Gentium S.p.A.
Form 20-F
April 01, 2013
As filed with the Securities and Exchange Commission on April 1, 2013

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

FORM 20-F

[ ]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, 2012

OR

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

OR

[ ]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 5373200
(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.

15,038,483 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 [ ] 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 [ ] 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 [ ]

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes [ ] No [x]

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 [ ] Accelerated filer [x] Non-accelerated filer [ ]

Indicate by check mark which basis of accounting the registrant has used to prepare the consolidated financial statements included in this filing:

U.S. GAAP [x] International Financial Reporting Standards as issued by the International Accounting Standards Board [ ] Other [ ]

If “Other has been checked in response to the previous question, indicated by check mark which financial item the registrant has elected to follow.

Yes [ ] No [ ]

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 [ ] No [x]

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PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

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 a mixture of single- and double-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 that occurs when veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation, that are administered prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is linked to multiple-organ failure and high rates of morbidity and mortality.

Defibrotide for the treatment and prevention of VOD has been given "orphan" status by the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide for the treatment and prevention of VOD has also been granted "orphan" status by the Korean Food and Drug Administration, or KFDA. In addition, defibrotide has been granted "fast-track product" designation by the FDA for the treatment of severe VOD prior to stem cell transplantation. To the best of our knowledge, there are no FDA or EMA approved treatments for this life-threatening disease.

We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD with multiple organ failure in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. We also have an ongoing study for the treatment of VOD through our Investigational New Drug, or IND, protocol. While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis througout the U.S. pursuant to our IND protocol, which we refer to as our cost recovery program, and throughout the rest of the world on a named patient basis, which we refer to as our named-patient program, or NPP. We expect to collect additional usage tolerability and safety data from patients of our cost recovery and named-patient programs to support our regulatory filings.

On May 10, 2011, we announced the filing of our Marketing Authorization Application, or MAA, under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. We plan to appeal this decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

On July 6, 2011, we announced the filing of our New Drug Application, or NDA, with the FDA for defibrotide for the treatment of VOD in adults and children undergoing hematopoietic stem cell transplantation. On August 17, 2011, we announced our voluntary withdrawal of our NDA following correspondence from the FDA identifying several potential "Refuse to File" issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with contract research organizations, or CROs, and consultants to address the issues raised by the FDA

and plan to resubmit our NDA in 2013.

We have entered into a license and supply agreement with Sigma-Tau Pharmaceuticals, Inc., or Sigma-Tau (as assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.) to commercialize defibrotide for the treatment and prevention of VOD in the Americas upon FDA approval, if any. Pursuant to the terms of this license agreement, between 2001 and 2010 we received US$ 11.35 million in milestone payments. We are entitled to an additional payment of US$ 6 million following regulatory approval from the FDA to market defibrotide in the U.S., and a further US$ 2 million payment following the transfer of the approved NDA to Sigma-Tau. In addition, in connection with such agreement, Sigma-Tau has agreed to reimburse us with certain costs associated with the development of defibrotide. We continue to work with Sigma-Tau on our U.S. regulatory strategy.

In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as headquarters for our commercial operations. We have entered into license and/or supply and distribution agreements with specialized regional partners to distribute debibrotide, including on a named-patient basis, in the following territories: the Asian Pacific, the Middle East and North Africa, Europe, the Nordics and Baltics, Turkey, Israel and the Palestinian Authority. Certain of these regional partners have also agreed to assist us with local registration, marketing authorization, reimbursement, marketing, sales and distribution and medical affairs activities following regulatory approval, if any. We plan to distribute defibrotide in major European countries upon regulatory approval, if any, on our own.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, or APIs, such as the defibrotide compound, sodium heparin, urokinase and sulglicotide. These APIs are subsequently used to make the finished forms of various drugs. With respect to defibrotide, we have contracted with Patheon S.p.A. to process the defibrotide compound into its finished form at Patheon's manufacturing facility. We believe that we are the sole worldwide producer of defibrotide. Our operating assets are located in Italy.

We have accumulated a deficit of approximately €92.07 million since our inception. We have been cash flow positive since 2010, primarily due to an up-front payment from Sigma-Tau Pharmaceuticals Inc. in connection with the expansion of the license for defibrotide in the Americas, and revenue and cash-flow generated from the cost recovery and named-patient programs. While we expect that existing cash and cash equivalents together with the anticipated cash flow from product sales will be sufficient to support our current operations for at least the next twelve months, if we have expenditures above our current expectations, or if we are unable to generate sufficient revenue and cash-flow through our cost recovery and named-patient programs, we may need to obtain additional capital through equity or debt financing, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all.

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. These risks are described in more detail under "Risk Factors" in this annual report. The risks described are not the only risks we face. Additional risks to which we are subject include those not presently known to us and those risks that we currently deem immaterial. Our business, financial condition and operations could be materially adversely affected by any of these risks. The trading price of our securities could decline as a result of any of these risks and you may lose all or part of your investment. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this annual report.

SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read in conjunction with "Operating and Financial Review and Prospects" and our consolidated financial statements and the related notes appearing elsewhere in this annual report. The selected consolidated financial data as of December 31, 2011 and December 31, 2012 and for the three years ended December 31, 2012 are derived from our audited consolidated financial statements, which are included in this annual report. The selected financial data as of December 31, 2008, December 31, 2009 and December 31, 2010 and for the years ended December 31, 2008 and December 31, 2009 are 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 is 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:	For the Years Ended December 31,					
(000s omitted except per share data)	2008	2009	2010	2011	2012	2012(1)
Revenues:						
Product sales to related party	€651	€195	€-	€-	€-	$-
API product sales	4,792	4,603	6,533	4,848	4,856	6,403
NPP product sales	-	4,904	13,182	16,886	22,774	30,030
Total product sales	5,443	9,702	19,715	21,734	27,630	36,433
Other revenues	25	129	289	123	152	201
Other revenues from related party	1,970	337	4,547	2,026	1,257	1,657
Total revenues	7,438	10,168	24,551	23,883	29,039	38,291
Operating costs and expenses:						
Cost of goods sold	5,596	4,002	5,786	6,035	5,778	7,619
Research and development	9,569	3,512	6,104	5,533	10,531	13,886
General and administrative	7,668	6,036	5,835	5,490	6,271	8,269
Sales and marketing	-	-	-	2,237	4,558	6,010
Charges from related parties	537	279	346	222	186	245
Restructuring charges	-	-	1,101	-	-	-
Depreciation and amortization	998	916	908	870	1,003	1,323
Write-down of assets	3,403	-	-	-	-	-
	27, 771	14,745	20,080	20,387	28,327	37,352
Operating income/(loss)	(20,333)	(4,577)	4,471	3,496	712	939
Foreign currency exchange gain (loss), net	173	162	90	46	(67)	(88)
Interest income/(expense), net	256	(110)	(87)	(21)	155	204
Pre-tax income/(loss)	(19,904)	(4,525)	4,474	3,521	800	1,055
Income tax expense:						
Total income tax expense	-	-	(397)	(811)	(26)	(34)
Net income/(loss)	€(19,904)	€(4,525)	€4,077	€2,710	€774	$1,021
Net income/(loss) per share:						
Basic	(1.33)	(0.30)	0.27	0.18	0.05	0.07
Diluted	€(1.33)	€(0.30)	€0.27	€0.18	€0.05	$0.07

The following table summarizes certain of our consolidated balance sheet data.

(000s omitted except shares)	2008	2009	2010	2011	2012	2012(1)
Balance Sheet Data:						
Cash and cash equivalents equivalents equivalent	€11,491	€1,392	€8,742	€9,990	€12,485	$16,463
Working capital	3,152	1,041	6,555	10,730	14,220	18,750
Property, net	10,751	9,717	8,598	8,508	7,449	9,822
Total assets	26,901	18,167	24,674	27,412	28,638	37,762
Long-term debt, net of current maturities	3,268	3,098	1,759	1,545	1,135	1,497
Shareholders' equity	10,451	7,330	12,930	17,383	20,350	26,834
Capital stock	€14,956	€106,962	€108,485	€110,228	€112,421	$148,238
Number of shares	14,956,317	14,956,317	14,956,317	14,969,150	15,038,483	15,038,483

(1) Euro amounts are translated into U.S. dollars using the Noon Buying Rate for the Euro on December 31, 2012, of U.S. 1.3186 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 American Depositary Shares, or 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
2008	1.4726	1.3919
2009	1.3935	1.4332
2010	1.3261	1.3269
2011	1.3931	1.2973
2012	1.2859	1.3186

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 based on the noon buying rate on each day of such period.

	U.S. Dollar per Euro	
Month	High	Low
September 2012	1.3142	1.2566
October 2012	1.3133	1.2876
November 2012	1.3010	1.2715
December 2012	1.3260	1.2930
January 2013	1.3584	1.3047
February 2013	1.3692	1.3054
March 2013 (through March 22, 2013)	1.3098	1.2888

Source: Federal Reserve Statistical Release H.10

On March 22, 2013, the noon buying rate was €1.00 to $1.2996.

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

Obtaining regulatory approval has been and continues to be increasingly difficult and costly and takes many years, and, once obtained, is costly to maintain. With the occurrence of a number of high profile safety events with certain pharmaceutical products, regulatory authorities, and in particular the FDA, members of Congress, the United States Government Accountability Office (GAO), Congressional committees, private health/science foundations and organizations, medical professionals, including physicians and investigators, and the general public are increasingly concerned about potential or perceived safety issues associated with pharmaceutical and biological products, whether under study for initial approval or already marketed.

This increasing concern has produced greater scrutiny, which may lead to fewer treatments being approved by the FDA or other regulatory bodies, as well as more restrictive labeling of a product or a class of products for safety reasons, potentially including a boxed warning or additional limitations on the use of products, pharmacovigilance programs for approved products or requirement of risk management activities related to the promotion and sale of a product.

On May 10, 2011, we announced the filing of our MAA under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. The EMA's Committee for Medicinal Products for Human Use, or CHMP, which reviewed the MAA, concluded that there were issues with certain documentation and the reporting of data in the prevention study. In the treatment study, the number of patients in the historical control group was considered to be too low and the CHMP was concerned about the fact that some patients who were originally chosen to be in the historical control group were excluded from the study. In addition, the CHMP concluded that there was a lack of data on the way the medicine is eliminated by the kidneys in children and patients with reduced kidney function, which concerned the CHMP since a safety concern was identified in children who received high doses of defibrotide. We plan to appeal the EMA's decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

In addition, on August 17, 2011, we voluntarily withdrew our NDA with the FDA following correspondence from the FDA identifying several potential "Refuse to File" issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with CROs and consultants to address the issues raised by the FDA and plan to resubmit our NDA in 2013.

We do not currently have regulatory approval to market and sell defibrotide anywhere in the world, and we may never obtain regulatory approval to market and sell defibrotide. While we have generated revenue on the distribution of defibrotide through our cost recovery and named-patient programs, we cannot guarantee that historical revenues from these programs will continue or whether we will be able to continue to distribute defibrotide on a pre-approval

basis. If we are unable to obtain regulatory approval to commercialize defibrotide or unable to distribute defibrotide on a pre-approval basis, our business and results of operations would be materially and adversely affected and we may be unable to continue as a going concern.

The FDA and EMA may require us to conduct additional clinical trials for defibrotide to treat VOD or prevent VOD and/or collect additional data, which will delay the commercialization of defibrotide and may require us to obtain additional capital.

The EMA and the FDA may require us to conduct one or more additional clinical trials prior to granting marketing approval for defibrotide. In addition, for the treatment indication, these regulators may require us to conduct a trial that requires a concurrent control group of untreated patients as opposed to a historical control arm, which may not be possible if patients are unwilling to enroll and/or investogators refuse to participate in such a trial.

Conducting clinical trials is a complex, time-consuming and expensive process. Our ability to complete any clinical trials in a timely fashion will depend in large part on a number of key factors, including protocol design, regulatory and institutional review board approval, the rate of patient enrollment in clinical trials, and compliance with extensive current Good Clinical Practices requirements. We have opened clinical sites and have enrolled patients in a number of new countries where our experience is more limited, and have required the use of the services of third party clinical trial service providers. If we fail to adequately manage the design, execution and regulatory aspects of any new clinical trials, our studies and ultimately our regulatory approvals may be delayed or we may fail to gain approval for our product candidates altogether.

We may lack sufficient capital to commence and complete new clinical studies for defibrotide. Obtaining additional capital through equity and/or debt financings, loans or collaborative arrangements with corporate partners may not be available to us on favorable terms, if at all. Even if we are able to obtain additional capital to conduct additional clinical trials for defibrotide, these studies will take years to complete.

While we have generated limited revenue from sales of defibrotide on a pre-approval basis, we have had significant losses to date, and we may not be able to meet our future cash requirements without obtaining additional capital from external sources or if we are prevented from or unsuccessful in distributing defibrotide on a pre-approval basis.

As of December 31, 2012, we had approximately €12.49 million in cash and cash equivalents. We have generated a significant portion of our revenue through the distribution of defibrotide on a pre-approval basis through our cost recovery and named-patient programs. Prior to the initiation of our cost recovery and named-patient programs, we were cash-flow negative and had only generated net losses. We may revert to incurring significant losses and may become cash-flow negative, particularly if we are required to conduct additional clinical studies, or if we are prevented from or unnuccessful in distributing defibrotide on a pre-approval basis. If we incur operating losses and become cash-flow negative for longer than we expect to and are unable to raise additional capital, we may become insolvent and unable to continue our operations. In addition, our fluctuating operating results may fail to meet the expectations of investors, which may cause the price of our ADSs to decline.

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

The development of defibrotide has required a commitment of substantial funds and we may need to commit a substantial amount of additional funds in order to obtain regulatory approval to market and commercialize defibrotide.

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

- the timing and cost to develop and obtain regulatory approvals to market defibrotide, including the potential need to conduct future clinical trials;
- future payments, if any, received or made under existing or possible future collaborative arrangements;
- our ability to continue to distribute defibrotide under our named-patient and cost recovery programs;
- the costs associated with building and maintaining a commercial infrastructure;
- the costs associated with implementing any upgrades to our manufacturing facility as required by the FDA, the EMA, or any other regulatory body;
- the costs associated with protecting and expanding our patent and other intellectual property rights;
- market acceptance of defibrotide; and
- the overall condition of the financial markets.

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 with respect to defibrotide. We may also be forced to curtail, cease or restructure our operations, enter into new funding arrangements with collaborators on unattractive terms, or relinquish rights to defibrotide that we would not otherwise relinquish in order to continue operating independently.

Even if we obtain regulatory approval to market defibrotide, we do not know whether we will ever generate significant revenues.

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. The FDA, EMA and KFDA have designated defibrotide to treat and prevent VOD, as "orphan drugs," which generally means that fewer than 200,000 people are affected by the disease or condition. If we are unable to distribute defibrotide at our expected price-points to this limited market, we may never generate significant revenue.

Following regulatory approval for defibrotide, if any, we plan on marketing and distributing defibrotide in major countries throughout Europe through our subsidiary, Gentium GmbH. However, we have alliances with regional partners to assist us with the distribution of defibrotide in certain territories post-approval, including an alliance with Sigma-Tau Pharmaceuticals, Inc. to market defibrotide for the treatment and prevention of VOD in North America, Central America and South America. Our future profitability may depend largely on our partners' efforts to market defibrotide, which may not be successful.

If we fail to comply with the extensive legal and regulatory requirements affecting the health care industry, we could face increased costs and penalties.

Our activities, and the activities of our collaborators and third-party providers, are subject to extensive government regulation and oversight both in the U.S. and in foreign jurisdictions. The FDA and comparable agencies in other jurisdictions directly regulate many of our most critical business activities, including the conduct of preclinical and clinical studies, product manufacturing, advertising and promotion, product distribution, adverse event reporting and product risk management. These risks may be heightened if we obtain regulatory approval for defibrotide.

Regulations governing the health care industry are subject to change, including:

- new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to health care availability, pricing or marketing practices, compliance with wage and hour laws and other employment practices, method of delivery, payment for health care products and services, tracking payments and other transfers of value made to physicians and teaching hospitals, and extensive anti-bribery and anti-corruption prohibitions;

- changes in the FDA and foreign regulatory approval processes that may delay or prevent the approval of new products and result in lost market opportunity;

- changes in FDA and foreign regulations that may require additional safety monitoring, labeling changes, restrictions on product distribution or use, or other measures after the introduction of our products to market, which could increase our costs of doing business, adversely affect the future permitted uses of approved products, or otherwise adversely affect the market for our products; and

- changes in the tax laws relating to our operations.

While these regulations may not impact our business directly, they may impact Sigma-Tau's distribution of defibrotide in the Americas, which would impact our royalty revenues upon FDA approval, if any.

We may be required to suspend or discontinue any current and future clinical trials 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, the 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 presents 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 condition associated with high dose chemotherapy and stem cell transplantation. Adverse events involving vascular disorders, coagulation and potentially life-threatening bleeding have been reported in VOD patients treated with defibrotide, which could potentially be related to the defibrotide therapy. Hypotension has been reported in patients participating in clinical trials of defibrotide to treat severe VOD, which may also be related to the drug. 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, when 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 assessed by the FDA and other regulatory authorities in determining whether defibrotide is, from a risk-benefit perspective, safe and effective to treat severe VOD, to prevent VOD, and to prevent deep vein thrombosis.

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

Product liability and other claims arising out of the testing of our product candidates in human clinical trials may reduce demand for our products or result in substantial damages.

We face an inherent risk of product liability exposure in connection with human clinical trial testing of defibrotide and the distribution of defibrotide through our named-patient and cost recovery programs. An individual may bring a product liability claim against us if defibrotide causes, or merely appears to have caused, an injury.

Product liability claims of this nature may result in:

- a decreased demand for defibrotide;
- injury to our reputation;
- withdrawal of clinical trial volunteers;
- significant litigation costs; and
- substantial monetary awards to plaintiffs.

Although we currently maintain product liability insurance, we may not have sufficient insurance coverage, and we may not be able to obtain sufficient coverage at a reasonable cost. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the commercialization of any products that we or our collaborators develop, including defibrotide. If we are successfully sued for any injury caused by our products or processes, then our liability could exceed our product liability insurance coverage and our total assets.

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 or unable to adapt to changes in existing regulatory requirements or the 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., with whom 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 the EMA. These authorities could force us to stop manufacturing our products if they determine that we or Patheon are not in compliance with applicable regulations or require us to complete further costly alterations to our facilities.

We manufacture our APIs at our manufacturing facility in Italy. In addition, we have hired Patheon S.p.A. to process 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 the manufacturing of APIs, including the defibrotide compound, and defibrotide. These facilities are also subject to inspection and regulation by the FDA and the EMA with respect to the manufacturing of the defibrotide API compound and defibrotide. Also, part of the process to obtain FDA and EMA approval for defibrotide is to obtain certification from those authorities that these facilities are in compliance with current good manufacturing practices. Following initial approval, if any, the FDA or the EMA will continue to inspect our manufacturing facilities, in some cases, unannounced, to confirm ongoing compliance with good manufacturing practices.

These regulators may deny approval to manufacture our APIs or otherwise require us to stop manufacturing our APIs if they determine that either our facility or Patheon's facility does not meet the standards of compliance required under applicable regulations. In addition, these regulators may require us to complete costly alterations to our facilities.

The Public Company Acounting Oversight Board is unable to enforce its review of the audits conducted by our independent registered public accounting firm operating in Italy; therefore, investors may be deprived of the benefits of such inspection.

Our independent registered public accounting firm, Reconta Ernst and Young S.p.A., that issues the audit reports included in our annual reports filed with the SEC, is required by the laws of the United States to undergo regular inspections by the Public Company Accounting Oversight Board, or PCAOB, to assess its compliance with SEC rules and PCAOB professional standards. While our audits are performed in accordance with the standards of PCAOB, our auditors are a registered public accounting firm in Italy, a jurisdiction where the PCAOB is currently unable, under Italian law, to enforce their inspection of our auditors audits and, therefore, our auditors, like other independent registered public accounting firms in Italy, are currently not inspected by the PCAOB.

