

Our estimated current production, production capacity, and percentage of utilization for urokinase for the fiscal year 2010 are set forth below:

Product	Estimated Current	Percentage of

	Production Level (millions of units/year)	Maximum Production Capacity With One Eight Hour Shift (millions of units/year)	Utilization
Urokinase	37,800	37,800	100%

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

The environmental management system was certified under the UNI EN ISO 14001 Standard on April 20, 2007 and the EMAS certification was obtained on July 26, 2007. We defined our environmental policy to be in compliance with current regulations on environmental protection, to provide for continuous improvement of our manufacturing performance, to protect our employees' health, to protect the safety of people working at our location and to respect the safety of people living close to our plant and the surrounding community.

We lease 2,350 square meters of office and laboratory space from FinSirton. In addition, we lease 100 square meters of laboratory and manufacturing space for urokinase from Sirton.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. 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 annual report. 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 annual report. These risks could cause our actual results to differ materially from any future performance suggested below.

OPERATING RESULTS

Overview

We are a biopharmaceutical company focused on the development and manufacture of our primary product candidate, defibrotide, an investigational drug based on single-stranded DNA extracted from pig intestines. Our development of defibrotide has been focused on the treatment and prevention of a disease VOD, a condition in which some of the veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation treatments, that are given prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is associated with multiple-organ failure and high rates of morbidity and mortality. We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. Defibrotide has been given orphan status by the FDA and EMEA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide has also been granted fast-track product designation by the FDA for the treatment of VOD. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approved basis under a treatment IND protocol in the U.S. and through a named-patient program throughout the rest of the world. We do not know of any FDA or EMEA approved treatments for VOD.

We are currently completing certain preclinical and clinical studies requested by regulatory authorities. As part of our overall strategy, we anticipate filing for regulatory approval for defibrotide in the U.S. and Europe by the end of our second quarter in 2011. We are also working closely on our U.S. regulatory strategy with our commercial partner, Sigma-Tau Finanziaria S.p.A. and its affiliate Sigma-Tau Pharmaceuticals, Inc., to which we have licensed our commercial rights to defibrotide for both the treatment and prevention of VOD in the Americas.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, which are subsequently used to make the finished forms of various drugs. We believe that we are the sole worldwide producer of defibrotide. In addition to defibrotide, we manufacture urokinase and sulglicotide, both of which are sold to third parties. All of the Company's operating assets are located in Italy.

Historically, we sold defibrotide as an active pharmaceutical ingredient to our affiliate, Sirton, who then filled and finished the defibrotide active pharmaceutical ingredient into ampoule and capsule forms. Sirton then sold these ampoules and capsules to Crinos S.p.A., a subsidiary of Stada Arzneimittel AG. Crinos, pursuant to a distribution agreement entered into with us, sold these products throughout Italy, under the trademarks Prociclide and Noravid, to treat and prevent vascular disease with risk of thrombosis in Italy.

In 2007, we changed our relationship with Sirton, from customer to a contract manufacturer, and sold the finished forms of Prociclide and Noravid to Crinos directly. On December 31, 2008, the distribution agreement with Crinos expired and, consistent with our overall strategy, we chose not to renew this agreement and discontinued the manufacture of defibrotide to be finished into Prociclide and Noravid. In August, 2009, the Italian Health Agency accepted the Company's request to withdraw the marketing authorization for Prociclide and Noravid but granted an extension of the marketing authorization through May 2010 in order to sell the products that were previously distributed.

In 2009 we launched a named-patient program, administered by IDIS Limited, and a cost recovery program, administered by US Oncology Clinical Development. Both of these programs are designed to provide defibrotide to patients on a pre-approval compassionate use basis. For the year ended December 31, 2009, sales of defibrotide through these programs amounted to approximately 51% of our total product sales.

In January 2010, we amended and expanded our existing license agreement with Sigma-Tau Pharmaceuticals, Inc. to include the prevention indication of defibrotide for the Americas. Following this amendment, we decided to close our New York office and consolidate our corporate activities within our headquarters in Italy.

Historically, we have also generated revenue from research and development agreements with co-development partners, 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), reimbursement of research and development expenses, and royalties from product sales in the licensed territories. Our revenues by type are as described below:

	For The Years Ended December 31,		
(in thousands)	2007	2008	2009
Product sales:			
Prociclide and Noravid	€ 2,756	€ 1,728	€ -
Urokinase	1,461	844	1,974
Sulglicotide	764	2,672	2,789
Other	113	199	35
Named-patient/cost recovery program sales	-	-	4,904
Total product sales	5,094	5,443	9,702
Other revenues	2,515	1,995	466
Total revenue	€ 7,609	€ 7,438	€ 10,168

Of our product sales in the periods shown in the table above, all were sales in Italy except for 13.5% during the year ended December 31, 2007 and 49.1% during the year ended December 31, 2008, which were primarily sales of sulglicotide in South Korea, and 85.9% for the year ended December 31, 2009, which were sales of sulglicotide in South Korea, sales of urokinase in Spain and sales of defibrotide through the named-patient and cost recovery programs. Substantially all of our other revenues is the result of a cost sharing arrangement with Sigma-Tau Pharmaceuticals, Inc., entered into in 2007, under which Sigma-Tau Pharmaceuticals, Inc. agreed to reimburse us for 50% of certain costs incurred in our Phase III clinical trial of defibrotide to treat severe VOD and milestone payments under our 2001 License and Supply Agreement entered into with Sigma-Tau Pharmaceuticals, Inc.

We expect to continue to incur net losses as we continue the development of defibrotide, apply for regulatory approvals and expand our operations. However, absent the need to fund any additional clinical trials, we believe that our cash and cash equivalents, including the upfront payment received from Sigma-Tau Pharmaceuticals, Inc. in connection with the expansion of the license for defibrotide in the Americas, together with revenues generated from our named-patient and cost recovery programs, will be sufficient to meet our obligations for at least the next twelve months. However, if we elect to increase our spending above current plans or perform additional clinical trials, we may need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all.

As of December 31, 2009, substantially all of our cash and cash equivalents were held in accounts at financial institutions located in the Republic of Italy and the United States, that we believe are of acceptable credit quality. We invest our cash in liquid instruments that meet high credit quality standards and generally mature within three months of purchase. We are exposed to exchange rate risk with respect to certain of our cash balances and accounts receivables that are denominated in U.S. dollars. As of December 31, 2009, we held a cash balance of $0.50 million, receivables of $0.96 million and payables of $1.99 million that were denominated in U.S. dollars. This dollar-based balances are available to be used for future purchases and other liquidity requirements that may be denominated in such currency. We are exposed to unfavorable and potentially volatile fluctuations of the U.S. dollar against the Euro (our functional currency).

Any increase (decrease) in the value of the U.S. dollar against the Euro will result in unrealized foreign currency remeasurement losses (gains) with respect to the Euro. The value of the Euro against the U.S. dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions. Any change in the value of the Euro relative to other currencies that we transact business with in the future could materially and adversely affect our cash flows, revenues and financial condition. To the extent we hold assets denominated in U.S. dollars, any appreciation of the Euro against the U.S. dollar could result in a non-cash charge to our operating results and a reduction in the value of our U.S. dollar denominated assets upon remeasurement.

In addition, we are exposed to foreign currency risks to the extent that we enter into transactions denominated in currencies other than our functional currency, such as investments, programming costs and accounts payable. Changes in exchange rates with respect to these items will result in unrealized or realized foreign currency transaction gains and losses upon settlement of the transactions.

We are exposed to changes in interest rates primarily as a result of our borrowings. Our primary exposure to variable rate debt is through the EURIBOR and we have entered into interest rate cap agreement to manage exposure to movements in interest rates. Interest rate cap agreements lock in a maximum interest rate should variable rates rise, but enable us to benefit from lower interest rates.

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, judgments and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ from those estimates.

We believe the following policies to be critical to understand 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

Our primary source of revenue was from the sale of products, named-patient and cost recovery programs and from collaborative arrangements. We recognize revenue from product sales when ownership of the product is transferred to and accepted by the customer, the sales price is fixed or determinable, and collectability 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. Revenues are recorded net of applicable allowance for contractual adjustments entered into with customers.