Inspections of audit firms that the PCAOB has conducted have identified deficiencies in those firms' audit procedures and quality control procedures, which may be addressed as part of the inspection process to improve future audit quality. The lack of PCAOB inspections in Italy prevents the PCAOB from regularly evaluating our auditor's audits and quality control procedures. As a result, the inability of the PCAOB to conduct inspections of auditors in Italy may deprive investors of the benefits of PCAOB inspections.

We currently rely upon a sole processor, Patheon S.p.A., to fill and finish defibrotide into marketable formulations, and we may not be able to quickly replace Patheon if it is unable to perform these services.

If Patheon does not or is not able to perform these services for any reason, it may take time and resources to implement and execute the necessary technology transfer to another processor, and such a delay could potentially cause us to breach contractual obligations into which we have entered or may enter, violate local laws requiring us to deliver the product to those in need, and impact our revenues.

We use hazardous materials in our manufacturing facility, and any claims relating to the improper handling, storage, release or disposal of these materials could be time-consuming and expensive.

Our manufacturing of active pharmaceutical ingredients involves the controlled storage, use and disposal of chemicals and solvents. We are subject to laws and regulations governing the use, transportation, treatment, storage, handling and disposal of solid and hazardous materials, wastewater discharges and air emissions. We obtained certification under the UNI EN ISO 14001 Standard for our environmental management system on April 20, 2007 and an Eco-management and Audit Scheme, or EMAS, certification on July 26, 2007. Both certifications were renewed in 2010 and we are currently working on obtaining renewals for the certifications for an additional three-year period following their expiration. Our environmental policy is designed to comply 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 in the surrounding community. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by these laws and regulations, we cannot completely eliminate the risk of contamination or injury from hazardous materials. If an accident occurs, an injured party could seek to hold us liable for any damages that result and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. We may incur significant costs to comply with current or future environmental laws and regulations.

We may have difficulty obtaining raw material for defibrotide.

Defibrotide is based on pig intestines. If our current sources of pig intestines encounter safety or other issues that impact their ability to supply the pig intestines to us as needed, 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.

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Due to our limited resources, we rely on third parties for the development of defibrotide and, if these third parties fail to comply with strict regulations, the development of defibrotide may be delayed or unsuccessful.

We do not have the personnel capacity to manage all aspects concerning the development of defibrotide. We depend on third-party providers to manage our clinical trials and will likely continue to depend on such third parties with respect to any future clinical trials conducted. If these third parties fail to comply with applicable regulations or if they fail to adequately execute such trials and/or manage or studies, we may not be able to enter into alternative arrangements without undue delay or additional expenditures and, as a result, the development of defibrotide may be delayed or we may fail to gain regulatory approval altogether.

If we are unable to attract and retain qualified personnel and key relationships, our business could be seriously harmed.

We are highly dependent on our senior management, whose services are critical to the successful implementation of research and development and manufacturing and regulatory strategies, and our ability to maintain relationships with key opinion leaders. If we lose one or more of the members of our senior management or other key opinion leaders, our business 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, obtain regulatory approval for and commercialize defibrotide. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel, if needed.

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 a 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 to treat and/or prevent VOD, we may need to obtain regulatory approval of the price we 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.

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 against losses that may be caused by any of these occurrences or events.

We conduct all of our manufacturing operations in a single facility located in Villa Guardia, near Como, Italy. This facility could be damaged by fire, flood, earthquake, power loss, telecommunication and information system failure, terrorism or a similar event. Our insurance covers damages to the facility, including the buildings, machinery, electronic equipment and goods, of up to approximately €22 million, but does not cover damages caused by any of the events 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 against business interruption and we do not have a replacement manufacturing facility readily available.

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 may have products or are currently developing products to treat some of the same disorders and diseases that defibrotide is designed to treat.

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

In May 2003, the FDA designated defibrotide as an orphan drug to treat VOD, and in January 2007, the FDA designated defibrotide as an orphan drug to prevent VOD. If the FDA approves NDAs for these uses of defibrotide, before approving a NDA filed by anyone else, the orphan drug status will grant us limited market exclusivity for seven years from the date of the FDA's approval of our NDA. However, a marketing authorization may be granted to another applicant for the same product if we give our consent to such authorization, if we are unable to supply sufficient quantities of defibrotide, or if 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. There is no guarantee that the FDA will approve our NDA, if and when we are ready to resubmit, before approving another company's product for the same uses, although we are not aware of any other company that is researching defibrotide for these uses at this time. In such a case, however, the first product approved would have market exclusivity and our products would not be eligible for approval until that exclusivity period expires.

In July 2004, the EMA designated defibrotide as an orphan medicinal product to both treat and prevent VOD. If the European regulators do grant us a marketing authorization for those uses of defibrotide, we will have limited market exclusivity for those uses for ten years following the date of the approval. However, a marketing authorization may be granted to another applicant for the same product if we consent to such authorization, 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 applications that we may file in the future, may not be granted. 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 the risk of bringing products to the market is too great, thus adversely affecting our operating results.

Because of the extensive time required to develop, test and complete a regulatory review of a product candidate, it is possible that our relevant patent rights may expire either before defibrotide can be approved for sale and commercialized or within a short time after 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. The patent expires in 2022 in most countries. This patent is important 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 not be an opportunity to extend this patent and thereby extend the exclusivity period related to the FDA and the EMA, 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, particularly when patent protection is inappropriate or unattainable. 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. To enforce a claim against a third party for illegally obtaining and 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 afford intellectual property rights and protections to the extent that United States and Europe do. 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 their public trading price has been volatile.

The market price of our common stock has been highly volatile. Between our initial public offering on June 21, 2005 and December 31, 2012, the closing price of our ADSs has fluctuated between $0.33 and $24.40 per share, with an average daily trading volume for the twelve-month period ended December 31, 2012 of approximately 21,724 ADSs. The market has experienced significant price and volume fluctuations for many reasons, some of which may be unrelated to our operating performance.

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

- public announcements of decisions made by regulators in both the United States and abroad;
- public announcements of improvements, new commercial products, failures of products, or progress toward commercialization by our competitors or peers;
- the influence of 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 fluctuation in our revenues and financial results.

We may not remain listed on the Nasdaq Global Market.

From the date of our public offering through 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 must be met in order for our ADSs to continue to be listed on the Nasdaq Global Market. We would be in violation of the continued listing requirements if:

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

In the event of any such violation, 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, 2012, our stockholders' equity was $26.83 million (€20.35 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.

One of our largest shareholders and our founder exercises significant control over us, which may make it more difficult for you to elect or replace directors or management and approve or reject mergers and other important corporate events, including obtaining potential financing.

One of our largest shareholders and our founder, F3F S.p.A. (formerly known as FinSirton S.p.A.) owned approximately 17% of our outstanding ordinary shares at December 31, 2012. Dr. Laura Ferro, our former Chief Executive Officer and President and a current member of our board of directors, together with members of her family, may be deemed to control F3F S.p.A.

In addition, Sigma-Tau Finanziaria S.p.A., along with its affiliates, owned approximately 18% of our outstanding ordinary shares at December 31, 2011. Dr. Marco Brughera, who holds various senior-level positions within the Sigma-Tau Group, 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 F3F S.p.A. 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 your best interest. Also, the concentration of our beneficial ownership may have the effect of delaying, deterring or preventing a change in 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," each of F3F S.p.A. and Sigma-Tau Finanziaria own a percentage of our ordinary shares sufficient to bring legal action against our board of directors and to possibly 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 participation in matters that present a conflict of interest. They are merely required to declare the conflict of interest that pertains to the matter. Accordingly, directors who 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 for 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 the ultimate sale of the securities in the markets may adversely affect the market for the ADSs.

You do not have the ability to exercise your voting rights in the same manner as the holders of our ordinary shares and may not receive voting materials in time to instruct the depository to exercise your right to vote.

Except as described in this annual report and in the deposit agreement for the ADSs with our depositary, The Bank of New York Mellon, 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 only have the right to instruct the depositary, as the holders' representative, to exercise these voting rights. In addition, you may not receive voting materials in time to instruct the depositary to vote, and it is possible that you, or persons who hold 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 offer to our existing shareholders the right to purchase our securities. Under our deposit agreement for the ADSs, 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 American Depositary Receipts, or 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 if we or the depositary deem it advisable to do so under any requirement of law, any government or governmental body, 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. With some exceptions, in order to issue new equity or debt securities convertible into equity, we must increase our authorized capital. In order to do so, our board of directors must meet and resolve to recommend that our shareholders approve an amendment to our bylaws increasing our capital. The holders of the majority of our outstanding shares must then approve that amendment at an extraordinary shareholders' meeting duly called. These meetings take time to call and it might be very difficult to get a majority of the holders of all outstanding shares to vote in favor of the proposed resolution. In addition, an Italian notary public must verify that the capital increase is in compliance with our bylaws and with applicable Italian law. Further, under Italian law, our existing shareholders and any holders of convertible securities have preemptive rights (except in specific cases) 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. Alternatively, our shareholders can delegate the power to increase our capital to the board of directors, but the board's right to exercise such power, if delegated, will expire after five years. If the board does not approve a capital increase by the end of those five years, our board and shareholders would need to meet again to re-delegate this authority.

With respect to shareholders' resolutions approving a capital increase, Italian law provides that in the absence of meeting minutes, or in the event of the 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 competent 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 consolidated 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 the members of our board of directors and our board of statutory auditors acted with serious irregularities, in violation of their duties as directors, in approving a potential financing because such financing was potentially harmful to the company. On August 18, 2008, the Court of Como issued a temporary order preventing us from moving forward with the potential financing. While this claim was later dismissed for lack of damages, the claim did, nonetheless, prevent the directors from implementing the financing. Any shareholder or 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.

Italian law places restrictions on the amount of debt securities that we may issue relative to our equity to the extent that such debt securities are not listed on regulated markets or do not otherwise provide the holder of such securities the right to purchase or convert the same into our shares.

Under Italian law, we may issue debt securities in an amount not to exceed twice the sum of our capital, our legal reserve and any other disposable reserves appearing on our latest Italian GAAP balance sheet approved by our shareholders, unless the debt securities are listed on regulated markets or provide the holder of such securities the right to purchase or convert the same into our shares, in which case such restrictions do not apply. 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, 2012, the sum of Gentium S.p.A. capital, legal reserves and other reserves on our unaudited Italian GAAP financial statements was €38.97 million. If, in the future, we issue debt securities that are not listed on regulated markets or do not provide the holder of the securities the right to purchase or convert the same into our shares, 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. In such a case, 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 through 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 us, although there can be no assurance that we would be able to find purchasers of 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 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, 2012, our unaudited Gentium S.p.A. Italian GAAP capital was approximately €15.04 million. If we suffer losses from operations that reduce our capital to less than €120 thousand, then we must either 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 do not take these steps, our company could be liquidated.

We apply our operational losses against our legal reserves and capital. If our capital is reduced 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, reducing the legal reserves and capital by the amount of the remaining losses, or carrying the losses forward for up to one year. If the shareholders vote to carry the losses forward up to one year, and the losses are still more than one-third of the amount of the capital at the end of the year, then we must reduce our capital by the amount of the losses.

Due to the differences between Italian and U.S. law, the depositary (acting as a shareholder on your behalf) may have fewer shareholder rights than you would have as 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 shareholder rights than you would have as a shareholder of a U.S. corporation. We have presented a detailed comparison of the Italian laws applicable to our company versus Delaware law in “Item 10, Additional Information, Comparison of Italian and Delaware Corporate Law.” We compare 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 which afford them consultation rights with respect to specific matters regarding their employers' business and operations, including the downsizing or closure of facilities and employee terminations. In particular: (i) Law no. 604/1966, regulates the individual dismissals; (ii) Law no. 223/1991, concerns the collective dismissal procedure; (iii) Law no. 428/1990 as amended by legislative decree no. 18/2001, provides for the information and consultation procedure in case of a transfer of the undertaking or a part thereof and (iv) Legislative decree no. 25/2007, introduces 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, including the uncertainty as to whether regulatory approval for our lead product candidate, defibrotide, will be obtained. When used in this annual report, the words "anticipate," "believe," "estimate," "may," "intent," "continue," "will," "plan," "intend," and "expect" and similar expressions identify forward statements. You should read statements that contain these words carefully because they discuss our future expectations, contain projections of our future results of operations or of our financial condition or state other "forward-looking" information. We believe that it is important to communicate our future expectations to our investors. Although we believe that our expectations reflected in any forward-looking statements are reasonable, these expectations may not be achieved. The factors listed in the section captioned "Risk Factors," as well as any cautionary language included in this 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 started as a group of pharmaceutical businesses founded in Italy in 1944 and have been involved in the research and development of drugs derived from DNA and DNA molecules since the 1970s. In 1993, we were formed by F3F S.p.A. (formerly known as FinSirton S.p.A.) as Pharma Research S.r.L., an Italian private limited company, for the purpose of pursuing research and development activities of prospective pharmaceutical specialty products. In July 2001 we changed our name to Gentium S.p.A.. F3F S.p.A. is one of our largest shareholders owning approximately 17% of our outstanding ordinary shares at December 31, 2012, and may be deemed to be controlled by the Dr. Laura Ferro, our former Chief Executive Officer and President and currently one of our directors, and her family. Under our current bylaws, our company's term of existence will expire on December 31, 2050. We are governed by the Italian Civil Code.

Our principal executive offices are located at Piazza XX Settembre 2, 22079 Villa Guardia (Como), Italy. Our telephone number is +39 031 5373200. 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 is CT Corporation System, located at 111 Eighth Avenue, 13th Floor, New York, New York 10011, telephone number (212) 894-8940.

We are focused on the development and manufacture of our primary product candidate, defibrotide, an investigational drug based on a mixture of single- and double-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 that occurs when veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation, that are administered prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is linked to 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 with multiple organ failure in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. We also have an ongoing study for the treatment of VOD through our IND protocol. While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis througout the U.S. pursuant to our IND protocol, which we refer to as our cost recovery program, and throughout the rest of the world on a named patient basis, which we refer to as our named-patient program. We expect to collect additional usage tolerability and safety data from patients of our cost recovery and named-patient programs to support our regulatory filings.

On May 10, 2011, we announced the filing of our MAA under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. We plan to appeal this decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

On July 6, 2011, we announced the filing of our NDA with the FDA for defibrotide for the treatment of VOD in adults and children undergoing hematopoietic stem cell transplantation. On August 17, 2011, we announced our voluntary withdrawal of our NDA following correspondence from the FDA identifying several potential "Refuse to File" issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with CROs and consultants to address the issues raised by the FDA and plan to resubmit our NDA in 2013.

We have entered into a license and supply agreement with Sigma-Tau (as assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.) to commercialize defibrotide for the treatment and prevention of VOD in the Americas upon FDA approval, if any. Pursuant to the terms of this license agreement between 2001 and 2010, we received US$ 11.35 million in milestone payments. We are entitled to an additional payment of US$ 6 million following regulatory approval from the FDA to market defibrotide in the U.S., and a further US$ 2 million payment following the transfer of the approved NDA to Sigma-Tau. In addition, in connection with such agreement, Sigma-Tau has agreed to reimburse us with certain costs associated with the development of defibrotide. We continue to work with Sigma-Tau on our U.S. regulatory strategy.

In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as headquarters for our commercial operations. We have entered into license and/or supply and distribution agreements with specialized regional partners to distribute debibrotide, including on a named-patient basis, in the following territories: the Asian Pacific, the Middle East and North Africa, Europe, the Nordics and Baltics, Turkey, Israel and the Palestinian Authority. Certain of these regional partners have also agreed to assist us with local registration, marketing authorization, reimbursement, marketing, sales and distribution and medical affairs activities following regulatory approval, if any. We plan to distribute defibrotide in major European countries upon regulatory approval, if any,on our own.

We have a manufacturing plant in Italy where we produce APIs such as the defibrotide compound, sodium heparin, urokinase and sulglicotide. These APIs are subsequently used to make the finished forms of various drugs. With respect to defibrotide, we have contracted with Patheon S.p.A. to process the defibrotide compound into its finished form at Patheon's manufacturing facility. We believe that we are the sole worldwide producer of defibrotide. Our operating assets are located in Italy.

We have Italian, United States and international trademark rights in "Gentium", United States and European Union trademarks in "Gentide", Italian, United States and European trademarks in "Defitelio", Italian and European trademarks in "Defrex", international and Italian trademark rights in "Oligotide" and Italian trademark rights in "Pharma Research" and "Dinelasi". 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. The FDA, the EMA and the KFDA have designated defibrotide to treat and prevent VOD, as "orphan drugs". If the FDA or the EMA grant us a marketing authorization for those uses of defibrotide, we will have market exclusivity for those uses for seven and ten years following the date of approval, respectively.

This annual report contains market data and industry forecasts that were obtained from industry publications and third parties.

CAPITAL EXPENDITURES

The following table sets forth our capital expenditures for each year in the three-year period ended December 31, 2012.

	For the Year Ended December 31,		
(in thousands)	2010	2011	2012

Land and buildings	€-	€8	€4
Plant and machinery	129	84	43
Industrial equipment	7	4	27
Other	9	213	52
Leasehold improvements	50	718	97
Computer Software	-	23	11
Construction in progress	10	228	159
Total	€205	€1,278	€393

All of these capital expenditures were in Italy with the exception of a few computer purchases. We financed these expenditures with revenue and cash-flow generated from the distribution and sale of our product candidates, on a pre-approval basis, under the cost recovery and named-patient programs.

BUSINESS OVERVIEW

We are building upon our experience with defibrotide, an investigational drug based on a mixture of single- and double-stranded DNA extracted from pig intestines and purified to a set of defined molecular weights and charges which our founding company discovered over 20 years ago. We are focused on the development and manufacture of defibrotide to treat and prevent VOD, a condition that occurs when veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation, that are administered prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is linked to multiple-organ failure and high rates of morbidity and mortality. We manufacture the defibrotide compound at our manufacturing facility near Como, Italy. We have contracted with Patheon S.p.A. to process this defibrotide compound into its finished form at Patheon's manufacturing facility. 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.

On May 10, 2011, we announced the filing of our MAA under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. We plan to appeal this decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

On July 6, 2011, we announced the filing of our NDA with the FDA for defibrotide for the treatment of VOD in adults and children undergoing hematopoietic stem cell transplantation. On August 17, 2011, we announced our voluntary withdrawal of our NDA following correspondence from the FDA identifying several potential "Refuse to File" issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with CROs and consultants to address the issues raised by the FDA and plan to resubmit our NDA in 2013.

While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis througout the U.S. pursuant to our IND protocol, which we refer to as our cost recovery program, and throughout the rest of the world on a named patient basis, which we refer to as our named-patient program, or NPP. We received €13.18 million, €16.89 million, and €22.77 million through our named-patient and cost recovery programs in 2010, 2011 and 2012, respectively.

We have entered into a license and supply agreement with Sigma-Tau (as assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.) to commercialize defibrotide for the treatment and prevention of VOD in the Americas upon FDA approval, if any. Pursuant to the terms of this license agreement, between 2001 and 2010 we received US$ 11.35 million in milestone payments. We are entitled to an additional payment of US$ 6 million following regulatory approval from the FDA to market defibrotide in the U.S., and a further US$ 2 million payment following the transfer of the approved NDA to Sigma-Tau. In addition, in connection with such agreement, Sigma-Tau has agreed to reimburse us with certain costs associated with the development of defibrotide. We continue to work with Sigma-Tau on our U.S. regulatory strategy.

In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as headquarters for our commercial operations. We have entered into license and/or supply and distribution agreements with specialized regional partners to distribute debibrotide, including on a named-patient basis, in the following territories: the Asian Pacific, the Middle East and North Africa, Europe, the Nordics and Baltics, Turkey, Israel and the Palestinian Authority. Certain of these regional partners have also agreed to assist us with local registration, marketing authorization, reimbursement, marketing, sales and distribution and medical affairs activities following regulatory approval, if any. We plan to distribute defibrotide in major European countries upon regulatory approval, if any, on our own.

We manufacture sulglicotide, sodium heparin and urokinase. These APIs are used to make other drugs. Our revenues from the sales of these APIs amounted to €6.53 million, €4.85 million and €4.86 million in 2010, 2011 and 2012,

respectively.

Market Overview

Chemotherapy, radiation therapy and hormone therapy treatments are used to target and kill cancer cells. In some cases, these therapies treat the cancer directly; in other cases, they are administered to prepare the patient for a stem cell or bone marrow transplant, which then 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 who are considered to be at high risk of developing these vascular system complications may not receive optimal cancer treatments or any treatment at all.

One disorder of the vascular system that can result from chemotherapy, radiation therapy, hormone therapy or 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 the cell damage 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, may lead to failure of the liver and other organs (multiple-organ failure), which usually results in death. According to 2003 data collected from the International Bone Marrow Transplant Registry and the European Bone Marrow Transplant Registry, approximately 21,000 people receive a bone marrow transplant, which is a type of stem cell transplant, each year in the United States. Based on our review of more than 200 articles in medical literature, we believe that approximately 12% of patients who undergo a stem cell transplant 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. A historical study conducted by Dana-Farber at three centers consisting of 38 patients showed that only approximately 11% of patients who develop severe VOD achieve a complete response within 100 days after stem cell transplantation and only approximately 20% survive for more than 100 days. The historical control arm of our Phase III trial achieved similar results, with approximately 9% of patients who developed severe VOD achieving a complete response within 100 days after stem cell transplantation and only approximately 25% surviving for more than 100 days. VOD poses a severe risk to the victim's health and life. To our knowledge, there are no FDA or EMA approved treatments for VOD at this time.

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., to commercialize defibrotide in the Americas. Outside of the Americas, we have developed and will continue to develop appropriate partnerships for the commercialization of defibrotide in other parts of the world, and we plan to commercialize defibrotide in the major European countries on our own through our wholly-owned subsidiary, Gentium GmbH.

· Obtain regulatory approval to use defibrotide to treat and prevent VOD. Gentium, as well as independent investigators, have conducted several studies that show the potential efficacy and safety of defibrotide as a treatment and a method of prevention of VOD (see detail under the "Product Candidate" section below). Defibrotide for the treatment and prevention of VOD has received orphan status from the FDA, the EMA and the KFDA. In addition, we have received fast track designation from the FDA for the use of defibrotide for the treatment of severe VOD prior to stem cell transplantation. The EMA recently denied our MAA for defibrotide for the prevention and treatment of VOD, and we have withdrawn our NDA for the treatment of VOD with the FDA. We plan to explore all opportunities to achieve regulatory approval, including a resubmission of our NDA in 2013, appealing the decision by the EMA regarding our MAA, and conducting additional clinical studies.

• Compassionate use programs to maximize pre-approval data. We distribute defibrotide for the treatment and prevention of VOD on a pre-approval compassionate use basis through our named-patient and cost recovery 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 conducted as necessary. In 2011 and 2012, approximately 1,000 and 1,200 patients received defibrotide through these programs.

• Explore other indications for defibrotide. Defibrotide may be beneficial to other diseases, such as acute graft versus host disease, or aGvHD, where it has shown promising preliminary data in a clinical trial. Similarly, defibrotide was shown to provide some benefit to multiple myeloma in a preliminary clinical trial.

• Expand our portfolio by adding additional compounds to our pipeline. It is our intention to continue evaluating opportunities for compounds that might be available and will allow us to expand our existing pipeline.

• Continue to increase the usage of defibrotide on a named-patient basis. We have entered into license and/or supply distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient basis in various territories, including the Asian Pacific, the Middle East and North Africa, Europe, the Nordics and Baltics, Turkey, Israel and the Palestinian Authority. We will continue to develop appropriate partnerships that will enable us to distribute defibrotide in additional territories in other parts of the world.

• Increase our marketing capacity, including the use of strategic partnerships. Following regulatory approval for defibrotide, if any, we plan on marketing and distributing defibrotide through our subsidiary, Gentium GmbH, in major countries throughout Europe and through strategic partnerships throughout the rest of the world, such as Sigma-Tau Pharmaceuticals, Inc., to which we have given the license to market defibrotide for the treatment and prevention of VOD in North America, Central America and South America upon regulatory approval.

Product Candidate

Defibrotide is an investigational drug based on a mixture of single- and double-stranded DNA extracted from pig intestines and purified to a set of defined molecular weights and charges, which is under development for the treatment and prevention of VOD, a disease caused by certain cancer treatments, such as chemotherapy and radiation, that are administered prior to stem cell transplantation. Currently, and to the best of our knowledge, there are no FDA

or EMA approved treatments for this life-threatening disease. Defibrotide for the treatment and prevention of VOD has been given "orphan" status by the FDA and the EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide for the treatment and prevention of VOD has also been granted "orphan" status by the KFDA. The FDA has also granted fast-track product designation to defibrotide 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-approval basis under our IND protocol in the U.S. and through a named-patient program throughout the rest of the world.

We manufacture the defibrotide compound at our plant near Como, Italy. This compound is then sent to Patheon S.p.A. to be processed into its finished form. We believe that we are the sole worldwide producer of defibrotide.

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 on defibrotide to treat VOD, which was conducted in 19 centers in Europe from December 1997 to June 1999. Twenty-two patients, or 55%, showed a complete response to the treatment. Nineteen patients, or 47%, survived more than 100 days after stem cell transplantation. The study showed that four of the 19 patients who had survived for more than 100 days subsequently died. Twenty-eight patients were deemed likely to die or exhibited 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 survived for at least 100 days. The study concluded that defibrotide was generally safely administered with no significant side-effects.

The December 15, 2002 edition of Blood published results of a study involving 88 patients who contracted severe VOD following stem cell transplants and were treated with defibrotide over a 6 year period from March 1995 to May 2001. 19 patients were treated under individual IND Applications and 69 patients were part of a multi-center Phase I/II clinical trial conducted under an IND Application submitted by a Dana-Farber investigator. The primary goal of the trial was to assess 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%, survived for at least 100 days after stem cell transplantation with only minimal adverse effects, with the primary effect being transient mild hypotension. Thirteen of those 31 patients who had survived more than 100 days died by October 2001, the last date on which survival information was available.

The Dana-Farber investigator also sponsored a Phase II clinical trial in the United States under his IND Application, involving 150 stem cell transplant patients with severe VOD, 141 of whom 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 defibrotide, including its impact on the survival rate of patients with severe VOD, the effectiveness of the dosages administered 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. The results showed that of the 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 for at least 100 days after stem cell transplantation, with minimal adverse effects.

The January 2004 edition of Bone Marrow Transplantation published the results of a study involving 45 children and adolescents who contracted VOD following stem cell transplants and were treated with defibrotide. Twenty-two of the 45 patients had severe VOD. Thirty-four of the 45 patients, or 76%, showed a complete response within 100 days after stem cell transplantation and 29 patients, or 64%, survived for at least 100 days after stem cell transplantation. Of the 22 patients with severe VOD, 11 patients, or 50%, showed a complete response within 100 days after stem cell transplantation and 8 patients, or 36%, survived for at least 100 days after stem cell transplantation. The study showed that defibrotide was well tolerated; about one-third of the patients developed a form of coagulopathy, and treatment was discontinued in two cases where a severe bleeding disorder was observed, although these events could not be clearly attributed to defibrotide.

In December 2005, we initiated a historical control Phase III clinical trial in the United States, Canada and Israel for this use of defibrotide on patients with severe VOD. We used a historical control arm because our clinical investigators believed it was unethical to refuse treatment to patients when such treatment could potentially save their lives. The primary endpoint was complete response within 100 days after stem cell transplantation and the secondary

endpoint was survival after 100 days. On December 7, 2009, final clinical trial results for our current Phase III clinical trial of defibrotide to treat severe VOD were presented at the American Society of Hematology Conference in New Orleans. On an intent to treat (ITT) basis, 24% of patients in the defibrotide arm achieved complete response at 100 days compared to 9% of patients in the historical control arm (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 of the patients were unequivocally diagnosed with 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.

In 2007, based on a request from the FDA, we initiated our expanded access program for defibrotide under our treatment IND protocol, which gives patients diagnosed with VOD in the United States access to defibrotide. During the course of these years, results from the ongoing IND protocol have been presented at scientific conferences. Under an expanded access program, the FDA allows early access to investigational drugs that are under development for the treatment of serious or life-threatening diseases for which there are no satisfactory alternative therapies. Our decision to launch this expanded access program was due to the large number of requests for access to defibrotide on a compassionate use basis, and the corresponding burden that sites and investigators have endured to obtain institutional review board and FDA approval for such compassionate use requests. We have been able to recover the costs associated with the distribution of defibrotide pursuant to our IND protocol for this expanded access program, which is why we now refer to this program as our cost recovery program. On September 29, 2009, we entered into an agreement with US Oncology, a clinical research organization, under which US Oncology agreed to administer and recover costs on our behalf in connection with this program. We expect to collect additional usage tolerability and safety data from patients of this program to support our planned NDA for the treatment and prevention of VOD.

On December 7, 2010, interim results of our IND study of defibrotide in the treatment of severe VOD were presented at the American Society of Hematology Conference in Orlando. This study is currently ongoing in the US. The interim analysis reported results of 104 patients with severe VOD, enrolled at 36 US institutions. Between December 2007 and September 2009, 31 patients (30%) achieved a complete response (CR) by D+100 and 33 patients (32%) survived to Day + 100 post stem cell transplant. In this population, no unexpected toxicities were observed and defibrotide-associated toxicities were consistent with prior studies. A poster on the safety of defibrotide was also presented. At time of the presentation, 1824 stem cell transplant patients had received defibrotide in controlled and uncontrolled studies for the treatment or prevention of VOD and severe VOD; the majority of these patients received the current 25 mg/kg/day dose. A review of safety for defibrotide was undertaken to assess the overall safety profile of defibrotide in this more compromised stem cell transplantation population that is predisposed to increased regimen related toxicities, including hemorrhagic and thrombotic complications. The safety database of 1824 includes data from the Phase II and the Phase III severe VOD treatment studies and the phase Phase II/III pediatric prevention of VOD study. Overall, the incidence of related adverse events was 1% (9 out of 772 patients) in VOD prophylaxis and 9% (96 out of 1052 patients) in patients who had received defibrotide for the treatment of VOD and severe VOD.

On July 6, 2011, we announced the filing of our new drug application, or NDA, with the FDA for defibrotide for the treatment of hepatic VOD in adults and children undergoing hematopoietic stem cell transplantation. On August 17, 2011, we announced a voluntary withdrawal of our NDA following correspondence from the FDA identifying several potential “Refuse to File” issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with contract research organizations, or CROs, and consultants to address the issues raised by the FDA and plan to resubmit our NDA in 2013.

On December 12, 2011, we announced the updated results on the ongoing treatment IND protocol for defibrotide. The analysis was based on 269 patients with severe VOD and multi-organ failure, or MOF, enrolled between December 2007 and March 2011 at 67 centers across the United States. 251 patients had undergone stem cell transplant (SCT) and the remaining 18 had developed VOD after chemotherapy alone. Of the 269 patients, 32% achieved a complete response (CR) and 50% survived to day 100 (D+100). Additional findings were as follows; In the subgroup of SCT patients, 31% (78/251) achieved a CR and 50% survived to D+100. In the 18 chemotherapy-only patients, CR was 39% and D+100 survival was 50%. Of 200 patients with severe VOD, CR was 28% and D+100 survival was 44%. Early initiation of defibrotide treatment (< 2 days, versus a delay of > 2 days) following VOD diagnosis resulted in increased CR (35% versus 23%, p=0.03) and survival (56% versus 37%, p=0.01). CR rate and D+100 survival for the 69 patients with non-severe VOD were 42% and 62%, respectively. 134 patients met entry criteria for the original Phase III trial of defibrotide and comparison to the Phase 3 historical control showed a statistically improved outcome in CR (30% vs 9%, p= < 0.01) and D+100 survival (46% vs 25%; p= < 0.01). The incidence of all grade graft versus host disease, or GvHD, in the allogeneic SCT patients (225/251) was 8%, similar to the observation of decreased GvHD in other studies of defibrotide. These results confirm the findings of previous trials and support early

intervention with defibrotide following diagnosis of VOD. Additionally, there were low incidences of GvHD in allogeneic-SCT patients treated with defibrotide and of treatment-associated toxicities, both consistent with prior studies of defibrotide.

On December 13, 2012, we announced that additional data from ongoing trials of defibrotide were presented at the 54th Annual Meeting and Exposition of the American Society of Hematology held at the Georgia World Congress Center in Atlanta. The Clinical Director of the Dana-Farber Cancer Institute reported updated results on our ongoing study of defibrotide for the treatment of hepatic VOD in hematopoietic stem cell transplant patients through our treatment IND protocol. The interim analysis was based on 333 patients with severe VOD and multi-organ failure, enrolled between December 2007 and September 2011 at 68 centers across the United States. 305 patients had undergone hematopoietic stem cell transplant and of those patients, 30% of patients achieved a complete response and 50% survived to day 100. In the subgroup of HSCT patients with severe VOD, 26% achieved a complete response and 45% survived to day 100. In patients with non-severe VOD, 39% achieved complete response and 65 % survived to day 100. In the treatment IND protocol, 155 patients matched the entry criteria for the original Phase III trial and comparison to the Phase III historical controls showed a statistically improved outcome in complete response (29% vs 9%, p=0.0019) and day 100 survival (49% vs 25%, p=0.0016). Delayed initiation of defibrotide treatment (>2 days, versus a delay of <2 days) following VOD diagnosis resulted in reduced complete response (20% versus 34%, p=0.0195) and survival (37% versus 56%, p=0.0118). The complete response rate and survival for the 69 patients with non-severe VOD were 42% and 62%, respectively. Children younger than 16 years old had higher complete rates than adults (33%vs 26%, p=0.187) and survival (56% vs 44%, p=0.277).

On December 13, 2012, an abstract titled "Evaluation of Defibrotide in the treatment of hepatic veno-occlusive disease in non stem cell transplant (non sct) chemotherapy patients: results from the Treatment IND (T-IND) expanded access protocol and the compassionate use program (CUP)" was presented at the 54th Annual Meeting and Exposition of the American Society of Hematology held at the Georgia World Congress Center in Atlanta. The analysis is based on a total of 89 patients who developed VOD after chemotherapy (chemo) alone: 61 patients in the CUP and 28 patients in the T-IND. Patients were enrolled in the CUP between December 1998 and March 2009; median age was 14 years (range 0.2–65) and 66% were male. In the T-IND the chemo patients were enrolled from December 2009 to September 2011; median age was 8 years (range 0.2–58) and 50% were male. The most common diagnoses were ALL (36% and 32%) and AML (30% and 25%) in the CUP and T-IND, respectively. Vincristine, cytarabine and cyclophosphamide were the most frequent chemotherapeutic agents associated with VOD, and with the exception of cyclophosphamide, their prior exposure was relatively similar between arms: patients in the CUP and in the T-IND, respectively, were treated with vincristine (31% and 46%), cytarabine (25% and 39%), and cyclophosphamide (16% and 61%). The median onset of VOD after chemotherapy was 19 days and 16 days in the CUP and T-IND, respectively, and sVOD was present in 46% and 50% of patients at study entry in the CUP and T-IND, respectively.

Overall, 53% (47/89) of patients achieved CR, with 53% (25/47) of patients with non-severe VOD achieving CR and 52% (22/42) of patients with sVOD achieving CR. Overall, 68% and 67% of patients were alive at D+100 (Kaplan-Meier estimate) in the CUP and T-IND, respectively, 65% and 69% of patients with non-severe VOD were alive at D+100 in the CUP and T-IND, respectively, and 72% and 64% of patients with sVOD were alive at D+100 in the CUP and T-IND, respectively. When VOD outcomes were compared to the SCT population of the T-IND (Richardson PG, et al. Blood [ASH Annual Meeting Abstracts] 2011;118:487), CR was 43% in non-SCT pts vs 30% in SCT and survival was 68% vs 50%, respectively.

Defibrotide to prevent VOD

We believe there is a significant opportunity to market defibrotide to patients who are at risk of developing VOD. Based on our research of VOD, we believe that recipients of high doses of chemotherapy, radiation therapy, hormone therapy, or of therapies that prepare for stem cell transplants have an elevated risk of developing VOD. With the support of the European Group for Blood and Marrow Transplantation, a not-for-profit scientific society, we conducted a Phase II/III clinical trial in Europe and Israel involving defibrotide to prevent VOD in children. Unlike our Phase III treatment trial in the United States, which used a historical control arm of untreated patients, this clinical trial included 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 involving 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 who received the drug experienced significant bleeding.

At the 2005 annual meeting of the European Group for Blood and Marrow Transplantation, the results of a study on defibrotide administered to patients who received chemotherapy and stem cell transplants were announced. Eight of 44 patients, or 18%, who received defibrotide developed VOD, three of which, or 7%, developed severe VOD. By comparison, four of 16 control group patients, or 25%, who received heparin instead of defibrotide developed VOD, two of which, 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 of a preliminary pilot clinical study conducted by the University Hospital of Geneva in Switzerland involving defibrotide administered to patients at high risk of VOD were announced. The results suggest that defibrotide may effectively and safely prevent 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, prior to the study, 10 of 52 patients

who underwent transplants in the same center developed VOD, which was fatal in three cases. The study report indicated that mild to moderate toxicities, including mild nausea, fever and abdominal cramps, were observed in patients who received defibrotide, although it was difficult to determine whether the toxicities were 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 toxicity.

The July 2007 edition of Bone Marrow Transplant published the results of a study on defibrotide administered to patients who received stem cell transplants. While a majority of these patients were recipients of reduced intensity cancer treatments, there were other factors putting each of them at risk 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, final clinical trial results from our Phase II/III pediatric prevention study to prevent VOD were presented 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 mortality was four times higher for patients with VOD, independent of severity, than for patients without VOD. Additionally, the incidence and severity of acute graft versus host disease, or GvHD, by day 100 in the allogeneic SCT recipients (246 patients) was significantly reduced from 63% in the control arm to 45% in 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.

On February 23, 2012, the final results of the Phase III randomized control trial which evaluated defibrotide for use in preventing hepatic VOD in pediatric patients were published in the medical journal, The Lancet (Vol 379). The results of Corbacioglu et al. showed that defibrotide led to a 40% a reduction in the incidence of VOD 30 days after hemopoietic stem cell transplantation, or HSCT, in patients receiving defibrotide, compared with those who did not receive defibrotide. Additionally, in allogeneic HSCT recipients, the incidence and severity of aGvHD were significantly lower in the defibrotide arm.

On May 10, 2011, we announced the filing of our MAA under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. We plan to appeal this decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

Defibrotide Pre-Approval

Defibrotide is being distributed in the United States through an expanded access program pursuant to a treatment IND protocol, which gives patients diagnosed with VOD access to defibrotide, and throughout the rest of the world on a named-patient basis, which we refer to our named-patient program.

On September 29, 2009, we entered into an agreement with US Oncology pursuant to which US Oncology agreed to administer and recover costs on our behalf in connection with our cost recovery program in the U.S.. Through our wholly-owned subsidiary, Gentium GmbH, we have entered into distribution agreements with certain regionalized partners to distribute defibrotide on a named-patient basis. We expect to collect additional usage tolerability and safety data from patients of these programs to support our regulatory applications.

We received €13.18 million, €16.89 million, and €22.77 million through our named-patient and cost recovery programs for 2010, 2011 and 2012, respectively.

Other Products

Sulglicotide

Sulglicotide is developed from swine duodenum and appears to have ulcer healing and gastrointestinal protective properties. We manufacture sulglicotide at our manufacturing facilities near Como, Italy. We sell sulglicotide primarily to a Korean partner, which uses this API to finish a drug that it markets in South Korea.

Urokinase

Urokinase is made from human urine and has the potential to dissolve fibrin clots. We manufacture urokinase at our facility near Como, Italy. Two companies purchase this API to create a finished drug that treats various vascular disorders such as deep vein thrombosis and pulmonary embolisms.

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, manufacturing, 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, as well as 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, denial of approval by the government, the 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 observed certain deficiencies in regard to the operation of our facility. We have corrected all of the deficiencies noted. In addition, 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, and we must receive verification and validation of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but since 2004 we have 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 endure a long and rigorous process before any of our product candidates may be marketed or sold in the United States. This regulatory process generally requires:

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

- submission to and acceptance by the FDA of an IND Application 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;

    - 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 resulted in a change in the oversight and approval process for certain therapeutic biologic drugs and a reassignment of responsibility for the process 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 now being regulated through the latter.