Collaborative arrangements generally contemplate that our technology or intellectual property will be utilized to commercialize or produce certain pharmaceutical products and that we will receive certain revenues pursuant to these agreements. Collaborative arrangements with multiple deliverables are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer and whether there is objective and reliable evidence of the fair value of the undelivered items. The consideration received from these arrangements is allocated among the separate units based on their respective fair value, and the applicable revenue recognition criteria are applied to each separate unit. Revenue associated with substantive at-risk milestones is recognized based upon the achievement of the milestones as defined in the respective agreements. We defer and recognize as revenue non-refundable payments received in advance that are related to the future performance over the life of the related research project. We recognize reimbursements to fund research and development efforts as the qualified expenditures are made. Finally, royalty revenues are recognized when earned when the applicable sales are made.

Inventories

Inventories consist of raw materials, semi-finished and finished active pharmaceutical ingredients and defibrotide distributed through the named-patient and treatment IND programs. 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 forecast 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.

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. We also review our inventory for quality assurance and quality control issues identified in the manufacturing process and determine if a write-down is necessary. In the context of reflecting inventory at the lower of cost or market, we will record an inventory reserve as soon as a need for such a reduction in net realizable value is determined.

Prior to commencement of selling defibrotide through the named-patient and cost recovery programs, we had expensed all costs associated with the production of defibrotide as research and development expense. Subsequent to signing the agreements associated with the named-patient and cost recovery programs, we capitalized the subsequent costs of manufacturing defibrotide as inventory, including costs to convert existing raw materials to active pharmaceutical ingredient and costs to package and label previously manufactured inventory whose costs had already been expensed as research and development expense. Until we sell the inventory for which a portion of the costs were previously expensed, the carrying value of our inventories and our cost of sales will reflect only incremental costs incurred subsequent to the signing of these agreements.

We expense costs relating to the production of clinical products as research and development expense in the period incurred, which are not expected to be sold through the named-patient and cost recovery programs and will continue to do so until we receive an approval letter from the United States Food and Drug Administration, or FDA, or European Medicines Agency, or EMEA, for a new product or product configuration. Upon receipt of an approval letter from FDA or EMEA for a new product or product configuration, we will begin to capitalize the subsequent inventory costs relating to that product configuration.

Impairment of Long-lived Assets

Our long-lived assets consist primarily of property and equipment. 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.

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 their related costs, that are included in research and development expenses. These activities include primarily salaries and benefits of our direct employees, employee stock based compensation expense, facility costs, overhead costs, clinical trial costs and related trial product manufacturing costs, contracted services and subcontractor costs. Clinical trial costs include costs associated with contract research organizations. The billings that we receive from contract research organizations for services rendered may not be received for several months following the service. 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 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. At December 31, 2009, we had €0.32 million of future payables under outstanding contracts with various contract research organizations that are not revocable. Most of these contracts are on a cost plus or actual cost basis.

Stock-Based Compensation

Employee stock-based compensation is estimated at the date of grant based on the employee stock award's fair value using the Black-Scholes option-pricing model and is recognized as expense ratably over the requisite service period, which is generally the vesting period, in a manner similar to other forms of compensation paid to employees. The Black-Scholes option-pricing model requires the use of certain subjective assumptions. The most significant of these assumptions are our estimates of the expected volatility of the market price of our stock, the expected term of the award and the expected forfeiture rate. When establishing an estimate of the expected term of an award, we consider the vesting period of the award, our recent historical experience of employee stock option exercise, the expected volatility and a comparison to relevant peer group data.

We review our assumptions periodically and, as a result, we may change our assumptions used to value share based awards granted in future periods. Such changes may lead to a significant change in the expense we recognize in connection with share based payments.

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

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

In our current valuation, we consider the volatility factor to be an important factor in determining the fair value of the options granted. We have used 60.65% factor based on what we believe is a representative sample of similar biopharmaceutical companies. However, this sample is not perfect as it omits, for example, Italian companies, due to the fact that there are a limited number of companies such as ourselves publicly traded in the U.S. market. Significant changes to these estimates could have a material impact on the results of our operations.

Recent Accounting Pronouncements

Please see Note 2 of our financial statements, “Summary of Significant Accounting Policies to our Financial Statements,” for a discussion of new accounting standards.

Results of Operations

The following tables set forth our results of operations:

	For The Years Ended December 31,		
	2007	2008	2009
Amounts in thousands except share and per share data			
Revenues:			
Product sales to related party	€ 2,704	€ 651	€ 195
Product sales to third parties	2,390	4,792	9,507
Total product sales	5,094	5,443	9,702
Other revenues	15	25	129
Other revenues from related party	2,500	1,970	337
Total Revenues	7,609	7,438	10,168
Operating costs and expenses:			
Cost of goods sold	4,584	5,596	4,002
Research and development	14,497	9,569	3,512
General and administrative	6,279	7,668	6,036
Depreciation and amortization	725	998	916
Charges from related parties	748	537	279
Write-down of assets	13,740	3,403	-
Total operating costs and expenses:	40,573	27,771	14,745
Operating loss	(32,964)	(20,333)	(4,577)
Foreign currency exchange gain/(loss), net	(4,001)	173	162
Interest income/(expense), net	1,357	256	(110)
Loss before income tax expense	(35,608)	(19,904)	(4,525)
Net loss	€ (35,608)	€ (19,904)	€ (4,525)
Net loss per share:			
Basic and diluted net loss per share	(2.52)	(1.33)	(0.30)
Weighted average shares used to compute basic and diluted net loss per share	14,105,128	14,956,263	14,956,317

Year Ended December 31, 2009 Compared to Year Ended December 31, 2008

Product sales.

Our product sales were €9.70 million for 2009 compared to €5.44 million for 2008, an increase of €4.26 million or 78.3%. The increase was primarily due to the launch in April 2009 of the named-patient program and the launch in September 2009 of the cost recovery program in the U.S. Named-patient program and cost recover program sales, for the year ended December 31, 2009 amounted to €4.90 million.

Sales to a related party, Sirton, for the year ended December 31, 2009 and 2008 represented 2% and 12% of the total product sales, respectively. The decrease in sales to a related party is primarily due to the fact that in the second quarter of 2009 we terminated our supply agreement with Sirton and entered into direct sales agreements with Sirton's customers in order to mitigate the risk associated with Sirton's poor financial condition. Additionally, after March

2008, we did not recognize product sales to a related party, unless paid in advance, amounting to €1.08 million, because one of the criteria stated by SAB 104 ("collectability is reasonably assured") was not met.

Sales to third parties increased to €9.51 million for 2009 compared to €4.79 million for 2008, an increase of €4.72 million or 98.5%. The increase was primarily due to the launch in 2009 of the named-patient and cost recovery programs, which amounted to €4.90 million in sales. Excluding such sales, sales to third parties related to the API business would have been €4.61 million and €4.79 million in 2009 and 2008, respectively, with a decrease of €0.18 million or 3.8%, primarily due to slight decrease on unit sold of sulglicotide, offset by price increase and higher volume of urokinase sold in 2009 compared to prior year.

Other revenues

Our other revenues were €0.47 million for 2009 compared to €1.99 million for 2008. The decrease versus the prior-year is primarily attributable to a decrease in activities that were reimbursed from Sigma-Tau under our cost sharing agreement, offset by a milestone payment from Sigma-Tau of €0.23 million ($0.35 million) for completion of the phase III clinical trial.

Cost of goods sold.

Our cost of goods sold was €4.00 million for 2009 compared to €5.60 million for 2008. Cost of goods sold as a percentage of product sales, was 41% in 2009 compared to 103% in 2008. The percentage decrease is primarily due to higher margin on defibrotide sold through the named-patient program and price increases in the API business. The Company fully expensed the cost of inventory in the prior year. Additionally, the higher percentage of cost of goods sold in 2008 was primarily due to the fact that product sales to a related party, Sirton, were not recognized in the amount of €1.08 million due to Sirton's poor financial condition and concerns over the ability to collect such receivables.

Research and development expenses.

We incurred research and development expenses of €3.51 million in 2009 compared to €9.57 million for 2008. Research and development expenses in 2009 and 2008 are net of €0.85 and €0.79 million, respectively, of government grants in the form of a tax credit. The reduction from the prior year is a result of a decrease in the activities related to the treatment and prevention studies.