Preclinical Testing

Preclinical testing generally includes laboratory evaluation of a product candidate, including its chemistry, formulation, stability and toxicity, as well as certain animal studies to assess the potential safety and effectiveness of the product candidate. 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 IND 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, prior to the expiration of this 30-day time period, the FDA raises concerns or questions regarding 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 IND Application based on those studies will become effective, and allow clinical testing to begin.

Clinical Trials

In addition to FDA review of an IND Application, each clinical institution that desires to participate in a proposed clinical trial must obtain approval of its clinical protocol by an Institutional Review Board. Institutional Review Boards review clinical trials for the purpose of protecting the rights and safety of human subjects. In this regard, in rendering decisions on approval, they review; among other things, ethical factors, and the processes for obtaining informed consent and the selection and safety of human subjects. Clinical trials must also be conducted in accordance with FDA regulatory requirements. The FDA, and/or the Institutional Review Board associated with the institution at which a clinical trial is being performed, may order the temporary or permanent discontinuation of a clinical trial if, at any time, it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an

unacceptable risk to the clinical trial subjects.

Human clinical trials are typically conducted in three sequential phases, which may overlap, and include the following:

Phase I

In Phase I clinical trials, a product candidate is typically administered either to healthy people or to 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. The trial may also be conducted to 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 potential 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, then 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 the overall risk-benefit relationship of the product candidate. The successful demonstration of clinical effectiveness and safety in one or more Phase III trials is generally a prerequisite to the filing of an application for FDA approval of the product candidate.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the product candidate is submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more indications, together with payment of a user fee, unless waived. An NDA includes all relevant data available from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the chemistry, manufacture, controls (CMC) and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the product candidate for its intended use to the satisfaction of the FDA.

If an NDA submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA's goal is to complete its initial review and respond to the applicant within 12 months of submission, unless the application relates to an unmet medical need in a serious or life-threatening indication and is designated for priority review, in which case the goal may be within eight months of NDA submission. However, PDUFA goal dates are not legal mandates and FDA response often occurs several months beyond the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests, or the NDA sponsor otherwise provides, additional information or clarification regarding information already provided in the NDA. The NDA review process can, accordingly, be very lengthy. During its review of an NDA, the FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical studies are not always conclusive and the FDA and/or any advisory committee it appoints may interpret data differently than the NDA sponsor.

After the FDA evaluates the NDA and inspects manufacturing facilities where the drug product and/or its API will be produced, it will either approve commercial marketing of the drug product with prescribing information for specific indications or issue a complete response letter indicating that the application is not ready for approval and stating the conditions that must be met in order to secure approval of the NDA. If the complete response letter requires additional data and the applicant subsequently submits that data, the FDA nevertheless may ultimately decide that the NDA does not satisfy its criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategies, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans,

or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing. Such post-marketing testing may include phase 4 clinical studies and surveillance to further assess and monitor the product's safety and efficacy after approval. Regulatory approval of products for serious or life-threatening indications may require that participants in clinical studies be followed for long periods to determine the overall survival benefit of the drug.

Post-Approval Regulations

Any approval of a product candidate is limited to specific clinical uses. Subsequent discovery of previously unknown side effects or other problems relating to a product may result in additional restrictions on its use or even the complete withdrawal of the product from the market. All FDA-approved products that we manufacture or distribute are subject to continuing regulation by the FDA, which requires record-keeping and reporting of adverse events or experiences. Drug manufacturers are required to register their establishments with the FDA and state agencies, and are subject to periodic inspections by the FDA and state agencies to ensure 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, a denial by the FDA of marketing approvals, or the withdrawal, suspension, or revocation of marketing approvals.

If the FDA approves one or more of our product candidates, we, along with our contract manufacturers, must provide certain safety and effectiveness information while the drug is being marketed. Changes in the product, as well as changes in the manufacturing process or facilities, 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 must also be in compliance with FDA requirements relating to, among others, disclosure of risk information, standards and regulations for communication of information relating to off-label uses, industry sponsored scientific and educational activities and other promotional activities, including those involving the Internet. The FDA has very broad enforcement authority, and failure to abide by these requirements can result in a warning letter mandating the correction of deviations from regulatory standards, or enforcement actions that can include seizures, fines, injunctions and criminal prosecution.

Fast track and orphan drug designation

The FDA has a "fast track" program which allows 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, and where there is a defined unmet medical need, particularly when no satisfactory alternative therapy exists or the new therapy is found to be 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. Approval of an application for a fast track review can be based on an effect on a clinical endpoint, or on a surrogate endpoint that is reasonably likely to predict a clinical benefit. The FDA may condition the approval of an application for fast track review on additional post-approval studies that validate the surrogate endpoint or confirm the effect on the clinical endpoint. Fast track status also provides the potential for a product candidate to obtain a "priority review." A priority review allows for a portion 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 of 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 after approval if the clinical trial results do not continue to support that the 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 FDA scrutiny of promotional materials.

The FDA may grant orphan drug status to drugs intended to treat a "rare disease or condition," which is generally characterized as 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 publicly disclosed 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 competing product candidates targeting the same uses. A product that has been designated as an orphan drug and subsequently receives the first FDA approval for the designated orphan use is entitled to orphan drug exclusivity, which means that, except in limited circumstances, the FDA may not approve any other applications for the same indication 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 grant program for clinical studies.

The FDA has designated defibrotide as an orphan drug for the treatment of VOD and the prevention of VOD and has provided funding for clinical studies for defibrotide to treat VOD. The FDA has approved our 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 apply for orphan drug status and fast track status for these other products.

Market Exclusivity

In addition to orphan drug exclusivity, a product regulated by the FDA as a "new drug" may be entitled to non-patent and/or patent exclusivity under the Federal Food, Drug and Cosmetic Act, or FFDCA, over 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 date of approval of the new chemical entity. With regard to any drug substance (active ingredient), drug product (formulation and composition) and method of use patent listed with the FDA, patent exclusivity under the FFDCA precludes the 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 either the NDA/patent holder does not file an infringement action within 45 days of receipt of notification of the certification, or an infringement action is filed 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 due to hardship or on other grounds.

HIPAA

Certain federal and state legislation may affect our ability to obtain certain health information in conjunction with our research activities. Specifically, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, and the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, mandate, among other things, that covered entities and business associates safeguard the privacy and security of individually identifiable health information in specific ways. In relevant part, the U.S. Department of Health and Human Services, or HHS, has released two rules to date, which mandate how the confidentiality and integrity of such information must be protected. The Privacy Rule imposes standards relating to the privacy of individually identifiable health information. These standards restrict the manner and circumstances under which covered entities and their business associates 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. HIPAA and the HITECH Act impose requirements on covered entities and business associates, including those covered entities and/or their business associates that conduct research activities regarding the use and disclosure of individually identifiable health information. As a result, unless covered entities conducting clinical trials for us obtain an effective authorization from each research subject for the release of the subject's individually identifiable health information meeting applicable requirements, such covered entities or their business associates may not be able to share with us all of the 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 receipt of marketing authorizations from the appropriate foreign regulatory authorities, regardless of whether or not FDA approval has been obtained. The foreign regulatory approval process in most industrialized countries generally involves risks similar to those associated with the FDA approval process, as described herein. The requirements governing the conduct of clinical trials and marketing authorizations, and the time required to obtain requisite approvals may widely vary from country to country and may 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 under a centralized, mutual recognition, or decentralized procedure.

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 information regarding the product candidate, including a description of the product applicant and the location of the production plant, along with payment of the application fees. The EMA formally evaluates the preliminary request and either indicates initial approval or a rejection of the preliminary request. If the EMA indicates an initial approval of the preliminary request, the applicant must then submit a full application to the EMA for review. 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 EMA (through its CHMP) 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 EMA may reject the application if the Agency decides that the quality, safety and effectiveness of the product candidate have not been adequately and sufficiently proven by the applicant, or if the information and documents filed are incomplete, or where the labeling and packaging information proposed by the applicant does not comply with the relevant European rules.

The EMA has also established an accelerated evaluation procedure applicable to product candidates intended to treat or prevent serious diseases or conditions for which no suitable therapy exists, and for which substantial beneficial effects on patients can be predicted.

The marketing authorization is valid for five years and may be renewed, upon application, for additional 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 generally accepted scientific methods.

We filed our MAA for defibrotide under the centralized procedure.

The mutual recognition procedure

Under the mutual recognition procedure, the holder of a national marketing authorization, obtained in accordance with the procedure and requirements applicable in the member state concerned, is entitled to submit an application to the remaining member states in which it seeks a marketing authorization. Within 90 days of receipt of the application and assessment report, each member state must decide whether or not to recognize approval. The mutual recognition process results in separate national marketing authorizations in the reference member state and each concerned member state.

The decentralized procedure

The decentralized procedure should be used for products that have not yet received authorization in a European Union member state. The applicant may request one or more concerned member state(s) to approve a draft assessment report, a summary of product characteristics, the product labeling and a package leaflet as proposed by the chosen reference member state. If a member state cannot approve the assessment report, the summary of product characteristics, the product labeling and the package leaflet on grounds of potential serious risk to human and animal health or to the environment, a pre-referral procedure should be commenced by the relevant coordination group. If the member states fail to reach an agreement during the 60-day pre-referral procedure, the matter is deferred to an arbitration proceeding.

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 any adverse reaction to the drug of which it becomes aware, regardless of the country in which the reaction occurs, and prepare periodic update reports on these adverse events. The holder of the authorization must hire and retain for its organization an expert who will be responsible for 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 sets the standards for and limitations on advertising messages generally, and specific promotional activities, such as the organization of conferences regarding certain drugs and the distribution of free samples.

The export of drugs (other than plasma and blood-related products) from Italy is not subject to authorization, but the import of drugs into Italy from non-European Union countries is subject to authorization 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, which 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 the EMA responsible for overseeing the requirements of the pediatric regulation. The PDCO may issue a waiver with respect to the use of a medicinal product in certain (or all) indications and/or certain (or all) pediatric age groups, or it may issue a deferral of the start or completion dates of all or some of the studies in the PIP. If a sponsor complies with a PIP agreed by PDCO, the sponsor may be eligible for a six-month extension on patents covering the product described in the plan. If the product has been designated an orphan drug by the EMA, it may be eligible for 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 a designation may include incentives for the research, development and marketing of these drugs, and allows for an extended period of market exclusivity in the event of a later successful application for a marketing authorization regarding the therapeutic indications for which orphan status was awarded.

A medicinal product, during any stage of its development but, in any case, prior to the filing of any application for the marketing authorization, may be designated as an orphan drug if the person/entity that has applied for the designation can establish that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five persons out of every ten thousand persons in the European Union, or

that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and, 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 no satisfactory method of diagnosis, prevention or treatment of the condition in question has been authorized in the European Union or, if a satisfactory method exists and has been authorized, 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 must submit an application to the EMA 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 EMA 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 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 becomes 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 registration, the product sponsor must submit an annual report to the EMA describing 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;
- before the market authorization is granted, if it is established that the requirements provided for in the European orphan drug legislation are no longer being 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 set forth in the legislation are no longer met by the orphan drug, or if 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 as 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 to the orphan drug.

Raw Materials

Our products and product candidates are produced from DNA extracted from pig intestines, using well-established processes that are used by others to manufacture various drugs. In particular, defibrotide is derived from swine intestinal mucosa and sulglicotide is derived 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, 2013, 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, 2013, 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 currently do not have arrangements with any other supplier for this critical raw material, we believe there are suitable alternative sources of pig intestines. The FDA and other regulatory bodies may evaluate La.bu.nat.'s or any other supplier's processing centers in connection with the approval of our product candidates and the ongoing production of our products.

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

Historically, there has been no significant price volatility for any of our raw materials. However, given the demand for swine mucosa for heparin, we may experience volatility in the price of pig intestines. In addition, the 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:

- manufacturing cost control;
- 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 that the drugs are designed to treat or prevent, 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 protections; and
- sales and marketing capabilities.

We face competition in the product candidate development and marketing arenas. During development, the existence or discovery of alternative treatments for similar or completely different disorders may limit our ability to acquire participants or co-sponsors in connection with clinical trials for our product candidates. Any product candidates that we successfully develop and 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. There may be organizations, including large pharmaceutical and biopharmaceutical companies, as well as academic and research organizations and government agencies, who are interested in pursuing the research and development of drug therapies that target the blood vessel wall. Many of these organizations have substantially greater research and development capabilities and experience and greater manufacturing, marketing and financial resources than we have. In addition, these companies' products and product candidates are in more advanced stages of development than our product candidates or have otherwise been approved for sale by the FDA and other regulatory agencies. As a result, our competitors may develop or license products or other novel technologies that are more effective, safe or cost efficient than our existing products or products that we are developing, 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 which have been involved in the research and development of drugs derived from DNA and DNA molecules since the 1970's. In 1993, we were formed by F3F S.p.A. (formerly known as FinSirton S.p.A.) as Pharma Research S.r.L., an Italian private limited company, for the purpose of pursuing research and development activities of prospective pharmaceutical specialty products. In December 2000, we converted into a corporation and in July 2001, we changed our name to Gentium S.p.A.. F3F S.p.A. is one of our largest shareholders, and may be deemed to be 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. Under our current bylaws, our terms of existence will expire on December 31, 2050.

In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as headquarters for our commercial operations. We plan to carry all commercial activities through this subsidiary.

PROPERTY, PLANT AND EQUIPMENT

Manufacturing and Facilities

We own a manufacturing facility near Como, Italy which, at December 31, 2012, is subject to a mortgage securing repayment of an aggregate of €1.32 million of debt owed to Banca Nazionale del Lavoro. The manufacturing facility is 2,350 square meters in size. We rely on a third party to generate steam used in our manufacturing process, but in 2013 we plan to install our own steam generator at an estimated cost of €250 thousand in order to satisfy this need.

In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets its current good manufacturing practices, or GMPs, including requirements for equipment verification of our manufacturing and cleaning processes. The FDA has not yet inspected our facility, but since 2004 we have spent more than €10 million on upgrades to our facility in anticipation of such inspection.

We produce defibrotide and sulglicotide at this facility and have the capability to produce sodium heparin. We typically operate our manufacturing facility on two eight hour shifts per day. Our estimated current production, maximum production capacity, and percentage of utilization for defibrotide for the fiscal year 2013 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%

Our estimated current production, production capacity, and percentage of utilization for sulglicotide for the fiscal year 2013 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	6,000	8,626	69%

Our estimated current production, production capacity, and percentage of utilization for urokinase for the fiscal year 2013 are set forth below:

Product	Estimated Current Production Level (millions of units/year)	Maximum Production Capacity With One Eight Hour Shift (millions of units/year)	Percentage of Utilization
Urokinase	39,600	39,600	100%

Our facility is subject to the regulation of regional agencies regarding worker health and safety, the fire department, and Azienda Sanitaria Locale and Agenzia Regionale Prevenzione e Ambiente with respect to water, air, noise and environmental pollution protection. 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 to encounter difficulties in complying with these regulations. We have also installed two scrubbers to reduce the odors and chemicals released into the air by the facility in order 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. Both certifications were renewed in 2010 and we are currently working on obtaining renewals for the certifications for an additional three-year period following their expiration. Our environmental policy is designed to comply 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 approximately 4,800 square meters of office and laboratory space from F3F S.p.A. (formerly known as FinSirton, S.p.A.). In addition, we lease 100 square meters of laboratory and manufacturing space for urokinase from Sirton S.p.A. (no longer an affiliate).

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion together with the consolidated 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.

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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 a mixture of single- and double-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 that occurs when veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation, that are administered prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is linked to multiple-organ failure and high rates of morbidity and mortality.

Defibrotide for the treatment and prevention of VOD has been given "orphan" status by the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide for the treatment and prevention of VOD has also been granted "orphan" status by the Korean Food and Drug Administration, or KFDA. In addition, defibrotide has been granted "fast-track product" designation by the FDA for the treatment of severe VOD prior to stem cell transplantation. To the best of our knowledge, there are no FDA or EMA approved treatments for this life-threatening disease.

We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD with multiple organ failure in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. We also have an ongoing study for the treatment of VOD through our IND protocol. While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis througout the U.S. pursuant to our IND protocol, which we refer to as our cost recovery program, and throughout the rest of the world on a named patient basis, which we refer to as our named-patient program. We expect to collect additional usage tolerability and safety data from patients of our cost recovery and named-patient programs to support our regulatory filings.

On May 10, 2011, we announced the filing of our MAA under a centralized procedure with the EMA for defibrotide for the treatment and prevention of VOD in adults and children. On March 21, 2013, the EMA announced its decision to deny the approval of our MAA. We plan to appeal this decision and explore all possible options, including conducting additional clinical studies, with respect to obtaining regulatory approval from the EMA for defibrotide.

On July 6, 2011, we announced the filing of our NDA with the FDA for defibrotide for the treatment of VOD in adults and children undergoing hematopoietic stem cell transplantation. On August 17, 2011, we announced our voluntary withdrawal of our NDA following correspondence from the FDA identifying several potential "Refuse to File" issues regarding, among other things, the completeness and accuracy of our datasets. We have been working with CROs and consultants to address the issues raised by the FDA and plan to resubmit our NDA in 2013.

In 2011, we entered into license and/or supply and distribution agreements with specialized regional partners to distribute defibrotide, including on a named-patient basis, in the Asian Pacific, Turkey, Israel and the Palestinian Authority. In 2012, we entered into license and/or supply and distribution agreements with additional regional partners to distribute defibrotide, including on a named-patient basis, in the Middle East and North Africa, Eastern Europe, and the Nordic and Baltic countries, accounting for 8% of our 2012 named-patient product sales.

We have generated a significant portion of our revenue through the distribution of our primary product candidate, defibrotide, under our cost recovery program in the U.S., and under our named-patient program throughout the rest of the world. For the years ended December 31, 2010, 2011 and 2012, sales of defibrotide through these programs amounted to approximately 67%, 78% and 82% of our total product sales, respectively.

We have a manufacturing plant in Italy where we produce APIs, such as the defibrotide compound, sodium heparin urokinase and sulglicotide. We also generate revenues from the sale of these APIs, which are used by other companies to make the finished form of various drugs. For the years ended December 31, 2010, 2011 and 2012, sales of APIs amounted to approximately 33%, 22% and 18% of our total product sales, respectively.

In addition, we have generated a significant amount of revenue from our license, supply and distribution agreement with Sigma-Tau Pharmaceuticals, Inc., pursuant to which we have licensed the right to market defibrotide to treat and prevent VOD in North America, Central America and South America to Sigma-Tau Pharmaceuticals, Inc. In connection with this agreement, we entered into a cost sharing agreement with Sigma-Tau, under which it has agreed to share in certain costs associated with the development of defibrotide. We have recognized other revenue of €4,547 thousand, € 2,026 thousand and € 1,257 thousand for the years ended December 31, 2010, 2011 and 2012, respectively, in connection with these agreements with Sigma-Tau.

Our revenue sources are detailed categorically below:

	For The Years Ended December 31,		
(in thousands)	2010	2011	2012
Product sales:			
API - Urokinase	€1,893	€1,612	€1,404
API - Sulglicotide	4,640	3,236	3,154
API – Other	-	-	298
Named-patient/cost recovery program sales	13,182	16,886	22,774
Total product sales	19,715	21,734	27,630
Other revenues	4,836	2,149	1,409
Total revenue	€24,551	€23,883	€29,039

Although we are incorporated in Italy, the majority of our product sales are generated through customers located outside of Italy, with the exception of limited volumes of sales of urokinase and other APIs. Product sales to customers outside of Italy amounted to 94%, 97% and 97% for the years ended December 31, 2010, 2011 and 2012, respectively. The API sulglicotide is mainly sold in South Korea and the API urokinase is principally sold in Spain. Defibrotide, which is still under development and for which we have not obtained a market authorization in any territory in the world, is sold in the US and Ex-US through our cost recovery and named-patient programs and accounted for 67%, 78% and 82% of our total product sales for the years ended December 31, 2010, 2011 and 2012, respectively. Substantially all of our other revenues are generated from a cost sharing arrangement with Sigma-Tau Pharmaceuticals, Inc., executed in 2007, under which Sigma-Tau Pharmaceuticals, Inc. agreed to reimburse 50% of certain costs we incurred during our Phase III clinical trial of defibrotide to treat severe VOD, and from milestone and up-front payments under our license and supply agreement with Sigma-Tau Pharmaceuticals, Inc., as amended, to include the prevention indication of defibrotide for distribution in the Americas. In 2012, Sigma-Tau agreed to reimburse the Company approximately $2.9 million over the next two years.

In 2012, we have been cash flow positive, primarily due to revenue generated from the cost recovery and named-patient programs. We expect that existing cash and cash equivalents together with the anticipated cash flow from product sales will be sufficient to support our current operations for at least the next twelve months. However, if we are unable to obtain regulatory approval to commercialize defibrotide, unable to continue to generate sufficient revenue and cash-flow through our cost recovery and named-patient programs as expected, or if our cash requirements exceed our current expectations, we may incur net losses and may have 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, 2012, substantially all of our cash and cash equivalents were held in accounts at financial institutions located in the Republic of Italy and in the United States, which 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 the purchase date. We are exposed to exchange rate risk with respect to certain of our cash balances, accounts receivable and accounts payable that are denominated in U.S. dollars. As of December 31, 2012, we held a cash balance of $2.06 million, receivables of $0.83 million and payables of $0.84 million that were denominated in U.S. dollars. These 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 re-measurement 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 the currencies in which we transact business in the future could materially

and adversely affect our cash flow, revenues and financial condition. To the extent that 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 re-measurement.

In addition, we are exposed to foreign currency risks to the extent that we engage in transactions, such as investments, programming costs and accounts payable, denominated in currencies other than our functional currency. With respect to these items, changes in the exchange rate 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 had entered into interest rate cap agreements to manage exposure to interest rate movement. These interest rate cap agreements expired on the dates on which greater than 50% of the original principal amounts of the underlying indebtenedness were repaid. Due to the current rate of the Euribor, the outstanding amounts of the principal due on our borrowings and the scheduling of repayment of such borrowings, we have determined the risk of interest rate movement to be low and did not renew these agreements. We monitor fluctuations in the interest rate market and will consider entering into new agreeements if we later determine that such risk has increased.

Critical Accounting Policies and Estimates

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated 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 the understanding our financial condition and operation results because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain.

Revenue Recognition

Our primary source of revenue is from the sale of products through our named-patient and cost recovery programs and from collaborative arrangements. We recognize revenue when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered, our price to the customer is fixed or determinable and collectability is reasonably assured. Revenues from product sales are recognized upon delivery, when title and risk of loss have passed to the customer. Provisions for returns and other adjustments related to sales are provided during the same period in which 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 such qualified expenditures are made. Finally, royalty revenues are recognized when earned after 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 cost recovery 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 to their estimated net realizable values as they become outdated or obsolete. 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 subject to our ability to reasonably forecast future sales levels versus quantities on hand and existing purchase commitments. Forecasting demand and resource planning are based, in part, on assumptions that we must make regarding expected market changes, overall demand, pricing incentives and raw material availability, among other variables. Significant changes in these estimates could indicate that inventory levels are excessive, which would require us to reduce inventories to their estimated net realizable values.

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

Prior to commencing the sale of defibrotide through the named-patient and cost recovery programs, we had expensed all costs associated with the production of defibrotide as research and development expenses. Subsequent to signing the agreements associated with the named-patient and cost recovery programs, we began to capitalize the costs of manufacturing defibrotide as inventory, including costs to convert existing raw materials to active pharmaceutical ingredients and costs to package and label previously manufactured inventory, which costs had already been expensed as research and development expenses. Until we sell the inventory for which a portion of the costs was previously expensed, the carrying value of our inventory 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 expenses in the period incurred, which are not expected to be sold through the named-patient and cost recovery programs. We will continue to do so until we receive an approval letter from the FDA or EMA for a new product or product designation. Upon receipt of an approval letter from the FDA or EMA for a new product or product designation, we will begin to capitalize the subsequent inventory costs relating to that product designation.

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 this 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 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 its carrying value. Fair value can be calculated using a number of different approaches, including discounted cash flow, comparables, and 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, an assessment of undiscounted cash flows, the selection of an appropriate discount rate, the calculation of the weighted average cost of capital and the discounts or premiums inherent in market prices require 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

Several of our activities and related costs are designated research and development expenses, which primarily include salary and benefits payments to our direct employees, employee stock-based compensation expenses, 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 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 constant communication with our contract research organizations to assess their progress on the underlying study and the reasonableness of their cost estimates. Differences between estimated trial costs and actual costs have not been material to date, and changes have been made when they become known. Under this policy, research and development expenses can vary due to accrual adjustments related to the underlying clinical trials and the expenses incurred by the contract research organizations. At December 31, 2012, we had €4.37 million of future payables under outstanding contracts. Most of these contracts are on a cost plus or actual cost basis.

Stock-Based Compensation

Employee stock-based compensation is estimated on the date of grant, based on the fair value of the employee stock award. Employee stock-based compensation is recognized 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 fair values of all option grants were estimated on the grant date using a binomial valuation model. The binomial model considers characteristics of fair value option pricing that are not available under the Black-Scholes model. Similar to the Black-Scholes model, the binomial model takes into account variables such as volatility, dividend yield rate, and risk free interest rate. However, unlike the Black-Scholes model, the binomial model also considers the contractual term of the option, the probability that the option will be exercised prior to the end of its contractual life, the probability of termination or retirement of the option holder in computing the value of the option, and the exchange rate between the euro and the dollar. For these reasons, we believe that the binomial model provides a fair value that is more representative of actual experience and future expected experience than the value calculated using the Black-Scholes model.

The option-pricing model requires the use of certain subjective assumptions or estimates regarding the expected volatility of the market price of our stock, the expected term of the award and the expected forfeiture rate. In estimating the expected term of an award, we consider the vesting period of the award, our historical experience with employee stock option exercise and the expected volatility, and use relevant peer group data as a comparative measure.

We review our assumptions periodically and we may change the assumptions we use to value share-based awards granted in future periods. Such changes may lead to a significant change in the expenses 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. For options granted in 2012, we have used a 93.55% 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 that are publicly traded in the U.S. market. Significant changes to these estimates could have a material impact on the results of our operations.

Valuation Allowance

As of December 31, 2012 and 2011, we had net operating loss (NOL) carryforwards of approximately €53.48 million and €51.32 million, respectively.

As required by ASC 740, our management has evaluated the positive and negative evidence bearing upon the ability to realize our deferred tax assets, which are comprised principally of NOL and research and experimentation credit carryforwards. Management has determined at this time that while it believes that the deferred tax assets will be realized, the weight of objective evidence requires a valuation allowance of approximately €21.16 million at December 31, 2012.

Recent Accounting Pronouncements

Reference should be made to Note 2 of our consolidated financial statements, “Summary of Significant Accounting Policies to our Consolidated Financial Statements,” for a discussion of new accounting standards.

Results of Operations

The following tables set forth our results of operations:

Amounts in thousands except share and per share data	For The Years Ended December 31, 2010	2011	2012
Revenues:			
API product sales	€6,533	€4,848	€4,856
NPP product sales	13,182	16,886	22,774
Total product sales	19,715	21,734	27,630
Other revenues	289	123	152
Other revenues from related party	4,547	2,026	1,257
Total Revenues	24,551	23,883	29,039
Operating costs and expenses:			
Cost of goods sold	5,786	6,035	5,778
Research and development	6,104	5,533	10,531
General and administrative	5,835	5,490	6,271
Sales and Marketing	-	2,237	4,558
Charges from related parties	346	222	186
Restructuring charges	1,101	-	-
Depreciation and amortization	908	870	1,003
Total operating costs and expenses:	20,080	20,387	28,327
Operating income	4,471	3,496	712
Foreign currency exchange gain/(loss), net	90	46	(67)
Interest income/(expense), net	(87)	(21)	155
Income before income tax expense	4,474	3,521	800
Income tax expense:			
Total income tax expense	(397)	(811)	(26)
Net income	€4,077	€2,710	€774
Net income per share:			
Basic	€0.27	€0.18	€0.05
Diluted	€0.27	€0.18	€0.05
Weighted average shares used to compute net income per share:			
Basic	14,956,317	14,964,021	15,014,411
Diluted	14,956,317	15,340,859	15,639,890

Year Ended December 31, 2012 Compared to Year Ended December 31, 2011

Product sales

Total product sales, which include sales of defibrotide and APIs, were €27.63 million for 2012 compared to €21.73 million for 2011, an increase of €5.90 million or 27%. The increase was primarily due to a higher volume of defibrotide distributed through the named-patient and cost recovery programs, which can be partially attributed to the partnerships entered into in 2012, an increased awareness of defibrotide and a decrease in service fees associated with the named-patient program managed by one of our European partners. Revenues from the distribution of defibrotide

through the named-patient and cost recovery programs amounted to €22.77 million for the year ended December 31, 2012, compared to €16.89 million for the year ended December 31, 2011, recording an increase of €5.88 million or 35%. For the years ended December 31, 2012 and 2011, named-patient and cost recovery program sales were net of €1.55 million and €3.17 million in service fees, respectively.

API sales were €4.86 million for 2012 compared to €4.85 million for 2011. Sulglicotide API sales were €3.15 million for 2012 compared to €3.24 million for 2011, accounting for 65% and 67% of our total API sales. The variance in sulglicotide sales was partially due to a decrease in volume which had a negative impact of €0.3 million, which was partially offset by €0.2 million due to an increase in the price of sulglicotide. Urokinase sales were €1.40 million for 2012 compared to €1.61 million for 2011. The variance is attributable to a decrease in volume versus the prior year. In 2012, we realized €0.30 million in sales of the API heparin, which we did not have in prior year.

Other revenues

Other revenues were €1.41 million for 2012 compared to €2.15 million for 2011, a decrease of €0.74 million or 34%. Other revenues for the prior year included a ratable recognition of the up-front payment of €5.11 million (US$7.0 million) made by Sigma-Tau in 2010 in connection with the amendment of an existing license and supply agreement with the Company to include the prevention indication of defibrotide in the Americas, which amounted to Euro 1.70 million (US$ 2.33 million). The decrease was partially offset by an increase in activities, such as clinical trials, that were eligible for reimbursement from Sigma-Tau under a cost sharing agreement with the Company, which amounted to €1.26 million and €0.32 million for the years ended December 31, 2012 and 2011, respectively.

Cost of goods sold

Our cost of goods sold was €5.78 million in 2012 compared to €6.04 million in 2011. Overall, the cost of goods sold as a percentage of product sales was 21% in 2012 compared to 28% in 2011 mainly due to a different composition of product mix with proportionately increased sales of defibrotide which has a higher margin compared to sales of our other APIs. Also contributing to the variance was a net release of an inventory reserve in the amount of €0.46 million, a slight increase in the margin of sulglicotide due to the renegotiation of the sales price and a slight decrease in labor costs due to temporary lay-offs of certain employees in connection with a temporary shut-down of our manufacturing activities.

Research and development expenses.

We incurred research and development expenses of €10.53 million in 2012 compared to €5.53 million for 2011, an increase of €5.00 million or 90%. 2011 research and development expenses include severance, employee termination benefits and other exit costs associated with a change in management in the amount of €0.43 million. Research and development expenses were primarily for the development of defibrotide to treat and prevent VOD. The increase from the comparable period in 2011 was primarily due to the engagement of contract research organizations and outside scientific, regulatory and quality consultants, travel and conference expenses and scientific advisory board meetings necessary to assist the Company in addressing issues raised by the FDA and support the Company through the EMA's regulatory review process.

General and administrative expenses

Our general and administrative expenses were €6.27 million for 2012 compared to €5.49 million for 2011, an increase of €0.78 million or 14%. The increase was primarily due to higher legal and tax consultant expenses, personnel and recruiting expenses in connection with an increase in our headcount, corporate governance expenses and stock-based compensation costs.

Sales and marketing

Sales and marketing expenses were €4.56 million for 2012 compared to €2.24 million for 2011, an increase of €2.32 million or 104%. Sales and marketing expenses relate to costs incurred in connection with the establishment of our subsidiary's European commercial team, which primarily occurred in the second half of 2011. Therefore, sales and

marketing expenses for the twelve-month period ended December 31, 2012 account for expenses related to new appointments for our commercial team that we did not have during the prior-year period. Sales and marketing expenses refer mainly to payroll and payroll related costs, health economic and marketing analysis, travel and conference expenses, and stock-based compensation costs.

Income tax expenses

Income tax expenses were €0.03 million for 2012 compared to €0.81 million for 2011, a decrease of €0.78 million. The decrease is mainly attributable to a decrease in profitability and lower taxable income compared to the prior year. In addition, we released previously accrued income taxes in the amount of €0.02 million, recorded a tax credit of €0.07 million in connection with the enactment of a new tax reform, and accrued Italian corporate taxes of €0.11 million and Swiss corporate taxes of €0.01 million.

Net income

Our net income was €0.77 million in 2012 compared to €2.71 million in 2011. The difference was primarily due to an increase in research and development expenses, an increase in sales and marketing expenses associated with the establishment of a commercial team, which did not exist until the second half of 2011, an increase in general and administrative expenses, a decrease in other income and revenues from a related party offset by an increase in the volume of defibrotide sold through the named-patient and cost recovery programs, an increase in gross margin and a decrease in income tax expenses.

Year Ended December 31, 2011 Compared to Year Ended December 31, 2010

Product sales.

Product sales were €21.73 million for 2011 compared to €19.72 million for 2010, an increase of €2.01 million or 10.2%. The increase was primarily due to a higher volume of defibrotide distributed through the named-patient and cost recovery programs, which can be partially attributed to the partnerships entered into in 2011 with specialized regional partners for the distribution of defibrotide on a named-patient basis, and an increased awareness of defibrotide. Revenues from the distribution of defibrotide through the named-patient and cost recovery programs amounted to €16.89 million for the year ended December 31, 2011, compared to €13.18 million for the year ended December 31, 2010, recording an increase of €3.71 million or 28%. For the years ended December 31, 2011 and 2010, named-patient and cost recovery program sales were net of €3.17 million and €2.13 million in service fees, respectively.

API sales were €4.85 million for 2011compared to €6.53 million for 2010, a decrease of €1.68 million or 26%. Of the €1.68 million decrease, €1.40 million is attributable to the sulglicotide API business, which suffered a drop in volume of sales of €0.82 million and a reduction in price of €0.58 million, mainly due to a 20% reimbursement cut from the South Korean government for a finished drug manufactured by a South Korean commercial partner that uses sulglicotide as an API. In addition, we experienced a decrease of €0.28 million in urokinase revenues, which was largely attributable to volume.

Other revenues

Other revenues were €2.15 million for 2011 compared to €4.84 million for 2010. The decrease versus the prior year is primarily attributable to a decrease in activities eligible for reimbursement from Sigma-Tau pursuant to a cost sharing arrangement, such as pre-clinical and clinical trials. Reimbursements for such activities amounted to €0.32 million and €1.14 million for 2011 and 2010, respectively. In addition, of the €5.11 million ($7.0 million) up-front payment advanced by Sigma-Tau in connection with the amendment of the existing license and supply agreement, to include the prevention indication of defibrotide in the Americas, we had a ratable recognition of €1.70 million ($2.33 million) for 2011compared to €3.41 million for 2010, a decrease of €1.71, or 50%.

Cost of goods sold.

Our cost of goods sold was €6.04 million in 2011 compared to €5.79 million in 2010. The cost of goods sold includes write-offs of €0.34 million and €0.38 million for 2011 and 2010, respectively, in order to adjust the carrying values of some APIs to their net realizable values. Overall, the cost of goods sold as a percentage of product sales was 28% in 2011 compared to 29% in 2010 mainly due to a different composition of product mix with proportionately increased sales of defibrotide which has a higher margin compared to sales of our other APIs. The increase in gross margin was partially offset by a decrease in the price of sulglicotide and unfavorable manufacturing costs associated with the reprocessing of some of the APIs.

Research and development expenses.

We incurred research and development expenses of €5.53 million in 2011 compared to €6.10 million for 2010. The decrease from the comparable period in 2010 was primarily due to the completion of a technology transfer, costs associated with pre-clinical and clinical trials, such as reproductive toxicity, hERG channel, QT/QTc, and pharmacokinetics of defibrotide in healthy volunteers, and stock-based compensation, offset by an increase in scientific consultancy, regulatory activities and severance, employee termination benefits and other exit costs associated with a change in management in early October 2011 totaling €0.43 million.

General and administrative expenses.

Our general and administrative expenses were €5.49 million for 2011 compared to €5.84 million for 2010. 2010 general and administrative expenses included the release of a reserve for doubtful accounts of €0.27 million due to the deemed payment of accounts receivable through the elimination of the same amount of accounts payable due to the same counterparty. The slight decrease from the prior year was primarily due to the elimination of administrative and payroll expenses incurred by our New York office, which closed in 2010, offset by an increase in administrative expenses incurred in connection with the formation of a wholly-owned subsidiary in Switzerland along with higher stock-based compensation expenses, which amounted to €1.35 million and €1.22 million for the years ended December 31, 2011 and December 31, 2010, respectively.

Restructuring charges.

Restructuring charges were none and €1.10 million for 2011 and 2010, respectively. For 2011, €0.43 million attributed to severance, employee termination benefits and other exit costs associated with a change in management in early October were classified as research and development expenses. For 2010, €0.95 million in such charges were attributable to employee termination benefits, outplacements costs, costs to terminate lease agreements and other exit costs resulting from the strategic decision to close our New York office and to consolidate our resources and corporate operations into our headquarter in Como, Italy. In addition, as a result of a workforce reduction, we recorded €0.15 million in one-time employee termination benefits, outplacements costs, termination notice and legal contractual compensation due upon early resolution of the employment agreements.

Income tax expense

Income tax expenses were €0.81 million for 2011 compared to €0.40 million for 2010, an increase of €0.41 million or 100%. The increase is mainly due to new corporate tax legislation enacted in December 2011 by the Italian Parliament to raise funds for the country's deficit. The corporate tax reform established that net operating losses, or "NOLs", can be carried forward for an indefinite period of time, as opposed to five years, and can offset up to 80% of the taxable income establishing a minimum corporate tax rate of 5.5% of the taxable income. We accrued €0.30 million in such tax in 2011.

Net income

Our net income was €2.71 million in 2011 compared to €4.08 million in 2010. The difference was primarily due to an increase in the volume of defibrotide sold through the named-patient and cost recovery programs, offset by a decrease in our API sales and other income and revenues under the cost sharing agreement entered into with Sigma-Tau (including the ratable recognition of a portion of the up-front payment made by Sigma-Tau in connection with the amendment of its existing license and supply agreement with us). Also contributing to the variance was a decrease in research and development expenses and restructuring charges, offset by an increase in sales and marketing expenses associated with the establishment of a commercial team, which was not present in 2010 as well as an increase in current income tax expenses as a consequence of the new corporate tax reform.

LIQUIDITY AND CAPITAL RESOURCES

	As of December 31,	
(in thousands)	2011	2012
Cash and cash equivalents	€9,990	€12,485

	Years Ended December 31,		
(in thousands)	2010	2011	2012

Net cash provided by operating activities	€8,237	€2,401	€3,422
Net cash used in investing activities	(205)	(393)	(611)
Net cash used in financing activities	(716)	(801)	(249)
Effect of exchange rate on cash and cash equivalents	34	41	(67)
Cash and cash equivalent, beginning of period	1,392	8,742	9,990
Cash and cash equivalents, end of period	€8,742	€9,990	€12,485

We require cash to fund our operating activities and our service debt. We have been cash flow positive in 2012, primarily due to revenue and cash-flow generated from the cost recovery and named-patient programs. Our excess funds are currently invested in short-term investments with a maturity date of three months. Based on our historical needs and on current estimates, our current cash position and expected cash flow from our revenues will be sufficient to fund our operations for the next twelve months. However, if we are unable to obtain regulatory approval to commercialize defibrotide, unable to generate sufficient revenue and cash-flow through our cost recovery and named-patient programs, or if we increase expenditures above our current expectations, we may need to obtain additional capital through equity or debt financing, loans and collaborative agreements with corporate partners and which may not be available to us on favorable terms, if at all.