General and administrative expenses.

Our general and administrative expenses were €6.04 million in 2009 compared to €7.67 million in 2008. In 2008, we established a reserve for doubtful accounts in the ammount of €1.78 million, of which €0.68 was releasedin 2009. Additionally, the Company had lower payroll costs due to the temporary layoffs under a special public fund used in Italy under the “Cassa Integrazione Guadagni” program.

Depreciation and amortization expense.

Depreciation and amortization expense was €0.92 million in 2009 compared to €1.00 million in 2008. Depreciation expense excludes depreciation of our manufacturing facilities included in our cost of goods sold.

Foreign currency exchange gain (loss), net

Our foreign currency exchange gain (loss) is primarily due to remeasurement at December 31, 2009 of U.S. dollar cash balances. The positive result between 2008 and 2009 is due to a more favorable exchange rate in 2009 and a lower cash balance.

Interest income/(expense), net.

Interest income /(expense), net amounted to €(0.11) million and €0.26 million in 2009 and 2008, respectively. The decrease in interest income /(expense), net is a result of a lower amounts of invested funds in 2009 compared to the prior period as well as a decrease in interest rates.

Net loss.

Our net loss was €4.53 million in 2009 compared to €19.90 million in 2008. The difference was primarily due to net sales generated with the launch of the named-patient program, decrease in general and administrative expense, research and development expense, and higher margin on products sold through the named-patient program.

Year Ended December 31, 2008 Compared to Year Ended December 31, 2007

Product sale.

Our product sales were €5.44 million for 2008 compared to €5.09 million for 2007, an increase of €0.35 million or 7%. The increase was primarily due to an increase in demand for our products from our customers. Sales to a related party, Sirton, for the year ended December 31, 2007 and 2008 represented 53% and 12% of the total product sales, respectively. The decrease in sales to a related party is primarily due to the fact that we did not recognize product sales to a related party for sale transactions consummated after March 2008, amounting to €1.08 million, because one of the criteria stated by SAB 104 ("collectability is reasonably assured") was not met. In addition, in contemplation of the expiration of our distribution agreement with Crinos, we stopped selling Prociclide and Noravid as a finished product to Crinos during the three month period ended December 31, 2008. Sales to third parties increased to €4.79 million for the year ended December 31, 2008 due to higher sales volume of sulglicotide. Sulglicotide is used by a South Korean manufacturer to produce a finished product.

Other revenues

Our other revenues were €1.99 million for 2008 compared to €2.51 million for 2007. Fluctuation versus the prior-year period is primarily due to timing on the recognition of reimbursement from Sigma Tau, under a cost sharing arrangement entered into during the third quarter of 2007, of certain costs incurred in our ongoing phase III clinical trial of defibrotide to treat severe VOD.

Cost of goods sold.

Our cost of goods sold was €5.60 million for 2008 compared to €4.58 million in 2007. Cost of goods sold as a percentage of product sales was 103% in 2008 compared to 90% in 2007. The decrease in gross margin was primarily due to the non-recognition of product sales to a related party, Sirton, for sale transactions consummated after March 2008. The Company did not recognize product sales due to Sirton's poor financial condition, which caused concerns over the collectability of such receivables.

If we would have recognized such revenue, cost of goods sold as a percentage of product sales would have been 86% for 2008 compared to 90% for 2007. The increase in gross margin would have been primarily due to change in product mix.

Research and development expenses.

We incurred research and development expenses of €9.57 million in 2008 compared to €14.50 million for 2007. Research and development expenses are net of €0.79 million government grants accrued as a reduction of expense. Excluding such grants, research and development expense would have been €10.36 million and €14.50 million in 2008 and 2007, respectively. Research and development expenses were primarily for the development of Defibrotide to treat and prevent VOD. The decrease from the comparable period in 2007 is the timing of performance of clinical research organizations and regulatory activities. Also contributing to the research and development expenses was stock based compensation of €0.38 million in 2008 compared to €0.44 million in 2007.

General and administrative expenses.

Our general and administrative expenses were €7.67 million in 2008 compared to €6.28 million in 2007. The 2008 general and administrative expenses reflect the establishment of an allowance for doubtful accounts of €1.78 million. General and administrative expenses include general corporate expenses, legal and other professional fees and stock based compensation expense of €1.50 million in 2008 compared to €1.36 million in 2007.

Depreciation and amortization expense.

Depreciation and amortization expense was €1.00 million in 2008 compared to €0.73 million in 2007. Depreciation expense excludes depreciation of our manufacturing facilities included in our cost of goods sold.

Write-down of assets

We recorded an impairment of €3.40 million in 2008 compared to €13.74 million in 2007. Write-down of assets include the write-down of acquired trademarks for Prociclide and Noravid (both forms of defibrotide), the Italian marketing authorizations for Prociclide and Noravid, inventory, and the Company's patents. The trademarks and marketing authorizations for Prociclide and Noravid have been written-down due to the expiration and non-renewal by the Company of the distribution agreement with Crinos S.p.A., which distributed Prociclide and Noravid in Italy to treat and prevent vascular disease with risk of thrombosis. Because the Company has decided to discontinue the distribution of Prociclide and Noravid, doubt has been raised concerning the recoverability of future cash flows expected to be derived from these assets. Therefore, the Company has impaired €1.70 million of the remaining net book value of the trademarks and Italian marketing authorizations for Prociclide and Noravid. In addition, the Company wrote down €1.23 million of the remaining book value of semi-finished and finished Prociclide and Noravid in our inventory, including such products expected to be returned by Crinos, as these products are no longer saleable. At December 31, 2008, we wrote down the remaining carrying value of the Company's patents amounting to €0.48 million, because there was no expected future cash flows to support the amounts to be derived over the remaining useful life of the patents.

Foreign currency exchange gain (loss), net

Our foreign currency exchange gain (loss) is primarily due to remeasurement at December 31, 2008 of U.S. dollar cash balances. The positive result between 2007 and 2008 is due to a more favorable exchange rate in 2008 and a lower cash balance in 2008 versus 2007.

Interest income, net.

Interest income, net amounted to €0.26 million and €1.36 million in 2008 and 2007, respectively. Gross interest income amounted to €0.59 million and €1.67 million in 2008 and 2007, respectively, a decrease of €1.08 million. The decrease is a result of a lower amount of invested funds in the 2008 period and decrease in interest rates. Interest expense totaled €0.33 million and €0.32 million in 2008 and 2007, respectively, an increase of €0.01 million attributable to an fluctuation in interest rate.

Net loss.

Our net loss was €19.90 million in 2008 compared to €35.61 million in 2007. The difference was primarily due to the write-down of assets acquired from Crinos amounting to €13.74 million, foreign exchange gain and lower research and development expenses, offset by an increase in general and administrative expenses due to the allowance for doubtful accounts of €1.78 million.

LIQUIDITY AND CAPITAL RESOURCES

During 2007, we used approximately €14.2 million of cash to fund operations and working capital requirements, €0.81 to reimburse current portions of long term debts and capital lease obligations, and approximately €7.1 million for capital expenditures and acquisition of intangible assets, including €8 million paid to Crinos. We funded these amounts from the following sources:

- €7.6 million in gross revenues;
- $47.5 million in gross proceeds from a private placement of 2,354,000 ordinary shares;
- $8.4 million in gross proceeds from the exercise of warrants and stock options;
- €279 thousand in short term borrowing; and
- €10.2 million from cash available at December 31, 2006.

During 2008, we used approximately €12.78 million of cash to fund operations and working capital requirements, €1.60 to reimburse current portion of long term debts, short term borrowings and capital lease obligations, and approximately €0.59 million for capital expenditures. We funded these amounts from the following sources:

- €7.44 million in gross revenues;
- €147 proceeds from long term debt, and
- €25.96 million from cash available at December 31, 2007.

During 2009, we used approximately €5.16 million of cash to fund operations and working capital requirements, €1.17 to reimburse current portion of long term debts and capital lease obligations, and approximately €4.25 million for

capital expenditures, including €4 million paid to Crinos. We funded these amounts from the following sources:

- €9.70 million in gross revenues;
- €0.26 million in sales of marketable securities; and
- €11.49 million from cash available at December 31, 2008.