Operating Activities

In 2012, our primary sources of funding have been our operating activities and working capital. We closed the year with a net income of €0.77 million. Of this net income, certain costs were non-cash charges, primarily depreciation and amortization costs of €1.46 million, stock-based compensation expenses of €1.92 million and a release of a previously accrued inventory reserve of €0.46 million related to inventory sold or destroyed. In addition to non-cash charges, we also had a net change in other operating assets and liabilities of €0.03 million, including a decrease in accounts receivable of €0.98 million, a decrease in inventory of €1.41 million, a decrease in accounts payable, other accrued expenses and income tax payables of €2.01 and a release of previously accrued deferred revenues of €0.33 million. In 2012, as compared to 2011, we recorded an increase in research and development expenses necessary to assist the Company in addressing issues raised by the U.S. FDA and supporting the Company through the EMA regulatory review process, along with an increase in sales and marketing expenses in connection with building out our European commercial team, which the Company did not establish until November 2011.

In 2011, our primary sources of funding were our operating activities and we closed the year with a net income of €2.71 million. Of this net income, certain costs were non-cash charges, such as depreciation and amortization costs in the amount of €1.32 million, stock-based compensation expenses of €1.66 million, a provision for income taxes of €0.58 million, and a write-off of inventory of €0.34 million. In addition to non-cash charges, we also had a net change in other operating assets and liabilities of €4.15 million, including an increase in accounts receivable of €1.28 million, an increase in inventory of €0.92 million, a decrease in accounts payable and other accrued expenses of €0.65 million, a decrease in termination indemnities of €0.13 million and a decrease in deferred revenues of €1.21 million, due to the recognition of €1.70 million of previously deferred revenue related to our license agreement entered with Sigma-Tau and the deferral €0.49 million relating to a commitment entered into with a partner to recognize free products if, in a given period, it buys certain volumes of that product. Cost accrual of free products is recorded in the period in which the related revenues are recognized resulting in a reduction of product revenue and the establishment of a liability which is included in other current liabilities. In 2011, we formed Gentium GmbH, a wholly-owned subsidiary organized under the laws of Switzerland, as the headquarters for our commercial operations. We also appointed our commercial leadership team in the major European countries.

In 2010, our primary sources of funding were an upfront payment of €5.11 ($7.00) million received from Sigma-Tau Pharmaceuticals, Inc. in connection with the amendment and expansion of a license agreement and proceeds from our operating activities. We closed the year with a net income of €4.07 million. Of this net income, certain costs were non-cash charges, such as depreciation and amortization costs in the amount of €1.32 million, stock-based compensation expenses of €1.52 million, a provision for income taxes of €0.40 million, a write-down of inventory of €0.37 million and non-cash income of €0.25 million due to the release of an allowance for doubtful accounts. In 2010, in addition to non-cash charges, we also had a net change in other operating assets and liabilities of €0.73 million, which principally included an increase in accounts receivable of €0.50 million, an increase in inventory of €1.18 million, a decrease in prepaid expenses and other current assets of €0.89 million and an increase in deferred revenue of €1.70 million related to our license agreement with Sigma-Tau. In 2010, we utilized a tax credit of €1.16 million to offset social security and withholding taxes due, and we sustained one-time employee termination benefits of €0.95 million

resulting from a strategic decision to consolidate our resources and operations into our headquarters in Como, Italy.

Investing Activities

In 2012 we had capital expenditures of €0.61 million which were principally allocated to leasehold improvements for our corporate office located in Villa Guardia, Como, Italy.

In 2011 we had capital expenditures of €0.72 million, which were principally allocated to furniture and leasehold improvements for our corporate office located in Villa Guardia, near Como, Italy. Such investment activities were partially financed through the sale of marketable securities for €0.26 million and partially compensated by the landlord.

In 2010, we had capital expenditures of €0.21 million.

Financing Activities

In 2012, we used approximately €0.53 million to reimburse a portion of our long term debt and capital lease obligations while proceeds from the exercise of stock options amounted to €0.28 million.

In 2011, we used approximately €0.88 million to reimburse a portion of our long term debt and capital lease obligations. Proceeds from the exercise of stock options amounted to €0.07 million.

In 2010, we used approximately €0.72 million to reimburse a portion of our long term debts and capital lease obligations. In 2010, in connection with a national agreement among the Italian Bank Association and the Italian Ministry of Economics and Enterprise Organizations, we obtained a deferment on the payment of principal debt outstanding for a twelve-month period. Such benefit terminated in November 2010.

At December 31, 2012, we had an aggregate of €1.54 million in debt outstanding and had €12.49 million in cash and cash equivalents. Additional information on the maturity, repayment obligations and interest rate structure with respect to this debt, and our material commitments for capital expenditures, is provided below under "Contractual Obligations and Commitments."

We expect to devote substantial resources toward the continuation of our research and development efforts and related regulatory expenses, the expansion of our licensing and collaboration efforts and building our sales and marketing team. Our funding requirements will depend on numerous factors including:

- the scope and results of our clinical trials, including any necessary future clinical trials;
- whether we are able to successfully commercialize and sell defibrotide for the uses for which it is being developed;
- the advancement of other product candidates under 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, taking legal action against, maintaining and enforcing patent claims and other patent-related costs, including litigation costs, and the outcome of litigation of any such claims;
- our ability to establish and maintain additional collaboration arrangements.

We do not expect our revenues to increase significantly until after we successfully obtain FDA and EMA 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 EMA regulatory marketing approval for, and to commercially launch, defibrotide to treat and prevent VOD;
- the receptiveness of the capital markets to financings, generally, and of biotechnology companies, specifically; and
- our ability to enter into additional collaboration arrangements with corporate and academic collaborators and the success of such relationships.

We have accumulated a deficit of approximately €92.07 million since our inception. We have been cash flow positive since 2010, primarily due to an up-front payment from Sigma-Tau Pharmaceuticals Inc. in connection with the expansion of the license for defibrotide in the Americas, and revenue and cash-flow generated from the cost recovery and named-patient programs. While we expect that existing cash and cash equivalents together with the anticipated cash flow from product sales will be sufficient to support our current operations for at least the next twelve months, if we have expenditures above our current expectations, or if we are unable to generate sufficient revenue and cash-flow through our cost recovery and named-patient programs, we may need to obtain additional capital through equity or debt financing, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all.

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

2013 Outlook

In 2013, we will continue to work 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 use defibrotide for both the treatment and prevention of VOD in the America, regarding the resubmission of our NDA and plan to resubmit our NDA in 2013.

With respect to our MAA with the EMA, we plan to appeal the EMA's decision denying our MAA. If we are required to conduct additional clinical studies by the FDA or the EMA, we will incur significant research and development expenses that may have an adverse effect on our profitability and cash flow.

We expect to explore other indications for defibrotide, such as acute graft versus host disease, or aGvHD, where it has shown promising preliminary data in a clinical trial. It is also our intention to continue evaluating opportunities for compounds that might be available to us to expand our existing pipeline.

We expect to continue to run our cost recovery program to give patients access to defibrotide in the United States for the treatment of VOD, and our named-patient program to give patients access to defibrotide throughout the rest of the world for the prevention and treatment of VOD. We intend to continue to expand our presence into new regional territories through license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient basis. We expect revenue associated with the distribution of defibrotide on a named-patient basis to increase as more patients throughout the world gain access to defibrotide.

We do not expect a material change to our API business. We plan to install a steam generator for our manufacturing activities at an estimated cost of €250 thousand and new grinding equipment at an estimated cost of €150 thousand. The improvements will both increase our manufacturing efficiency and improve the safety conditions of our manufacturing facility. Additionally, we are working to build a back entrance to our manufacturing plant to facilitate vehicle access.

We are mindful of the fact that external conditions could affect our ability to achieve our goals, including our ability to raise additional capital, and healthcare policy changes, increasing concerns and scrutiny regarding potential or perceived safety issues associated with pharmaceutical and biological products and continued government pricing pressures. Based on our historical needs and our current estimates, our current cash position and expected cash flow from our revenues will be sufficient to fund our operations for the next twelve months.

RESEARCH AND DEVELOPMENT

We have had to engage multiple third parties, such as contract research organizations and consultants, to assist us in the development of defibrotide, and we will likely have to engage similar third parties to develop any other product candidate. We expense research and development costs as they are incurred.

Research and Development Expenses

Our research and development expenses consist primarily of salaries and benefits of our direct employees, employee stock-based compensation expenses, 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 CROs. The billings that we receive from CROs for services rendered may not be received for several months following the services. Development timelines and costs are difficult to estimate and may vary significantly for each product candidate and from quarter to quarter. We accrue the estimated costs of the CROs related services based on our estimate of management fees, site management and monitoring costs and data management costs. Differences between estimated and actual trial costs 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 CROs. During the years ended December 31, 2010, 2011 and 2012, we had three major categories of research projects relating to our product candidates: defibrotide to treat VOD, defibrotide to prevent VOD and assorted other projects. The table below presents our research and development expenses by project for each of the years ended December 31, 2010, 2011 and 2012.

	For The Years Ended December 31,		
(in thousands)	2010	2011	2012
Defibrotide to treat VOD	€5,028	€3,156	€5,841
Defibrotide to prevent VOD	521	1,583	4,336
Others	555	794	354
Total	€6,104	€5,533	€10,531

We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD with multiple organ failure in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. We also have an ongoing study for the treatment of VOD through our IND protocol. While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis througout the U.S. pursuant to our IND protocol, which we refer to as our cost recovery program, and throughout the rest of the world on a named patient basis, which we refer to as our named-patient program. We expect to collect additional usage tolerability and safety data from patients of our cost recovery and named-patient programs to support our regulatory filings.

The successful development of defibrotide is uncertain. On May 10, 2011 and July 6, 2011, respectively, we announced the filing of our MAA for defibrotide with the EMA and our NDA for defibrotide with the FDA. The EMA recently denied our MAA for defibrotide for the prevention and treatment of VOD, and we have withdrawn our NDA for the treatment of VOD with the FDA. We plan to explore all opportunities to achieve regulatory approval, including a resubmission of our NDA in 2013, appealing the decision by the EMA regarding our MAA, and conducting additional clinical studies.

The exact nature, timing and estimated costs of the efforts necessary to complete the development of defibrotide to treat or prevent VOD or the other uses for which we may develop defibrotide and the date of completion of these development efforts are difficult to ascertain due to the numerous risks and uncertainties associated with development, including:

• potentially insufficient data necessary to obtain marketing approval from the FDA or EMA;

• the need to conduct additional clinical trials;

• the uncertainty of clinical trial results; and

• extensive governmental regulation, both foreign and domestic, for approval of new therapies.

If we fail to complete the development of defibrotide to treat or prevent VOD, it will have a material adverse effect on our future operating results and financial condition. In addition, any failure to obtain, or any delay in obtaining, regulatory approvals will also have a material adverse effect on our results of operations and financial condition. A further discussion of the risks and uncertainties associated with the development of defibrotide and certain consequences of failing to successfully develop the product candidate, 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, 2012, we had 3 U.S. patents issued with 6 U.S. patent applications pending, 33 foreign patents issued with 24 foreign patent applications pending, and 2 international patent application (not yet nationalized) pending. The United States Patent & Trademark Office issued a patent covering our process for manufacturing 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, for the use of defibrotide in stem cell transplants. This patent expires in 2021.

Patent rights and other proprietary rights are an important component of our business. We have sought and intend to continue to seek patent protection for our inventions, and we 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, as such, the enforceability of any patents we obtain cannot be guaranteed with any degree of certainty. The patents that we hold, those that are licensed to us, and those that may be issued to us in the future, may be challenged, invalidated or circumvented, and may not provide the intended protections against or competitive advantages over competitors with similar technology. Furthermore, it is possible that our competitors will independently develop similar technologies or duplicate our efforts while our product candidates are in development. Because of the extensive time required to develop, test and complete the regulatory review of a product candidate, it is possible that our relevant patent rights may expire before defibrotide can be approved for sale and commercialized, or within a short time after commercialization.

We have Italian, United States and international trademark rights in "Gentium", United States and European Union trademarks in "Gentide", Italian, United States and European trademarks in "Defitelio", Italian and European trademarks in "Defrex", international and Italian trademark rights in "Oligotide" and Italian trademark rights in "Pharma Research" and "Dinelasi".

OFF-BALANCE SHEET ARRANGEMENTS

We do not have any off-balance sheet arrangements.

TABULAR DISCLOSURE OF CONTRACTUAL OBLIGATIONS

Contractual Obligations and Commitments

Contractual obligations represent future cash commitments and liabilities under agreements with third parties, and exclude contingent liabilities for which we cannot reasonably predict future payment. The following chart represents our total contractual obligations, at December 31, 2012, aggregated by type (in thousands):

(in thousands)	Total	1 Year	2 Years	3 Years	4 Years	5 Years	Thereafter
Long-Term Debt Obligations:							
Mortgage loans	€1,320	240	240	240	240	240	120
Finance loans	123	81	42	-	-	-	-
Equipment loans	101	88	13	-	-	-	-
	€1,544	409	295	240	240	240	120
Operating leases	€1,126	349	222	185	185	185	-
Research and Development Programs	4,368	3,959	361	45	3	-	-
Sales and Marketing Programs	895	766	63	54	12	-	-
General and Administration Programs	671	542	92	31	4	2	-
	€7,060	5,616	738	315	204	187	-
Total	€8,604	6,025	1,033	555	444	427	120

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 and bears interest at the six-month Euribor rate plus 1.00%. Originally, the principal was repayable in fourteen installments, every six months, from December 27, 2007 until final maturity in 2014, and interest was payable every six months from June 27, 2006. In December 2009 and in June 2011, Banca Nazionale Del Lavoro S.p.A. agreed to defer payment of the loan principal for 48 months, extending the original term of the loan to 2018. At December 31, 2012, the principal amount outstanding under this loan was €1,320 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, bearing interest at the three-month Euribor rate plus 1.20%. On June 15, 2008, the rate was decreased to 1.02% over the Euribor rate. 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, 2012. In December 2009 and June 2011, San Paolo IMI S.p.A agreed to defer payment of the loan principal for 24 months, extending the original term of the loan to 2013. At December 31, 2012, the amount outstanding under this loan was €62 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 an original term of 60 months, maturing on December 31, 2011. Principal and interest are due in quarterly installments beginning on March 31, 2007. The loan bears interest at the three-month Euribor rate plus 1%. In December 2009 and June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal for 30 months, extending the original term of the loan to 2014. At December 31, 2012, the amount outstanding under this loan was €39 thousand.

The second loan is in the amount of €500 thousand for an original term of 60 months, maturing on December 31, 2011. Principal and interest are due in monthly installments beginning on January 31, 2007. The loan bears interest at the three-month Euribor rate plus 1%. In December 2009 and June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal due for 30 months, extending the original term of the loan to 2014. At December 31, 2012, the amount outstanding under this loan was €84 thousand.

The third loan is in the amount of €225 thousand for an original term of 57 months (after a technical pre-amortization period from December 20, 2006 to March 15, 2007) maturing on December 15, 2011. Under the terms of the Loan Agreement, the loan funds were required to be used within six months of disbursement 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. The loan bears interest at the three-month Euribor rate plus 0.8%. In December 2009 and June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal for 30 months, extending the original term of the loan through 2014. At December 31, 2012, the amount outstanding under this loan was €39 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 the related consulting services for advice regarding FDA issues.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

DIRECTORS AND SENIOR MANAGEMENT

Set forth below are the names, ages, positions and a brief account of the business experience of each of our executive officers, significant employees and directors as of April 1, 2013. Dr. Glenn Cooper resigned from the Board of Directors on March 27, 2013 due to a disagreement with the other board members over the need for additional oversight on clinical and scientific matters.

Name	Age	Position
Dr. Khalid Islam (1)	57	President and Chief Executive Officer
Salvatore Calabrese	43	Chief Financial Officer and Senior Vice President, Finance
Carin Heringa	52	Scientific Director and Senior Vice President
Gigliola Bertoglio (2)	78	Director
Dr. Marco Brughera (3)	57	Director
Dr. Laura Ferro (1)	61	Director
Dr. Bobby W. Sandage, Jr. (4)	59	Director
Elmar Schnee (5)	53	Director

(1) Member of the scientific oversight committee.

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

(3) Member of the compensation committee.

(4) Member of the scientific oversight committee (chairperson), and nominating and corporate governance committee.

(5) Member of the nomination and corporate governance 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 has over 22 years of experience in the pharmaceutical sector. From 1999 to 2008, he was the President and Chief Executive Officer of the SWX-listed anti-infective company Arpida AG. Prior to joining Arpida, he held various research and development roles at Hoechst Marion Roussel and Marion-Merrell Dow, both global pharmaceutical companies. He is the founder/co-founder of several companies and has previously served as a member of the Board of Directors for Arpida AG in Switzerland, Rheoscience A/S in Denmark and Chairman of Arpida Inc. In addition, Dr. Islam is currently the Chairman of the Board of Directors of C10 Pharma in Norway, an advisor to the venture capital group Kurma Biofund in Paris, a member of the International Scientific Advisory Board of the Network of Excellence in Pathogenomics, and a member of the Editorial Board of Current Drug Discovery and Technologies. He received a Bachelor of Science from Chelsea College, University of London, and his Ph.D. from Imperial College, University of London. He has published over 80 articles in scientific journals and holds numerous patents.

Salvatore Calabrese has served as our Chief Financial Officer since December 2010, 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. 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 his 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.

Dr. Carin Heringa has served as Scientific Director and Senior Vice President since March 2012. Dr. Heringa joined Gentium in November 2011 as Head of Global Medical Affairs. Prior to joining Gentium, Dr. Heringa held various managerial positions at several pharmaceutical companies. Most recently, she served as Medical Director of the Integrated Hospital Care Franchise at Novartis Pharmaceuticals Corporation. Dr. Heringa was formerly Drug Development Project Leader at Astellas Pharma Inc., where she was responsible for oversight of clinical programs relating to Hematology, Neuroscience, Cardiovascular Disease, Urology and Gastroenterology, and also previously served as Medical Director of the International Department at Yamanouchi Pharmaceuticals Co. Ltd., and the Medical Affairs Manager and International Coordinator for Clinical Research at Brocades Pharma BV. Dr. Heringa's experience also includes membership roles on the leadership team of the Integrated Hospital Care Franchise at Novartis, and on the Project Review Board at Astellas. Her experience in the pharmaceutical industry spans over two decades, during which time she has effectively managed multinational project teams and successfully led programs through all stages (Phase I - Phase IV) of clinical development. Dr. Heringa has played an important role in facilitating successful interactions between pharmaceutical companies and European and US regulatory authorities, including NDA, MAA, IND and IMPD submissions, registrations or line extensions with respect to Lucentis®, Ilaris®, Exelon® Patch, Omnic®, and Locoid®.

Gigliola Bertoglio has served as one of our directors since December 2004. 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, 2003, 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.

Dr. Marco M. Brughera has served as one of our directors since December 2011. Since January 2011, Dr. Brughera has held several positions for the Sigma-Tau Group, including Global Head Rare Disease Franchise, Corporate R&D Managing Director of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., President of Sigma-Tau Research Switzerland SA, Board Member of Sigma-Tau Pharmaceuticals Inc. and of Sigma Tau Rare Diseases SA. From 2004 to 2010, Dr. Brughera was the Vice President of Preclinical Development at Nerviano Medical Sciences, a pharmaceutical research and development facility in Italy and one of the largest oncology-focused integrated discovery and development companies in Europe. During that time, Dr. Brughera also served as the Managing Director at Accelera, Srl, an independent contract research organization within the Nerviano Medical Sciences Group. From 1999 to 2004, Dr. Brughera held various positions at Pharmacia & Upjohn and Farmitalia Carlo Erba SpA, an Italian pharmaceutical company. Dr. Brughera earned a degree in veterinary medicine from the University of Milan in 1981. He is also a Eurotox Registered Toxologist.