At December 31, 2009, we had an aggregate of €3.51 million in debt outstanding and had €1.39 million in cash and cash equivalents. In connection with the closure of our New York office, we will be using approximately €1.51 ($1.71) million of cash, which will be funded by cash available and approximately €5.11 ($7.00) million from the upfront payment received in connection with the amendment and expansion of the license agreement with Sigma-Tau Pharmaceuticals, Inc. Additional information about the maturity and repayment obligations for this debt and interest rate structure and our material commitments for capital expenditures is provided below under "Contractual Obligations and Commitments."

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

- the scope and results of our clinical trials;
- whether we are able to commercialize and sell defibrotide for the uses for which we are developing it;
- advancement of other product candidates in development;
- the timing of, and the costs involved in, obtaining regulatory approvals;
- the cost of manufacturing activities;
- the costs associated with building a future commercial infrastructure;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims and other patent-related costs, including litigation costs and results of such litigation; and
- our ability to establish and maintain additional collaborative arrangements.

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

- our ability to obtain FDA and European regulatory marketing approval for and to commercially launch defibrotide to treat severe VOD;
- the receptivity of the capital markets to financings, generally, and of biotechnology companies, specifically; and
- our ability to enter into additional collaborative arrangements with corporate and academic collaborators and the success of such relationships.

Through December 31, 2009, the Company had accumulated losses of approximately €100 million. However, absent the need to fund any additional clinical trials, management believes that the Company's cash and cash equivalents, including the upfront payment received from Sigma-Tau Pharmaceuticals, Inc. in connection with the expansion of the license agreement for defibrotide in the Americas, together with revenues generated from the Company's named-patient and cost recovery programs, will be sufficient to meet the Company's obligations for at least the next twelve months. If the Company elects to increase its spending above current plans or perform additional clinical trials, it may need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to the Company on favorable terms, if at all.

Italian law provides for limits and restrictions on our issuance of debt securities, described in our risk factor entitled, "We are restricted under Italian law as to the amount of debt securities that we may issue relative to our equity." In order to issue new equity or debt securities convertible into equity, with some exceptions, we must increase our authorized capital through a process described in our risk factor entitled, "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."

RESEARCH AND DEVELOPMENT

We discover, research and conduct initial development of our product candidates at our facilities in Italy, and also hire consultants to do so in various countries in Europe and the United States. We typically conduct preclinical laboratory and animal studies of product candidates either ourselves or through other research facilities. We typically engage medical centers to conduct clinical trials of our product candidates. In certain cases, where we believe the development costs will be substantial, we may enter into collaborative arrangements to help us develop those product candidates. We expense research and development costs as incurred.

Research and Development Expenses

Our research and development expenses consist primarily of costs associated with research, preclinical development contract research organization charges, regulatory activities, laboratory supplies and materials, manufacturing costs, contracted services and clinical trials for our product candidates. During the years ended December 31, 2007, 2008 and 2009, we had three major categories of research projects relating to 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, 2007, 2008 and 2009.

	For The Years Ended December 31,		
(in thousands)	2007	2008	2009
Defibrotide to treat VOD	€ 11,035	€ 7,131	€ 641
Defibrotide to prevent VOD	869	1,055	2,102
Others	2,593	1,383	769
Total	€ 14,497	€ 9,569	€ 3,512

We expect to continue to incur expenses for the development of defibrotide to treat and prevent VOD. We will need additional funds before we have completed the development of defibrotide to treat and prevent VOD. A further discussion of the risks and uncertainties associated with developing defibrotide 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.

Intellectual Property Rights And Patents

As of December 31, 2009, we had nine issued U.S. patents, eight pending U.S. patent applications, 26 issued foreign patents, 46 pending foreign patent applications and one international patent application (not nationalized yet). These include the following. The United States Patent & Trademark Office issued a patent covering our manufacturing process of defibrotide in 1991, which expired on January 15, 2008. In April 2001, we filed a patent application with the United States Patent & Trademark Office and corresponding patent applications in certain foreign countries regarding the use of defibrotide in stem cell transplants, which expires in 2021.

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

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

expire or remain in force for only a short period following commercialization.

OFF-BALANCE SHEET ARRANGEMENTS

We do not have any off-balance sheet arrangements.

TABULAR DISCLOSURE OF CONTRACTUAL OBLIGATIONS

Contractual Obligations and Commitments

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

The following table summarizes our long-term commitments as of December 31, 2009.

(in thousands)	Total	1 Year	2 Years	3 Years	4 Years	5 Years	More than 5 Years
Long-Term Debt Obligations:							
Mortgage loans	€ 1,800	€ 400	€ 400	€ 400	€ 400	€ 200	€ -
Finance loans	375	250	125	-	-	-	-
Equipment loans	706	415	291	-	-	-	-
Research loan	217	166	51	-	-	-	-
	€ 3,098	€ 1,231	€ 867	€ 400	€ 400	€ 200	€ -
Operating leases	47	16	16	15	-	-	-
Capital lease obligation	91	70	21	-	-	-	-
Research and Development Programs	323	323	-	-	-		
Total	€ 3,559	€ 1,640	€ 904	€ 415	€ 400	€ 200	€ -

We received various loans from the Minister for University and Research granted through San Paolo-IMI Bank (now Intesa SanPaolo) in September 2000 and December 2008. The loans are for financing research and development of defibrotide to treat and prevent VOD and bears interest at 1.0% per annum. We will need to repay the first loan in installments every six months beginning six months after the completion of the related research and development, but no later than January 2012. At December 31, 2009, the amount outstanding under this loan was €145 thousand. We will need to repay the second loan in seven installments due every six months, beginning January 2009. At December 31, 2009, the amount outstanding under this loan was €85 thousand.

On July 9, 2004, we obtained a loan in the approximate amount of €487 thousand from Cassa di Risparmio di Parma e Piacenza. The loan was obtained pursuant to Law No. 1329 of 28 November 1965 (Legge Sabatini), a law that facilitates the purchase and the lease of new production equipment. The loan is secured by a lien on our equipment and machinery. On August 4, 2004, we obtained an additional loan in the amount of €388 thousand from Cassa di Risparmio di Parma e Piacenza under the same terms and conditions. At December 31, 2009, these loans were fully reimbursed.

On April 20, 2006, we obtained a five year financing facility from Banca Intesa Mediocredito S.p.A. of up to €1 million to finance our purchase and installation of two reactors in our manufacturing facility. The financing has a five-year term and bears interest at the three-month Euribor rate plus 1.7%. It is secured by Banca Intesa debt securities in the aggregate amount of €263 thousand that we purchased and which expire on May 10, 2011. We make installment payments on the facility of €131 thousand every six months until its final maturity in April 2011. In December 2009, Banca Intesa Mediocredito S.p.A agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2012. At December 31, 2009, the aggregate amount outstanding under this facility was €394 thousand.

On June 14, 2006, we obtained a loan in the amount of €2,800 thousand from Banca Nazionale Del Lavoro S.p.A. The loan is secured by a mortgage on certain of our land and buildings. It bears interest at the six-month Euribor rate plus 1.00%, the principal of which will be repaid in 14 installments, every six months, starting from December 27, 2007 until final maturity in 2014 and the interest on which will be paid every six months starting from June 27, 2006. In December 2009, Banca Nazionale Del Lavoro S.p.A. agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2015. At December 31, 2009, the principal amount outstanding under this loan was €2,000 thousand.

On June 30, 2006, we obtained a loan in the amount of €750 thousand from San Paolo IMI S.p.A (now Banca Intesasanpaolo S.p.A.). for the acquisition and installation of manufacturing equipment. The loan bears interest at the three month Euribor rate plus 1.20%. Beginning on June 15, 2008, the rate will be decreased to 1.02% over the Euribor rate. The loan is payable in thirteen quarterly installments of approximately €58 beginning on June 15, 2008 through June 15, 2011. Interest is due quarterly beginning on September 15, 2006. The agreement requires us to maintain a minimum level of net shareholders' equity determined in accordance with Italian generally accepted accounting principles. The Company was in compliance with this provision of the agreement at December 31, 2009. In December 2009, San Paolo IMI S.p.A agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2012. At December 31, 2009, the amount outstanding under this loan was €437 thousand.

On December 20, 2006 we obtained three loans from Banca Intesa S.p.A (now Banca Intesasanpaolo S.p.A.).

The first of these loans is in the amount of €230 thousand for a term of 60 months, maturing on December 31, 2011. Principal and interest are due in 20 quarterly installments beginning on March 31, 2007. It bears interest at the three-month Euribor rate plus 1%. In December 2009, Banca Intesa S.p.A agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2012. At December 31, 2009, the amount outstanding under this loan was €110 thousand.

The second loan is in the amount of €500 thousand for a term of 60 months, maturing on December 31, 2011. Principal and interest are due in 60 monthly installments beginning on January 31, 2006. It bears interest at the three-month Euribor rate plus 1%. In December 2009, Banca Intesa S.p.A agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2012. At December 31, 2009, the amount outstanding under this loan was €222 thousand.

The third loan is in the amount of €225 thousand for a term of 57 months (after a technical pre-amortization period from December 20, 2006 to March 15, 2007) maturing on December 15, 2011. It must be used within six months for investments in the innovation of products and/or production processes or to buy manufacturing equipment. Principal and interest payments are due in quarterly installments starting on June 15, 2007. It bears interest at the three-month Euribor rate plus 0.8%. In December 2009, Banca Intesa S.p.A agreed to defer payment of principal due for 12 months, extending the original term of the loan to 2012. At December 31, 2009, the amount outstanding under this loan was €113 thousand.

Our commitments for clinical research consist of fixed price contracts with third-party research organizations related to clinical trials for the development of defibrotide and related consulting services for advice regarding FDA issues.

In connection with our purchase of the Italian marketing rights to defibrotide and related trademarks from Crinos, we paid Crinos €4 million in 2006, placed another €4 million in escrow, which was released to Crinos in April 2007, paid Crinos an additional installment of €4 million in December 2007, and paid Crinos a final installment of €4 million in January 2009.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

DIRECTORS AND SENIOR MANAGEMENT

Set forth below is the name, birth date, position and a brief account of the business experience of each of our executive officers, significant employees and directors as of March 31, 2010.

Name	Age	Position
Dr. Khalid Islam (1)	54	President and Chief Executive Officer
Gary Gemignani (2)	44	Executive Vice-President and Chief Financial Officer
Dr. Massimo Iacobelli	50	Senior Vice-President, Scientific Director
Salvatore Calabrese	40	Senior Vice-President, Finance
Gigliola Bertoglio (3)	75	Director
Marco Codella	50	Director
Dr. Glenn Cooper (4)	57	Director
Dr. Laura Ferro (1)	59	Director
Dr. Bobby W. Sandage, Jr. (5)	56	Director

(1) Member of the scientific oversight committee.

(2) Will be leaving as of March 31, 2010 in connection with our previously disclosed closure of our New York office.

(3) Member of the audit committee (chairperson), nominating and corporate governance committee and compensation committee.

(4) Member of the compensation committee (chairperson), nominating and corporate governance committee (chairperson) and audit committee.

(5) Member of the scientific oversight committee (chairperson) and audit committee.

Dr. Khalid Islam has served as our Chairman of our Board of Directors since December 2009 and our Chief Executive Officer since November 2009. Dr. Islam is the founder and current Chairman of Ki Consulting AG, a consulting firm specializing in the development of pharmaceutical drugs. Dr. Islam is also the co-founder of Sirius Healthcare Partners, an advisory firm for mid-cap and small-cap life science companies. From July 1999 until May 2008, Dr. Islam was the President and Chief Executive Officer for Arpida AG, a Swiss biopharmaceutical company that focuses on novel products for the treatment of microbial infections. Prior to that, Dr. Islam worked as an Alliance Manager for Hoechts Marion Roussel, a global pharmaceutical company, where he assisted with drug discovery and development. Dr. Islam has extensive experience working on behalf of pharmaceutical companies with both the United States Food and Drug Administration (FDA) and European Medicines Agency (EMEA) and has been involved with the development and marketing of several pharmaceutical products. Dr. Islam has previously served as a member of the Board of Directors for Arpida AG, Rheoscience A/S, and Arpida Inc. Dr. Islam received a B.S. in Biochemistry from Chelsea College, University of London, in 1977 and his Ph.D. from Imperial College, University of London, in 1983.

Gary G. Gemignani has served as our Executive Vice-President and Chief Financial Officer since June 2006. From 2004 to 2005, Mr. Gemignani was the Vice President and Controller for the US Pharmaceuticals Division of Novartis AG, a pharmaceutical and consumer health company. From 1998 to 2004, he held a variety of vice-president level positions for Prudential Financial Inc., a financial products and services provider. From 1993 to 1998, Mr. Gemignani

held a variety of senior financial positions at Wyeth, a pharmaceutical, consumer healthcare and animal health company. From 1986 to 1993, he was an employee of Arthur Andersen & Co. Mr. Gemignani received a bachelor of science in accounting from St. Peter's College.

Dr. Massimo Iacobelli has served as our Senior Vice-President, Scientific Director since 2002 and as our Vice President, Clinical Development and Chief Medical Office from 1995 to 2002. From 1990 to 1994, he was the Senior Vice-President, Medical Marketing, at Sirton. From 1988 to 1989, Dr. Iacobelli directed the Drug Safety Department at Bayer S.p.A. He received a medical degree from Università degli Studi, Napoli, Italy.

Salvatore Calabrese has served as our Senior Vice-President of Finance since February 2010 and our Vice-President of Finance since February 2005. From December 2003 until February 2005, he was an Accounting and Finance Manager for Novuspharma, S.p.A., a development stage biopharmaceutical company focused on the discovery and development of cancer drugs and a subsidiary of Cell Therapeutics, Inc., a public reporting company, which then merged into Cell Therapeutics, Inc. He reported to the Chief Financial Officer of Cell Therapeutics, Inc. and was responsible for cost containment, budgeting, financial reporting and the implementation of Sarbanes-Oxley compliance. From September 1996 until November 2003, Mr. Calabrese was employed by PricewaterhouseCoopers as an accountant and was a Manager in Assurance Business Advisory Services at the time of departure. From October 2000 to June 2003, Mr. Calabrese worked in the Boston, MA office of PricewaterhouseCoopers. He earned a Bachelors' Degree in Economics at the University of Messina and a Masters' Degree in Accounting, Audit and Financial Control at the University of Pavia. He is also a chartered accountant in the Republic of Italy.

Gigliola Bertoglio has served as one of our directors from December 2004. Following the termination of our board of directors in August 2009, Ms. Bertoglio was re-elected to our board of directors on October 15, 2009. Ms. Bertoglio has been a partner of Audirevi S.r.l., an Italian registered public accounting firm, since January 2005 and was a self-employed consultant during 2004. From 1970 through 2003 she was employed by Reconta Ernst & Young (the Italian affiliate of Ernst & Young LLP) and its predecessors and was an audit partner beginning in 1977. From 1998 until leaving the firm, she was responsible for the firm's Capital Market Group in Italy. From 1989 to 1998, she was responsible for directing the firm's Professional Standards Group, a member of the Accounting and Auditing Standards Group of Ernst & Young International and a coordinating audit partner for clients with international operations. From 1977 to 1989, Ms. Bertoglio was a partner of the Italian firm of Arthur Young & Co. (the predecessor to Ernst & Young) where she was responsible for directing the firm's Professional Standards Group, served in an advisory role to the Accounting and Auditing Standards Group of Arthur Young International and was a coordinating audit partner for clients with international operations. From 1970 to 1977, she was an Audit Manager (1970 to 1974) and an Audit Principal (1975 to 1977) with the Italian firm of Arthur Young & Co. in its Rome and Milan offices. Prior to 1970, Ms. Bertoglio was employed in the New York offices of Horwath & Horwath and LKH&H, both of which were public accounting firms. She earned a degree in Public Accounting from New York University and a Diploma in Accounting from Economics Institution in Biella, Italy. She is a Certified Public Accountant (active license to August 31, 2002, inactive after that) in the United States and included in the Register of Authorized Auditors of Consob, the Italian Stock Exchange's regulatory agency for public companies.