Dr. Laura Ferro is our former President and Chief Executive Officer (1991 until 2009) and has served as one of our directors since 1991. Dr. Ferro is the former President and Chief Executive Officer of our largest shareholder, FinSirton (now F3F S.p.A.). From 1991 to 2010, Dr. Ferro also held various positions at Sirton Pharmaceuticals S.p.A., a subsidiary of F3F S.p.A. (formerly known as FinSirton S.p.A.) 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. Dr. Sandage currently serves as President of Coronado Biosciences, Inc., a clinical stage biopharmaceutical company focused on cancer care, and has held this position since December 2012. He served as the President and CEO of Coronado Biosciences, Inc. from April 2011 until December 2012. From March 2010 until April 2011, Dr. Sandage served as Vice President of Embedded Therapeutics at NYSE-listed Covidien plc. 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 of 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 previously served as 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.

Elmar Schnee was appointed to our Board of Directors on May 9, 2012. Mr. Schnee has more than twenty years of experience in the international pharmaceutical industry, with specific expertise in strategic planning, business development and marketing acquired through various positions held at Merck KGaA, Fisons Pharmaceutical PLC, Sanofi-Synthélabo and UCB Pharma. Since 2011, Mr. Schnee has served as Executive Chairman of Cardiorentis Ltd., a biopharmaceutical company specializing in the development and commercialization of therapies for the treatment of acute heart failure (AHF). Previously, Mr. Schnee spent several years in the global pharmaceutical and chemical group at Merck KGaA. He joined Merck in 2003 as Managing Director of Merck Santé s.a.s. in Lyon, France. In January 2004, he assumed responsibility for global operations of the ethical pharmaceuticals division of Merck KGaA and in November 2005 was appointed as Deputy Member of the Executive Board responsible for the pharmaceuticals business sector. In 2006, Mr. Schnee was appointed as Regular Member of the Executive Board and General Partner of Merck KGaA, with responsibility for pharmaceutical products oversight. Mr. Schnee holds a degree in Marketing Management from the Swiss Institute for Business Administration in Zurich.

All of our directors' terms expire on the date of our ordinary shareholders' meeting approving our 2012 Italian GAAP financial statements, which will be held on April 29, 2013 (first call) and, if necessary, May 10, 2013 (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, 2010, compensation to our executive officers and directors, excluding amounts due to termination of employments agreements, was €1.15 million and €0.32 million, respectively. For the year ended December 31, 2011, cash compensation to our executive officers and directors was €1.24 million and €0.27 million, respectively. For the year ended December 31, 2012, cash compensation to our executive officers and directors was €0.83 million and €0.32 million, respectively.

During the year ended December 31, 2010 we granted options to purchase an aggregate of 1,170,000 ordinary shares to executive officers and directors at exercise prices ranging from $4.57 to $5.49, which options terminate on dates ranging from September 30, 2019 to December 1, 2020. In addition, options previously granted to officers and directors in the amount of 683,981 and 84,970, respectively, were forfeited following termination of their employment agreements. During the year ended December 31, 2011 we granted options to purchase an aggregate of 380,000 ordinary shares to executive officers and directors at exercise prices ranging from $6.00 to $9.26, which

options terminate on dates ranging from September 30, 2019 to November 14, 2021. In addition, options previously granted to officers and directors in the amounts of 386,033 and 15,000, respectively, were forfeited upon separation and termination of their employment agreements. During the year ended December 31, 2012, we granted options to purchase an aggregate of 110,000 ordinary shares to an executive officer and directors at exercise prices ranging from $9.20 to $9.30, which options terminate on November 14, 2021.

Share-Based Compensation Plans

2004 Equity Incentive Plan

On September 2, 2004, our board of directors proposed a capital increase in connection with our 2004 Equity Incentive Plan, which was recommended to our shareholders for approval. 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 September 30, 2004, which were approved by the shareholders on April 28, 2005. On July 31, 2006, our board of directors approved an amended and restated version of our 2004 Equity Incentive Plan reflecting minor revisions, including the requirement under Italian law that all shares issued under the plan be paid for in cash, in an amount equal to at least €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 the issuance of 1,500,000 ordinary shares. 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, 2012, there were 1,116,379 shares underlying outstanding options, with a weighted average exercise price of $7.38. 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 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 the grant of 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 the recipients of the awards and the 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. Share appreciation rights 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 prohibits publicly held companies from taking a deduction for certain compensation paid to specified employees in a taxable year to the extent such 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 earlier 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 of the Italy sub-plan may not transfer a share award except pursuant to 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 earlier terminated by our board of directors.

2007 Stock Option Plan, As Amended

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

The 2007 Stock Option Plan authorizes 3,200,000 ordinary shares for issuance. At December 31, 2012, there were 1,144,838 shares underlying outstanding options, with a weighted average exercise price of $6.61. 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.

Share options granted under the 2007 Stock Option Plan generally have a term expiring at the earlier of ten years or 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 and approved by our board. 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 two years following the first anniversary of the grant date, and options granted to board members vest in full on the first anniversary of the grant date.

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.

On March 10, 2010, the Board of Directors adopted, and on April 30, 2010 at an ordinary shareholders' meeting, the shareholders approved, an amendment to the 2007 Stock Option Plan increasing the maximum number of authorized ordinary shares of the Company that may be issued under the 2007 Stock Option Plan by 2,200,000 for a total of

3,200,000 authorized ordinary shares for issuance. While these resolutions were approved at the ordinary shareholders' meeting, the capital increase necessary to the implementation of the share increase was not approved at the extraordinary shareholders' meeting following the ordinary shareholders' meeting. Even though a substantial majority voted in favor of the resolution, the vote did not reach a majority of all outstanding shares, as required under Italian law. The capital increase was later approved at an extraordinary meeting held on May 9, 2011.

Other pension and retirement plans

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

BOARD PRACTICES

Board Composition

Our board of directors currently consists of six members: Ms. Bertoglio, Dr. Brughera, Dr. Ferro, Dr. Islam, Dr. Sandage and Mr. Schnee. Dr. Glenn Cooper, who served as the seventh member of the board of directors in 2012, submitted his resignation on March 27, 2013. Ms. Bertoglio, Dr. Sandage and Mr. Schnee have never been employed by us or any of our subsidiaries and are independent directors. F3F S.p.A. (formerly known as FinSirton S.p.A.) also agreed to vote its shares in favor of electing one person designated by Sigma-Tau Finanziaria S.p.A. Dr. Brughera is the designee of Sigma-Tau. Dr. Brughera was elected as a director on December 6, 2011, replacing Mr. Marco Codella, the former Chief Financial Officer of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., who had served as a member of the board since June 2005. 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 director compensation to our shareholders and our board of directors. Under Italian law, our shareholders determine director compensation relating to basic board service, such as annual fees for serving on the board and fees for attending board meetings. Our shareholders have approved the following director compensation for the period from our 2012 Annual Ordinary Shareholders' Meeting to our 2013 Annual Ordinary Shareholders' Meeting:

- an annual cash retainer of $45,000 thousand for each non-employee director; and
- a stock option for 9,000 ordinary shares.

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 and Mr. Schnee, each of whom is an independent director. Ms. Bertoglio is an audit committee financial expert. Dr. Cooper also served on this committee until his resignation from the board on March 27, 2013. 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 we receive 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 deems necessary to carry out its duties, and to determine the compensation of such counsel and advisors, as well as ordinary administrative expenses of the committee; and
- approves related party transactions.

Our audit committee directly oversees our independent accountants and 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 appoint, terminate and determine the compensation for our independent accountants, although our audit committee can and 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 Ms. Bertoglio, who is an independent director and Dr. Brughera, who is not an independent director. Dr. Cooper served as the chairperson of this committee until his resignation from the board on March 27, 2013. Our board chose to appoint Dr. Brughera to our compensation committee following a determination that it was in the best interest of the company to have a three-person compensation committee and that Dr. Brughera, being the only director not serving on any committee of the board, was best suited for this position. Under Nasdaq rules, the compensation of a U.S. domestic company's chief executive officer and all other officers must be determined either by a compensation committee comprised entirely of independent directors or by a majority vote of independent directors serving on the board. Because our compensation committee is not comprised entirely of independent directors, officer compensation is determined by the vote of independent directors serving on our board based on recommendations made by the compensation committee. 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 the individual compensation of those officers or directors.

Nominating and Corporate Governance Committee. Our nominating and corporate governance committee consists of Mr. Schnee, Dr. Sandage and Ms. Bertoglio, each of whom is an independent director. Under Nasdaq rules, the directors of a U.S. domestic company must be 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, which includes 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 board of directors on 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 an adequate organizational structure, internal controls and administrative and accounting system, and also oversees our independent accountants with respect to our Italian GAAP financial statements.

The following table sets forth the name and position of each of the three members of our board of statutory auditors and the alternate statutory auditors, as of the date of this annual report. The current board of statutory auditors was elected on May 9, 2012 for a term that ends at the date of the ordinary shareholders' meeting to approve our 2014 Italian GAAP financial statements.

Name	Position

Giorgio Iacobone	Chairman
Carlo Ciardiello	Member
Augusto Belloni	Member
Putignano Oronzo	Alternate
Domenico Ferrari	Alternate

Mr. Iacobone and Mr. Belloni also serve as members of the board of statutory auditors of Sirton (now Vifarma S.p.A.).

In 2010, the board of statutory auditors met four times and attended twelve board of directors' meetings and one shareholders' meeting. In 2011, the board of statutory auditors met six times and attended eight board of directors' meetings and one shareholders' meeting. In 2012, the board of statutory auditors met five times and attended 6 board of directors meetings and 1 shareholders' meeting. In 2012, we accrued €73 thousand as compensation for their service on our board of statutory auditors.

Indemnification of Directors and Executive Officers and Limitation of Liability

We have entered into indemnification agreements with each of our directors and executive officers, which may, in some cases, provide indemnification that is broader in scope than the specific indemnification provisions of Italian law.

At present, there is no pending litigation or proceeding involving any of our directors, officers, employees, or agents in which indemnification by us will be required or permitted, nor are we aware of any threatened litigation or proceeding that may result in a claim for such indemnification.

We have purchased directors and officers' liability insurance, which covers liabilities arising under the Securities Act, and we intend to maintain this insurance in the future.

EMPLOYEES

The table below shows the number, activity and geographic location of our permanent employees as of December 31, 2010, 2011 and 2012. As of December 31, 2012, Gentium S.p.A. had 66 employees, 2 of them were based in the United States and the remaining were based in Italy, while Gentium GmbH had 11 employees.

	As of December 31,		
	2010	2011	2012
Administration, accounting, finance, business development	13	15	21
R&D, clinical, regulatory	15	14	17
Sales and marketing	-	9	7
Production, quality assurance control	33	30	32
Total	61	68	77

Italian law imposes certain confidentiality obligations on our employees and provides that we are entitled to either ownership of, or a right of option on, any intellectual property created by our employees while under our employ, although we must compensate our employees for such intellectual property creation. Our employees in Italy are also subject to national collective bargaining agreements. National agreements are negotiated collectively between the national associations of companies within a given industry and the respective national unions. National agreements provide a basic framework on working conditions, including pay, security and other provisions. With the exception of our executive officers in Italy, all of our employees were subject to a collective bargaining agreement that expires on December 31, 2015. Our executive officers in Italy are subject to a collective bargaining agreement that was renewed on November 25, 2009 and expires on December 31, 2013. Our work force is unionized and we believe that we maintain satisfactory relations with our employees.

Under Italian law, employees who leave employment for any reason, including termination for cause or resignation, are entitled to a severance payment based on salary and years of service. Our liability for these termination indemnities at December 31, 2012 was €384 thousand. In accordance with Italian law, we make social security and national healthcare contributions to the Italian Government on behalf of our employees, which provides pension and healthcare insurance benefits.

SHARE OWNERSHIP

Dr. Laura Ferro directly owns 100,000 shares of our Company as of April 1, 2013. Dr. Ferro also holds options that, within 60 days of April 1, 2013 are vested as to 64,000 ordinary shares. Dr. Ferro and members of her family control F3F S.p.A. (formerly known as FinSirton S.p.A.). Accordingly, Dr. Ferro may also be deemed to beneficially own shares of our company owned by F3F S.p.A.. Dr. Ferro disclaims such beneficial ownership.

Dr. Khalid Islam, our Chairperson, Chief Executive Officer, and Salvatore Calabrese, our Chief Financial Officer and Senior Vice President, Finance, hold options that, within 60 days of April 1, 2013, are vested as to 410,767 and 227,715 shares respectively.

To our knowledge, none of our other directors and officers listed herein owned one percent or more of our ordinary shares at April 1, 2013. See “Item 7, Major Shareholders and Related Party Transactions.”

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

MAJOR SHAREHOLDERS

The following table shows information with respect to the beneficial ownership of our ordinary shares as of April 1, 2013 based on information known to us or public filings by:

- each person, or group of affiliated persons, who we know beneficially owns 5% or more of our ordinary shares, and
- all of our directors and executive officers as a group.

At April 1, 2013, we had 15,038,483 ordinary shares outstanding. Except as indicated in the footnotes to this table, and subject to community property laws where applicable, the persons named in the table have sole voting and investment power with respect to all ordinary shares shown as beneficially owned by them. Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC. Ordinary shares underlying our convertible securities that are exercisable within 60 days from April 1, 2013 are deemed outstanding for computing the amount and percentage owned by the person or group holding such convertible securities, but are not deemed outstanding for computing the percentage owned by any other person or group.

	Number of Shares Beneficially Owned	Percent
Principal Shareholders		
Laura Ferro (1)	2,727,000	18.13 %
Paolo Cavazza (2)	2,611,995	17.37 %
F3F S.p.A.(formerly FinSirton S.p.A.) (3)	2,550,000	16.96 %
Claudio Cavazza's estate (4)	2,474,943	16.53 %
Sigma-Tau Finanziaria S.p.A. (5)	2,311,011	16.46 %
FMR LLC (6)	1,517,392	7.70 %
Defiante Farmaceutica, S.A. (7)	1,011,001	6.72 %
All directors and executive officers as a group (9 persons) (8)	4,093,403	27.22 %

(1) Dr. Laura Ferro, who is our former Chief Executive Officer and President and one of our current directors, may be deemed to share voting or dispositive control with F3F S.p.A. (formerly known as FinSirton S.p.A.) over the ordinary shares in Gentium that F3F S.p.A. beneficially owns. Dr. Ferro disclaims beneficial ownership of such shares. Assumes that Dr. Ferro is deemed to beneficially own the ordinary shares beneficially owned by F3F S.p.A. and includes 73,000 ordinary shares issuable upon exercise of options currently excercizable within 60 days of April 1, 2013.

(2) Based upon the information obtained from a Schedule 13D filed with the SEC, as amended. Address is Via Tesserte, 10, Lugano, Switzerland. Consists of (i) 1,300,000 outstanding ADSs held by Sigma-Tau Finanziaria S.p.A., (ii) 1,011,001 outstanding ADSs held by Defiante Farmaceutica S.A.; and (iii) 300,994 outstanding ADSs held by Chaumiere Consultadoria e Servicos S.A (now Sinaf). Mr. Paolo Cavazza owns, directly and indirectly, 40% of the outstanding equity of Sigma-Tau Finanziaria S.p.A. and so may be deemed to beneficially own the shares beneficially owned by Sigma-Tau Finanziaria S.p.A. In connection with a purchase by Sigma-Tau Finanziaria S.p.A. of 800,000 ordinary shares from F3F S.p.A. in April 2005, F3F S.p.A. agreed that, if the per share price in a sale by our shareholders of all of our ordinary shares is less than $5.00 per share, F3F S.p.A. will transfer to Sigma-Tau Finanziaria S.p.A. an additional number of ordinary shares equal to (x) $3.2 million divided by the product determined by multiplying (i) 0.8 by (ii) the per share sale price less (y) 800,000 ordinary shares. Sigma-Tau Finanziaria S.p.A. owns, directly and indirectly, 100% of the outstanding equity of Defiante

and so may be deemed to be the beneficial owner of the outstanding ordinary shares and ADSs held by Defiante. Mr. Paolo Cavazza and members of his family indirectly own Chaumiere (now Sinaf) and so may be deemed to beneficially own the ADSs beneficially owned by Chaumiere (now Sinaf).

(3) Address is Piazza XX Settembre 2, 22079 Villa Guardia (Como), Italy. The board of directors of F3F S.p.A. including Dr. Laura Ferro, may be deemed to share voting or dispositive control with F3F S.p.A. over the ordinary shares in Gentium that F3F S.p.A. beneficially owns. Dr. Ferro disclaims beneficial ownership of such shares.

(4) Based upon the information obtained from a Schedule 13G filed with the SEC, as amended. Address is Via Sudafrica, 20, Rome, Italy 00144. Consists of (i) 1,300,000 outstanding ADSs held by Sigma-Tau Finanziaria S.p.A., (ii) 1,011,001 outstanding ADSs held by Defiante Farmaceutica L.d.A., and (iii) 163,942 ADSs held by Inverlochy Consultadoria e Servicos LdA (now Taufin International). Mr. Claudio Cavazza owns, directly and indirectly, 60% of the outstanding equity of Sigma-Tau Finanziaria S.p.A. and so may be deemed to beneficially own the shares beneficially owned by Sigma-Tau Finanziaria S.p.A. In connection with a purchase by Sigma-Tau Finanziaria S.p.A. of 800,000 ordinary shares from F3F S.p.A. in April 2005, F3F S.p.A. agreed that, if the per share price in a sale by our shareholders of all of our ordinary shares is less than $5.00 per share, F3F S.p.A. will transfer to Sigma-Tau Finanziaria S.p.A. an additional number of ordinary shares equal to (x) $3.2 million divided by the product determined by multiplying (i) 0.8 by (ii) the per share sale price less (y) 800,000 ordinary shares. Sigma-Tau Finanziaria S.p.A. owns, directly and indirectly, 100% of the outstanding equity of Defiante and so may be deemed to be the beneficial owner of the outstanding ordinary shares and ADSs held by Defiante. Inverlochy Consultadoria e Servicos, LdA (now Taufin International) is indirectly wholly-owned by Mr. Claudio Cavazza's estate. By nature of such relationship, Mr. Cavazza may be deemed to beneficially own the ADSs held by Inverlochy Consultadoria e Servicos, LdA (now Taufin International).

(5) Based upon the information obtained from a Schedule 13D filed with the SEC, as amended. Address is Via Sudafrica 20, 00144 Roma, Italy. Consists of (i) 1,300,000 outstanding ADSs held by Sigma-Tau Finanziaria S.p.A. and (ii) 1,011,001 outstanding ADSs held by Defiante. Sigma-Tau Finanziaria S.p.A. owns, directly and indirectly, 100% of the outstanding equity of Defiante and so may be deemed to be the beneficial owner of the outstanding ordinary shares and ADSs held by Defiante. The board of directors of Sigma-Tau Finanziaria S.p.A. may be deemed to share voting or dispositive power with Sigma-Tau Finanziaria S.p.A. over the ordinary shares in our company that Sigma-Tau Finanziaria S.p.A. beneficially owns, and so may be deemed to beneficially own the ordinary shares that Sigma-Tau Finanziaria S.p.A. beneficially owns. In connection with a purchase by Sigma-Tau Finanziaria S.p.A. of 800,000 ordinary shares from F3F S.p.A. in April 2005, F3F S.p.A. agreed that, if the per share price in a sale by our shareholders of all of our ordinary shares is less than approximately $5.00 per share, F3F S.p.A. will transfer to Sigma-Tau Finanziaria S.p.A. an additional number of ordinary shares equal to (x) $3.2 million divided by the product determined by multiplying (i) 0.8 by (ii) the per share sale price less (y) 800,000 ordinary shares.

(6) Based upon the information obtained from a Schedule 13G filed with the SEC, amended. Address is 82 Devonshire Street, Boston, MA 02109.

(7) Based upon the information obtained from a Schedule 13G filed with the SEC, as amended. Address is Rua dos Ferreios, 260, Funchal-Madeira (Portugal) 9000-082.

(8) Assumes that Dr. Laura Ferro is deemed to beneficially own the ordinary shares beneficially owned by F3F S.p.A. and includes 73,000 ordinary shares issuable upon exercise of options currently exercisable and exercisable within 60 days of April 1, 2013.

Other than our depositary, the Bank of New York Mellon, as of March 26, 2013, there were no record holders of our ordinary shares located in the United States.