Marco Codella has served as one of our directors from June 2005. Following the termination of our board of directors in August 2009, Mr. Codella was re-elected to our board of directors on October 15, 2009. Mr. Codella has been the Chief Financial Officer of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., an international family of pharmaceutical companies, since May 1999 and he has been Chief Financial Officer of Sigma-Tau Finanziaria S.p.A. since July 2008. Mr. Codella was a professor of Economics and Management Accounting at University of Rome, La Sapienza from 2001 to 2007. From 1997 to 1999, Mr. Codella was the Finance, IT and Logistics Director of Crown Cork & Seal Italy S.p.A., an Italian subsidiary of Crown Holdings, Inc., a manufacturer of packaging products to consumer marketing companies. From 1994 to 1997, Mr. Codella was the Finance and IT Director of Crown Cork & Seal Italy S.p.A. From 1990 to 1994, Mr. Codella held various finance positions at Digital Equipment Italia S.p.A., an Italian subsidiary of Digital Equipment Corporation, a computer company. From 1987 to 1990, Mr. Codella was the Finance Manager of an Italian subsidiary of Ampex Corporation, a provider of technology for acquisition, storage and processing of visual information. From 1984 to 1987, Mr. Codella was an auditor at Deloitte, Haskins & Sells, an accounting firm. Mr. Codella is a director of Sigma-Tau Finanziaria S.p.A. He is also a Director of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Biosint S.p.A., Tecnogen S.p.A., Sigma-Tau Healthscience LLC, Sigma-Tau India, Sigma-Tau BV, and Sigma-Tau Healthscience International BV, each of which is a subsidiary of Sigma-Tau Finanziaria S.p.A. Mr. Codella is an Italian certified public accountant. Mr. Codella graduated summa cum laude from Rome University in 1984 with a degree in economics.

Dr. Glenn Cooper has served as one of our directors since October 2009. Dr. Cooper served as Chairman and Chief Executive Officer of Nasdaq-listed Indevus Pharmaceutical, a specialty pharmaceutical company focused on urology and endocrinology, from 1993 until 2009 when Indevus Pharmaceutical was acquired by Endo Pharmaceuticals. Prior to joining Indevus in 1993, Dr. Cooper held numerous executive level positions, including President and Chief Executive Officer of Progenitor, Inc., Executive Vice President and Chief Operating Officer of Sphinx Pharmaceuticals Corporation, and various clinical and regulatory positions with NYSE-listed Eli Lilly and Company. Dr. Cooper has participated in the development and commercialization of numerous drugs, including Prozac®, Axid®, Lorabid®, Ceclor®, SANCTURA®, SANCTURA XR®, Supprelin-LA®, and Vantas®. Dr. Cooper is currently a member of the Board of Directors of Repligen Corporation, listed on Nasdaq. Dr. Cooper received an M.D. from Tufts University School of Medicine, performed his postdoctoral training in Internal Medicine and Infectious Diseases at the New England Deaconess Hospital and the Massachusetts General Hospital and received a B.A. from Harvard University.

Dr. Laura Ferro is our former President and Chief Executive Officer and has served as one of our directors from 1991. Following the termination of our board of directors in August 2009, Dr. Ferro was re-elected to our board of directors on October 15, 2009. Dr. Ferro is the former President and Chief Executive Officer of our largest shareholder, FinSirton. From 1991 to 2010, Dr. Ferro also held various positions at Sirton Pharmaceuticals S.p.A., a subsidiary of FinSirton that specializes in manufacturing pharmaceutical products. Prior to that, Dr. Ferro was a practicing physician for 15 years. Dr. Ferro is a member of the executive committee of Farmindustria, an Italian pharmaceutical industry group. She is also the President of the Gianfranco Ferro Foundation, a not-for-profit Italian organization with the mission of stimulating research, education and dissemination of information on the correct use of medications and adverse effects of medicines. Dr. Ferro received her M.D. and Ph.D. degrees from the University of Milan, and a MBA from Bocconi University in Milan in 1994. Dr. Ferro is a licensed physician. She was certified in psychiatry at the University of Milan in 1981 and in Clinical Pharmacology at the University of Milan in 1994.

Dr. Bobby W. Sandage, Jr. has served as one of our directors since October 2009. From 1991, and until Indevus Pharmaceuticals was acquired by Endo Pharmaceuticals in 2009, Dr. Sandage held various positions at Indevus Pharmaceuticals, including as Executive Vice President of Research and Development and Chief Scientific Officer. Following the acquisition of Indevus Pharmaceuticals, Dr. Sandage served as the Executive Vice President for Endo Pharmaceuticals, a pharmaceutical company listed on Nasdaq that is engaged in the research, development, sale and marketing analgesic products and products to treat various urological and endocrinological conditions. Prior to joining Indevus Pharmaceuticals, Dr. Sandage held senior drug development positions DuPont Merck Pharmaceutical Company, DuPont Critical Care (formerly American Critical Care) and Merrell Dow Pharmaceuticals. Dr. Sandage is currently a member of the Board of Directors of Osteologix Inc., a public pharmaceutical company that focuses on the treatment and prevention of diseases of bone and joint tissue. He has also served as a member of the Board of Directors of Genta, Inc., also a public company. Dr. Sandage has a B.S. in Pharmacy from the University of Arkansas and Ph.D. in Clinical Pharmacy from Purdue University.

All of our directors' terms expire at the date of our ordinary shareholders' meeting approving our 2009 Italian GAAP financial statements, which will be held on April 26, 2010 (first call) and, if necessary, April 30, 2010 (second call). All of our current directors have been nominated for re-election.

COMPENSATION

Compensation of Directors and Executive Officers

For the year ended December 31, 2007, the aggregate cash compensation to our executive officers and directors as a group was approximately €1.29 million. For the year ended December 31, 2008, the cash compensation to our executive officers and directors were €0.90 million and €0.47 million, respectively. For the year ended December 31, 2009, the cash compensation to our executive officers and directors were €1.18 million and €0.30 million, respectively. During the year ended December 31, 2007, we granted options to purchase an aggregate amount of 429,000 ordinary shares to executive officers and directors at exercise prices ranging from $16.52 to $18.95 that terminate on dates ranging from March 26, 2017 to November 9, 2017. During the year ended December 31, 2008, we granted options to purchase an aggregate of 220,648 ordinary shares to executive officers and directors at exercise prices ranging from $5.20 to $13.98 that terminate on dates ranging from January 2, 2018 to May 9, 2018. We did not grant any options during the year ended December 31, 2009.

Share-Based Compensation Plans

2004 Equity Incentive Plan

Our board of directors proposed a capital increase for our 2004 Equity Incentive Plan to our shareholders on September 2, 2004. Our shareholders approved that capital increase on September 30, 2004. Our board of directors approved the specific terms of our 2004 Equity Incentive Plan effective as of September 30, 2004. Our shareholders approved the specific terms of our 2004 Equity Incentive plan on April 28, 2005. On July 31, 2006, our board of directors approved an amended and restated version of our 2004 Equity Incentive Plan to reflect minor revisions, including an Italian law requirement that all shares issued under the plan be paid for in cash in at least an amount equal to €4.50 per share, which was the net worth of our company at the time of the capital increase relating to the plan. On March 26, 2007, our board of directors approved an amendment to the Amended and Restated 2004 Equity Incentive Plan, extending the term of the plan to 2019. Our shareholders approved this amendment on April 27, 2007.

The incentive plan authorizes 1,500,000 ordinary shares for issuance. The maximum number of shares that may be issued under the incentive plan subject to incentive share options is 1,500,000. At December 31, 2009, there were 1,355,000 shares underlying outstanding options, with a weighted average exercise price of $12.18. Shares subject to share awards that have expired or otherwise terminated without having been exercised in full again become available

for the grant of awards under the incentive plan. In the event of a share split or other alteration in our capital structure, without the receipt of consideration, appropriate adjustments will be made to outstanding awards to prevent dilution or enlargement of participant's rights. The plan is governed by Italian law.

Our incentive plan provides for the grant of incentive share options (as defined in Section 422 of the U.S. Internal Revenue Code) to employees, including officers and employee-directors, and nonstatutory share options, restricted share purchase rights, restricted share unit awards, share appreciation rights and share bonuses to employees, including our officers, directors and consultants who are subject to tax in the United States. The incentive plan also provides for the periodic automatic grant of nonstatutory share options to our non-employee directors.

The incentive plan is administered by our board of directors or a committee appointed by our board of directors. The board or the committee determines recipients and types of awards to be granted, including the number of shares subject to an award, the vesting schedule of awards, the exercisability of awards, and subject to applicable restrictions, other terms of awards. The board of directors has delegated administration of the incentive plan to the compensation committee.

The term of share options granted under the incentive plan generally may not exceed ten years, although the capital increase relating to the ordinary shares issuable upon exercise of such options expires on September 30, 2019. Our compensation committee determines the price of share options granted under the incentive plan, provided that the exercise price for an incentive share option cannot be less than 100% of the fair market value of our ordinary shares on the date of grant. No incentive share option may be granted to any person who, at the time of the grant, owns (or is deemed to own) ordinary shares possessing more than 10% of our total voting ordinary shares, unless the option exercise price is at least 110% of the fair market value of the ordinary shares on the date of grant and the term of the incentive share option does not exceed five years from the date of grant. The exercise price for a nonstatutory share option can vary in accordance with a predetermined formula while the option is outstanding. In addition, the aggregate fair market value, determined at the time of grant, of the ordinary shares with respect to which an incentive share option first becomes exercisable during any calendar year (under the incentive plan and all of our other equity compensation plans) may not exceed $100 thousand.

Options granted under the incentive plan vest at the rate determined by our compensation committee. Typically, options granted under the incentive plan vest over three years, with one-third of the shares covered by the option vesting on the first anniversary of the grant date and the remainder vesting monthly over the next two years.

Generally, the optionee may not transfer a share option other than by will or the laws of descent and distribution unless the optionee holds a nonstatutory share option that provides otherwise. However, an optionee may designate a beneficiary who may exercise the option following the optionee's death. An optionee whose service relationship with us ceases for any reason may exercise the option to the extent it was vested for the term provided in the share option agreement. Options generally expire three months after the termination of an optionee's service. However, if an optionee is permanently disabled or dies during his or her service, that person's options generally may be exercised up to 12 months following disability or death.

Share appreciation rights granted under our incentive plan may be paid in our ordinary shares, cash or a combination of the two, as determined by our board of directors. The grant of a share appreciation right may be granted subject to a vesting schedule determined by our board of directors.

Restricted share purchase rights granted under the incentive plan may be granted pursuant to a repurchase option in our favor that will lapse in accordance with a vesting schedule and at a price determined by the board of directors (or a committee appointed by the board of directors). Rights under a share bonus or a restricted share purchase award are transferable only upon such terms and conditions as are set forth in the relevant agreement, as determined by the board of directors (or the committee appointed by the board of directors) in its sole discretion.

When we become subject to Section 162(m) of the Internal Revenue Code which denies a deduction to publicly held companies for certain compensation paid to specified employees in a taxable year to the extent the compensation exceeds $1.0 million, no person may be granted share options and/or share appreciation rights under the incentive plan covering more than 500,000 ordinary shares in any fiscal year. In addition, no person may be granted restricted share purchase rights, share units and/or share bonuses under the incentive plan covering more than 250,000 ordinary shares in any fiscal year. However, in connection with a participant's first year of employment, such participant may be granted options and/or share appreciation rights covering up to 600,000 ordinary shares and restricted share purchase rights, share units and/or share bonuses covering up to 500,000 ordinary shares.

In the event of certain corporate transactions (including, but not limited to, a sale or other disposition of all or substantially all of our assets, a merger or a consolidation), all outstanding awards under the incentive plan will be subject to the terms and conditions of the agreement memorializing the transaction. The agreement may provide for the assumption or substitution of awards by any surviving entity, the acceleration of vesting (and exercisability, if applicable) or the cancellation of awards with or without consideration. In addition, at the time of grant, our board of directors may provide for acceleration of vesting in the event of a change in control. In the event of a change in control, non-employee director options outstanding under the incentive plan will automatically become vested and will terminate if not exercised prior to such a change in control.

The board of directors may amend the incentive plan at any time. Amendments will be submitted for shareholder approval to the extent required by applicable laws, rules and regulations. The incentive plan will terminate on September 30, 2019 unless sooner terminated by the board of directors or a committee appointed by the board of directors.

2004 Italy Stock Award Sub-Plan

Our Amended and Restated 2004 Italy Stock Award Sub-Plan is a part of our Amended and Restated 2004 Equity Incentive Plan and provides for the grant of share options and the issuance of share grants to certain of our employees who reside in the Republic of Italy and who are liable for income tax in the Republic of Italy. Generally, the exercise price for a share option under the Italy sub-plan cannot be less than the average of the closing price of our ordinary shares listed on the American Stock Exchange or The Nasdaq Global Market System, as applicable, over the 30 days preceding the date of grant. No share option granted under our Italy sub-plan may cover more than 10% of the voting rights in our annual meeting of shareholders or 10% of our capital or equity. Share grants will be made in consideration for past services.

Generally, a participant under the Italy sub-plan may not transfer a share award other than by applicable law. However, a participant under the Italy sub-plan may designate a beneficiary who may exercise the award following the participant's death.

In the event of certain corporate transactions (including, but not limited to, a sale or other disposition of all or substantially all of our assets, a merger or a consolidation), all outstanding awards under the Italy sub-plan will be subject to the terms and conditions of the agreement memorializing the transaction. The agreement may provide for the assumption or substitution of awards by any surviving entity, the acceleration of vesting (and exercisability, if applicable) or the cancellation of awards with or without consideration. In addition, at the time of grant, our board of directors may provide for acceleration of vesting in the event of a change in control.

The Italy sub-plan will terminate on September 30, 2019 unless sooner terminated by our board of directors.

2007 Stock Option Plan

Our board of directors proposed a capital increase for our 2007 Stock Option Plan and the specific terms of such plan on March 26, 2007. Our shareholders approved the capital increase and the terms of the plan on April 27, 2007.

The 2007 Stock Option Plan authorizes 1,000,000 ordinary shares for issuance. At December 31, 2009, there were 242,030 shares underlying outstanding options, with a weighted average exercise price of $7.45. Shares subject to options that have expired or otherwise terminated without being exercised in full again become available for issuance under the plan. In the event of a share split or other alteration in our capital structure, without the receipt of consideration, appropriate adjustments will be made to the outstanding awards to prevent dilution or enlargement of a participant's rights. The plan is governed by Italian law.

The 2007 Stock Option Plan provides for the grant of incentive stock options (as defined in Section 422 of the U.S. Internal Revenue Code) to employees, including officers and employee-directors, and nonstatutory stock options. The plan also provides for the periodic automatic grant of nonstatutory stock options to our non-employee directors.

The 2007 Stock Option Plan is administered by our board of directors or a committee appointed by our board of directors. The board or the committee determines recipients and types of options to be granted, including the number of shares subject to an option, the vesting schedule of options, the exercisability of options, and subject to applicable restrictions, other terms of options. The board of directors has delegated administration of the 2007 Stock Option Plan to the compensation committee.

The term of share options granted under the 2007 Stock Option Plan generally may not exceed the earlier of ten years and March 26, 2022. Our compensation committee determines the price of share options granted under the 2007 Stock Option Plan, subject to certain limitations.

No incentive share option may be granted to any person who, at the time of the grant, owns (or is deemed to own) ordinary shares possessing more than 10% of our total voting ordinary shares, unless the option exercise price is at least 110% of the fair market value of the ordinary shares on the date of grant and the term of the incentive share option does not exceed five years from the date of grant. The exercise price for a nonstatutory share option can vary in accordance with a predetermined formula while the option is outstanding. In addition, the aggregate fair market value, determined at the time of grant, of the ordinary shares with respect to which an incentive share option first becomes exercisable during any calendar year (under the 2007 Stock Option Plan and all of our other equity compensation plans) may not exceed $100 thousand.

Options granted under the 2007 Stock Option Plan vest at the rate determined by our compensation committee. Typically, options granted to employees under the 2007 Stock Option Plan vest over three years, at the rate of

one-third of the shares covered by the option vesting on the first anniversary of the grant date and the remainder vesting monthly over the next two years.

Generally, the optionee may not transfer a share option other than by will or the laws of descent and distribution unless the optionee holds a nonstatutory share option that provides otherwise. However, an optionee may designate a beneficiary who may exercise the option following the optionee's death. An optionee whose service relationship with us ceases for any reason may exercise the option to the extent it was vested for the term provided in the share option agreement. Options generally expire three months after the termination of an optionee's service. However, if an optionee is permanently disabled or dies during his or her service, that person's options generally may be exercised up to 12 months following disability or death.

In the event of certain corporate transactions (including, but not limited to, a sale or other disposition of all or substantially all of our assets, a merger or a consolidation), all outstanding options under the 2007 Stock Option Plan will be subject to the terms and conditions of the agreement memorializing the transaction. The agreement may provide for the assumption or substitution of options by any surviving entity, the acceleration of vesting (and exercisability, if applicable) or the cancellation of options with or without consideration. In addition, at the time of grant, our board of directors may provide for acceleration of vesting in the event of a change in control. In the event of a change in control, non-employee director options outstanding under the 2007 Stock Option Plan will automatically become vested and will terminate if not exercised prior to such a change in control.

The board of directors may amend the 2007 Stock Option Plan at any time. Amendments will be submitted for shareholder approval to the extent required by applicable laws, rules and regulations. The 2007 Stock Option Plan will terminate on March 26, 2022 unless sooner terminated by the board of directors or a committee appointed by the board of directors.

The board of directors has proposed that the shareholders approve an amendment to the 2007 Stock Option Plan increasing the number of shares authorized under such plan to 2,200,000 at our Annual Ordinary Shareholders' Meeting on April 26, 2010 (first call) and, if necessary, April 30, 2010 (second call). In addition, as part of the overall director compensation package, the board of the directors has proposed that the shareholders approve a stock option grant with an economic value of $110,000 using the Black-Scholes model. We expect these options to only be issued to our non-employee directors.

Other pension and retirement plans

We do not have any other pension or retirement plans, other than a 401(k) plan for our U.S. employees.

BOARD PRACTICES

Board Composition

Our board of directors currently consists of six members: Ms. Bertoglio, Dr. Cooper, Mr. Codella, Dr. Ferro, Dr. Islam and Dr. Sandage. Ms. Bertoglio, Dr. Cooper and Dr. Sandage have never been employed by us or any of our subsidiaries and are independent directors. FinSirton also agreed to vote its shares in favor of electing one person designated by Sigma-Tau Finanziaria S.p.A. Mr. Codella is the designee of Sigma-Tau. We do not have any agreements with any of our directors that provide for benefits upon termination of employment, although under Italian law, if directors are removed by the vote of shareholders at an ordinary shareholders' meeting prior to the end of their term without cause, they may have a claim for damages against us. These damages may include, but are not limited to, compensation that would otherwise have been paid to the director for the remainder of his or her term and damage to his or her reputation.

Our Compensation Committee recommends the compensation of our directors to our shareholders and our board of directors. Under Italian law, our shareholders determine the compensation of our directors relating to basic board service, such as annual fees for serving on the board and fees for attending board meetings. Our directors then determine "additional" compensation for our directors for serving on the various board committees and attending committee meetings. Our compensation committee and board of directors have approved the following total director compensation for the term from our October 2009 ordinary shareholders' meeting to our ordinary shareholders' meeting approving our 2009 Italian GAAP financial statements, prorated on an annualized basis:

- an annual cash retainer of $45 thousand for each non-employee director, subject to shareholder approval; and
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$20 thousand to the chairperson of the audit committee; $10 thousand to the chairperson of the compensation committee; $15 thousand to the chairperson of the scientific oversight committee; $7.5 thousand to the chairperson of the nominating and corporate governance committee; and $5 thousand to all the other non-employee members of committees.

Board Committees and Code of Ethics

Our board of directors has established an audit committee, a compensation committee, a nominating and corporate governance committee, and a scientific oversight committee.

Audit Committee. Our audit committee consists of Ms. Bertoglio, Dr. Cooper and Dr. Sandage, each of whom is an independent director. Ms. Bertoglio is an audit committee financial expert. The audit committee is a standing committee of, and operates under a written charter adopted by, our board of directors. The audit committee:

- establishes procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls or auditing matters and the confidential, anonymous submission by our employees of concerns regarding questionable accounting or auditing matters;

- has the authority to engage independent counsel and other advisors, as it determines necessary to carry out its duties, and determine the compensation of such counsel and advisors, as well as its ordinary administrative expenses; and
- approves related party transactions.

Our audit committee directly oversees our independent accountants, including the resolution of disagreements between management and the independent accountants. As discussed below, under Italian law, our board of statutory auditors also oversees our independent accountants with respect to our Italian GAAP financial statements. Under Italian law, our shareholders must be the party that appoints, terminates and determines the compensation for our independent accountants, although our audit committee does make recommendations on such matters to our board of directors, which in turn makes recommendations to our shareholders.

Compensation Committee. Our compensation committee consists of Dr. Cooper and Ms. Bertoglio, each of whom is an independent director. Under Nasdaq rules, the compensation of a U.S. domestic company's chief executive officer and all other officers must be determined, or recommended to the board of directors, either by a compensation committee comprised of independent directors or a majority of the independent directors of its board of directors. Disclosure of individual management compensation information is mandated by the Exchange Act proxy rules, but foreign private issuers are generally exempt from that requirement. Our compensation committee makes recommendations to our board of directors regarding salaries, benefits, and incentive compensation for our executive officers and directors. Part of the compensation of our directors is fixed periodically by our shareholders at their annual ordinary shareholder meetings. We disclose the aggregate compensation of our executive officers and directors in our Exchange Act reports, but not individual compensation of those officers or directors.

Nominating and Corporate Governance Committee. Our nominating and corporate governance committee consists of Dr. Cooper and Ms. Bertoglio, each of whom is an independent director. Under Nasdaq rules, the directors of a U.S. domestic company must be either selected or recommended for the board of directors' selection by either a nominating committee comprised solely of independent directors or by a majority of the independent directors. Under Italian law, directors may also be nominated by our shareholders. Our nominating and corporate governance committee performs the duties required by Nasdaq, including assisting the board of directors in fulfilling its responsibilities by:

- identifying and approving individuals qualified to serve as members of our board of directors;
- selecting director nominees for our annual meetings of shareholders;
- evaluating our board's performance; and
- developing and recommending to our board corporate governance guidelines and oversight with respect to corporate governance and ethical conduct.

Our shareholders are able to nominate directors other than those nominated by the nominating committee.

Scientific Oversight Committee. Our scientific oversight committee consists of Dr. Sandage, Dr. Islam and Dr. Ferro. Our scientific oversight committee assists the board of directors in fulfilling its oversight responsibilities with respect to clinical and regulatory matters. The scientific oversight committee's primary purposes are to:

- oversee management's design and execution of clinical trials;
- provide input and advice to management regarding the same; and

- periodically update the rest of the board of directors regarding the company's performance of the clinical trials and the committee's advice regarding the same.

Other Committees. Our board of directors may establish other committees as it deems necessary or appropriate from time to time, including, but not limited to, an executive committee.

Board of Statutory Auditors

Under Italian law, in addition to electing our board of directors, our shareholders also elect a board of statutory auditors. The statutory auditors are elected for a term of three years, may be reelected for successive terms and may be removed only for cause and with the approval of a competent court. Each member of the board of statutory auditors must provide certain evidence that he or she is qualified to act in that capacity under Italian law, and that he or she meets certain professional standards. The board of statutory auditors is required to verify that we comply with applicable law and our bylaws, respect the principles of correct administration and maintain adequate organizational structure, internal controls and administrative and accounting system, and oversees our independent accountants with respect to our Italian GAAP financial statements.

The following table sets forth the names of the three members of our board of statutory auditors and the two alternate statutory auditors and their respective positions, as of the date of this annual report. The current board of statutory auditors was elected on June 30, 2009 for a term that ends at the date of the ordinary shareholders' meeting to approve our 2011 annual financial statements.