There were no changes in percentage ownership by the holders listed above since January 1, 2007 except for the following:

- All shareholders of our company prior to our February 2007 private placement were substantially diluted by the shares issued in that private placement.
-

In our February 2007 private placement, Chaumiere (now Sinaf) acquired 87,667 ordinary shares, Defiante acquired 87,666 ordinary shares and Inverlochy (now Taufin Intenational) acquired 87,667 ordinary shares. Paolo Cavazza may be deemed to have acquired the ordinary shares acquired by Chaumiere (now Sinaf). Paolo Cavazza, Claudio Cavazza's heirs and Sigma-Tau Finanziaria S.p.A. may be deemed to have acquired the ordinary shares acquired by Defiante. Claudio Cavazza's heirs may be deemed to have acquired the ordinary shares acquired by Inverlochy (now Taufin International).

- In June 2007, Biomedical Value Fund, L.P. sold 227,447 ordinary shares to Sigma-Tau Finanziaria S.p.A. and 304,468 ordinary shares to Defiante, and Biomedical Offshore Value Fund, Ltd. sold 272,553 ordinary shares to Sigma-Tau Finanziaria S.p.A. and 259,362 ordinary shares to Defiante.

- From July 2005 to March 26, 2013, our company issued stock option awards to our officers and directors. 1,044,482 ordinary shares are issuable upon exercise of stock option awards granted to our officers and directors within 60 days of March 26, 2013.

The holders of 5% or more of our outstanding ordinary shares do not have different voting rights than other holders of our ordinary shares. Dr. Ferro and her family may effectively control all decisions and actions that must be made or taken by holders of our ordinary shares by virtue of their ownership of 100% of the outstanding ordinary shares of F3F S.p.A., which beneficially owned 16.96% of our outstanding ordinary shares at March 26, 2013.

Change of Control Arrangements

We are not aware of any arrangements that could result in a change of control, other than F3F S.p.A.'s arrangement to vote its ordinary shares in favor of electing a nominee to our board of directors designated by Sigma-Tau Finanziaria S.p.A.

RELATED PARTY TRANSACTIONS

Except as described below, we have not entered into or proposed to enter into any transaction or loan with any of our affiliates, directors, executive officers (other than employment agreements), holders of 10% or more of our ordinary shares, immediate family members of such persons, or with any enterprise over which any such person is able to exercise a significant influence.

Control by Dr. Ferro's Family

Dr. Laura Ferro, who is our former Chief Executive Officer and President and one of our current directors, together with members of her family, may be deemed to control F3F S.p.A. (formerly known as FinSirton S.p.A.). As a result, Dr. Ferro and her family may be deemed to indirectly control approximately 17% of our outstanding ordinary shares as of March 26, 2013.

Agreements with Various Entities

On January 1, 2012, we entered into a commercial lease with F3F S.p.A.. The area leased is approximately 4,800 square meters in size and is used for offices, manufacturing, laboratories and storage facilities. The lease provides for an annual fee of €185 thousand for the initial six-year term, which may be adjusted annually based on the cost of living index, and, in the event we exercise our six-year renewal option, €215 thousand on an annual basis, subject to cost of living adjustments.

On January 7, 2010, we amended our existing license with Sigma-Tau Pharmaceuticals, Inc. to encompass a license for the intravenous formulation of defibrotide for the prevention of VOD in the Americas and to transfer the NDA post approval in the United States. Pursuant to the amended terms, in addition to payments of $11.35 million received between 2001 and 2010, we will receive an additional payment of $6 million following approval from the FDA to market defibrotide in the U.S. and a further $2 million following the transfer of the approved NDA to Sigma-Tau. In addition, we agreed to establish a joint steering committee with Sigma-Tau to engage in good faith discussions regarding the development, filing and relevant funding of defibrotide for any therapeutic indication licensed to Sigma-Tau.

On October 12, 2007, we entered into a letter agreement with Sigma-Tau Pharmaceuticals, Inc., pursuant to which Sigma-Tau agreed to reimburse 50% of certain costs we incurred relating to our Phase III clinical trial of defibrotide to treat severe VOD. This agreement was amended effective January 7, 2010. While Sigma-Tau will continue to share development costs for studies currently required for the filing of a NDA for defibrotide, we have agreed to engage in good faith negotiations with Sigma-Tau regarding the funding of certain additional costs that may be required to obtain regulatory approval in the U.S., and we have further agreed that $1.0 million in costs reimbursed by Sigma-Tau will be deductible from royalty payments owed to us in the future under the license and supply agreement. In 2012, Sigma-Tau agreed to reimburse us approximately $2.9 million over the next two years.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and officers, which may require us to indemnify against liabilities that arise by reason of the status of such directors and officers or service as directors or officers and may also require us to advance expenses incurred by our directors and officers in connection with any proceeding against them. However, we will not indemnify directors or officers with respect to liabilities arising from willful misconduct of a culpable nature.

INTERESTS OF EXPERTS AND COUNSEL

Not applicable.

ITEM 8. FINANCIAL INFORMATION

CONSOLIDATED STATEMENTS

Please refer to Item 18, "Consolidated Financial Statements" of this annual report.

OTHER FINANCIAL INFORMATION

Legal Proceedings

As of the date of this report, we are not a party to any legal or governmental proceeding that is pending or, to our knowledge, threatened or contemplated against our company that, if determined adversely to us, would have a materially adverse effect, either individually or in the aggregate, on our business, financial condition, results of operations and cash flow.

Dividend Policy

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

Any dividend we declare will be paid to the holders of ADSs, subject to the terms of the deposit agreement, to the same extent as holders of our ordinary shares, less the fees and expenses payable under the deposit agreement. Any dividend we declare will be distributed by the depositary to the holders of the ADSs.

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

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

Under Italian law, Italian companies are required to furnish certain information to the Italian tax authorities regarding the identity of non-resident shareholders in connection with the payment of dividends. Shareholders are required to provide their Italian tax identification number, if any, or alternatively, in the case of legal entities, their name, country of establishment and address, or in the case of individuals, their name, address and place and date of birth, or in the case of partnerships, the information required for individuals with respect to one of their representatives. In the case of ADSs owned by non-residents of Italy, we understand that the provision of information concerning the depositary, in its capacity as a holder of record of the ordinary shares underlying the ADSs, will satisfy this requirement. However,

beneficial U.S. ADS holders are entitled to a reduction of the withholding taxes applicable to dividends paid to them under the income tax convention for the avoidance of double taxation between the United States and Italy, which was signed on August 25, 1999 and went into effect on December 16, 2009 (the “Income Tax Convention”); provided, however, that conditions set out in the Income Tax Convention are met and subject to the applicable anti-avoidance provisions contained therein. In order for you to benefit from that reduction, we are required to furnish certain information about you to the Italian tax authorities and, therefore, any claim by you for those benefits would need to be accompanied by the required information.

SIGNIFICANT CHANGES

ITEM 9. THE OFFER AND LISTING

OFFER AND LISTING DETAILS

Our ADSs are listed on Nasdaq under the symbol "GENT." Neither our ordinary shares nor our ADSs are listed on a securities exchange outside the United States. The Bank of New York is our depositary for purposes of issuing the ADRs representing the ADSs. Each ADS represents one ordinary share.

Trading of our ADSs on the Nasdaq Global Market System commenced on May 16, 2006. Prior to this date, our ADSs were traded on the American Stock Exchange, beginning June 16, 2005 and ending on May 15, 2006, the date we de-listed. The following table sets forth the high and low closing prices per ADS reported by the American Stock Exchange and Nasdaq, as applicable, for each of the periods indicated.

	Price Range of ADSs	
	High	Low
2008	$13.98	$0.44
2009	$3.87	$0.33
2010	$7.20	$1.32
2011		
First Quarter	$12.13	$6.88
Second Quarter	$10.38	$9.05
Third Quarter	$9.99	$6.00
Fourth Quarter	$6.32	$5.65
Full Year	$12.13	$5.65
2012		
First Quarter	$9.20	$5.51
Second Quarter	$9.75	$8.76
Third Quarter	$11.16	$9.13
Fourth Quarter	$12.35	$9.92
Full Year	$12.35	$5.51
Month Ended		
January 31, 2013	$12.00	$11.29
February 28, 2013	$12.59	$8.34
March 31, 2013 (through March 27, 2013)	$8.41	$7.74

The closing price of the ADSs on NASDAQ on March 27, 2013 was $8.20.

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Sources: Nasdaq Stock Market

PLAN OF DISTRIBUTION

Not applicable.

MARKETS

Our ADSs are listed on The Nasdaq Global Market under the symbol “GENT.” The closing price of the ADSs on the Nasdaq Global Market on March 27, 2013 was $8.20. Neither our ordinary shares nor our ADSs are listed on a securities exchange outside the United States.

SELLING SHAREHOLDERS

Not applicable.

DILUTION

Not applicable.

EXPENSES OF THE ISSUE

Not applicable.

ITEM 10. ADDITIONAL INFORMATION.

SHARE CAPITAL

Not applicable.

MEMORANDUM AND ARTICLES OF ASSOCIATION

Bylaws

The following is a summary of certain information concerning our ordinary shares and bylaws (Statuto) and of the Italian law provisions applicable to companies whose shares are not listed in a regulated market in the European Union, as in effect at the date of this annual report. The summary contains all the information that we consider to be material regarding the shares but does not purport to be complete and is qualified in its entirety by reference to our bylaws or Italian law, as the case may be.

Under Italian law, most of the procedures regulating our company, including certain rights of shareholders, are contained in our bylaws as opposed to our articles of association. Amendments to our bylaws require approval at an extraordinary meeting of shareholders, as described below.

In January 2003, the Italian government approved a wide-ranging reform of the corporate law provisions of the Italian Civil Code, which came into force on January 1, 2004. On September 30, 2004, our shareholders approved a number of amendments to our bylaws, which were dictated or made possible by the 2003 corporate law reform. Our bylaws were further amended on April 28, 2005, November 29, 2005, April 28, 2006, April 27, 2007, June 30, 2009, April 30, 2010, and May 9, 2011. The following summary takes into account the 2003 corporate law reform and the consequent amendments to our bylaws.

General

As of March 26, 2013, our issued and outstanding share capital consisted of 15,038,483 ordinary shares, without a par value. The Euro currency was adopted in Italy on January 1, 2002. The redenomination of the ordinary shares from Italian Lira to Euro was approved by our shareholders on December 27, 2000. All the issued and outstanding shares are fully paid, non-assessable and in registered form.

We are registered with the Companies' Registry of Como. Our registered offices are located in Piazza XX Settembre n. 2, Comune di Villa Guardia, frazione Civello, Como, Italy, registration number 02098100130.

Our corporate purpose is the manufacturing, on behalf of our company and third parties, and marketing in both Italy and other countries, of pharmaceutical preparations, pharmaceutical products, raw materials for pharmaceutical and para-pharmaceutical use and in general all and any products sold by pharmacies or for hospital use, excluding, in all cases, the retail sale in Italy of pharmaceutical preparations and products, medical articles and clinical apparatuses in general and organic and inorganic products that may be used in agrotechnical and/or zootechnical fields. We may also

prepare and organize for our own account or on behalf of third parties, the documentation required for obtaining authorizations for marketing pharmaceutical products in compliance with the regulations in force in the countries of destination and be the holders of those authorizations. We may grant and/or transfer licenses to Italian and foreign enterprises or corporate bodies or acquire licenses for ourselves or third parties. For each product contemplated by our corporate purposes, we may carry out research programs in general and in particular technological, chemical, pharmacotoxicological and clinical research programs in the hospital and pharmaceutical field. We are generally authorized to engage in any commercial transactions necessary or useful to achieve our corporate purpose, with the exclusion of investment services and other financial or professional activities reserved by Italian law for authorized entities.

Authorization of shares

Our shareholders may authorize the issuance of additional shares at any time at an extraordinary shareholders' meeting. However, the newly issued shares may not be purchased before all the outstanding shares (i.e., the shares already subscribed) are entirely paid for. On September 30, 2004, following a recommendation by our board of directors, our shareholders approved a capital increase to allow for the issuance of:

- up to 1,560,000 ordinary shares available for grant under our share option plans;
- up to 1,335,000 ordinary shares upon the conversion of the Series A senior convertible promissory notes;
- up to 881,100 ordinary shares upon the exercise of the warrants; and
- 4,554,000 ordinary shares, including the shares underlying the ADSs in our initial public offering (including ordinary shares underlying the underwriters' purchase option and the over-allotment option).

The authorization for the issuance of ordinary shares authorized at this meeting expired on September 30, 2009, except that the authorization of the issuance of the 1,560,000 shares available for grant under our Amended and Restated and 2004 Equity Incentive Plan and our Amended and Restated Nonstatutory Plan and Agreement is valid until September 30, 2019, and with the further exception that 1,353,297 of these ordinary shares were authorized for issuance in connection with our issuance of the Series A notes and related warrants, but were not actually issued, and so became unauthorized and unissuable under Italian law.

On November 29, 2005, after a recommendation by our board of directors, our shareholders approved a capital increase of 713,518 ordinary shares to be reserved for issuance upon exercise of the warrants we issued to the participants in our October 2005 private placement and the placement agent for that private placement.

On April 28, 2006, following a recommendation by our board of directors, our shareholders approved an amendment to our bylaws, which granted certain powers to the board of directors for a five-year period, pursuant to articles 2443 and 2420-ter of the Italian Civil Code, including the power to:

• increase the capital of our company in cash, up to €90 million of par value, in one or more transactions, and to reserve all or part of such amount for the exercise of warrants issued by means of the same resolution of our board of directors providing for the relevant capital increase;

• issue convertible bonds (including subordinated) and increase the capital of our company, in one or more transactions, up to €10 million of par value, through the issuance of ordinary shares reserved for the conversion of such convertible bonds, and to reserve all or part of such convertible bonds for issuance upon the exercise of warrants issued by means of the same resolution of our board of directors providing for issuance of the convertible bonds; and

• in each case, exclude or limit the option right of our shareholders in favor of "strategic investors" (as defined by our bylaws) if our board of directors determines that exclusion or limitation to be in the interest of our company.

Such delegation of powers expired without having been exercised by the board of directors.

On May 31, 2006, pursuant to the board powers granted by the shareholders at the meeting of April 28, 2006, our board of directors resolved upon a capital increase of 466,446 ordinary shares, to be reserved for issuance upon exercise of warrants. On December 15, 2006, pursuant to the powers granted by the shareholders at the meeting dated April 28, 2006, our board of directors resolved upon a capital increase of 151,200 ordinary shares to be reserved for issuance upon exercise of warrants.

On February 6, 2007, pursuant to the powers granted by the shareholders at the meeting dated April 28, 2006, our board of directors resolved upon a capital increase of 2,354,000 ordinary shares to be subscribed within March 9, 2007, by "strategic investors."

On April 27, 2007, following a recommendation by our board of directors, our shareholders approved a capital increase relating to 1,000,000 ordinary shares to be reserved for issuance pursuant to exercise of options available for grant under our 2007 Stock Option Plan.

On June 30, 2009, our shareholders resolved to (i) remove the par value of our ordinary shares, including the par value of the ordinary shares previously issued by the company, and (ii) grant the board of directors with the power to increase the capital in cash up to an amount equal to Euro 100,000,000 on a separable basis, in one or more transactions, for a rights offering, through the issuance of up to a maximum of 120,000,000 shares, without par value, with the faculty to reserve all or part of such amount to the exercise of warrants issued by means of the same resolution of the Board of Directors approving the relevant capital increase, and with the faculty to reserve 1/4 of any such capital increase to employees as equity incentive under our equity incentive plans in effect from time to time.

On April 30, 2010, our shareholders resolved to update the text of article 6 of the Company's Bylaws as a consequence of the completion of certain capital increases and the expiration of the term for the subscription of certain other capital increases.

On May 9, 2011, our shareholders resolved to increase the capital of the Company in cash, by a maximum amount of Euro 2,200,000, on a separable basis, with the exclusion of the pre-emptive right of the shareholders, for the issuance of options to purchase a maximum of 2,200,000 shares, without a par value, in favor of the Company's employees, directors and consultants.

In addition, on May 9, 2011, following a recommendation by our board of directors, our shareholders approved an amendment to our bylaws which granted certain powers to the board of directors for a five-year period, pursuant to articles 2443 and 2420-ter of the Italian Civil Code, including the powers to:

· increase the capital of our company in cash, up to €90 million of par value, in one or more transactions, and to reserve all or part of such amount for the exercise of warrants issued by means of the same resolution of our board of directors providing for the relevant capital increase;

· issue convertible bonds (including subordinated) and increase the capital of our company, in one or more transactions, up to €10 million of par value, through the issuance of ordinary shares reserved for the conversion of such convertible bonds, and to reserve all or part of such convertible bonds for issuance upon the exercise of warrants issued by means of the same resolution of our board of directors providing for issuance of the convertible bonds; and

· in each case, exclude or limit the option right of our shareholders in favor of "strategic investors" (as defined by our bylaws) if our board of directors determines that exclusion or limitation to be in the interest of our company.

Form and transfer of shares

Our ordinary shares are not represented by share certificates; rather, they are registered in book-entry form. All of our ordinary shares are issued through Monte Titoli, an Italian clearinghouse and depositary, and held through various participants, primarily financial institutions, on Monte Titoli's system. Transfers in our ordinary shares are processed on Monte Titoli's system. We update our shareholder book (libro soci) that we keep at our corporate offices for Italian law purposes from time to time, with the names of the record shareholders based on information that will be provided to us by Monte Titoli participants.

This shareholder book is the controlling register of our record shareholders for Italian law purposes, including the purposes of establishing the record shareholders for shareholder meetings and declaring dividends and stock splits or a combination of the two. A shareholders' name must be entered in this shareholder book in order for the shareholder to establish its rights against us.

There are no limitations on the right to own or vote our ordinary shares, which applies to non-Italian residents and foreign residents. However, owners of our ordinary shares must establish an account with a Monte Titoli participant. Owners of ADSs representing our ordinary shares are subject to certain limitations on their rights, as explained in our risk factors entitled, "Risks Relating to Being an Italian Corporation – 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," "- You may not be able to participate in rights offerings and may experience dilution of your holdings as a result" and "- You may be subject to limitations on transfer of your ADSs." There are no provisions in our articles of association or bylaws that would have the effect of delaying, deferring or preventing a change of control of our company and that would operate only with respect to a merger, acquisition or corporate restructuring involving our company. There are no provisions in our bylaws governing the ownership threshold above, which shareholder ownership must be disclosed. There are no provisions discriminating against any existing or prospective holder of our ordinary shares as a

result of such shareholder owning a substantial number of our shares. There are no sinking fund provisions or provisions providing for liability for further capital calls by our company.

Dividend rights

Our payment of any annual dividend must be proposed by our board of directors to the shareholders and is subject to the approval of our shareholders at the annual ordinary shareholders' meeting. Before dividends may be paid out of our unconsolidated net income in any year, we must allocate an amount equal to 5% of the Italian GAAP net income to our legal reserve until such reserve is at least equal to 20% of our capital. If a loss in our capital occurs, we may not pay dividends until the capital is reconstituted or reduced by the amount of such losses. We may pay dividends out of available retained earnings from prior years, provided that after such payment, we will have a legal reserve at least equal to the legally required minimum of 20% of the capital. We may not approve or pay dividends until this minimum (i.e., 20% of the capital) is met. If the minimum is met, the board of directors could propose the issuance of a dividend to the shareholders and the shareholders' resolution might approve that issuance. The shareholders' resolution will specify the manner and the date for dividend payment. Any dividends which shareholders do not collect within five years of the date on which they become payable will be forfeited by those shareholders and come back to us. The board of directors may not approve interim dividends at times between our annual ordinary shareholders' meetings.

Board of directors

Pursuant to our bylaws, our board of directors must consist of no less than three and no more than eleven individuals. Our board of directors is elected at an ordinary shareholders' meeting and the term of board membership is one year. Our directors, who may but are not required to be shareholders, may be re-elected. Directors do not stand for reelection at staggered intervals. Cumulative voting rights are not permitted or required. There are no provisions in our articles of association or bylaws regarding retirement or non-retirement of our directors under an age limit requirement.

Our board of directors has complete power of our ordinary and extraordinary administration and, in particular, may perform all acts it deems advisable for the achievement of our corporate purposes, except for the actions reserved, by applicable law or the bylaws, to a vote of the shareholders at an ordinary or extraordinary shareholders' meeting. See also, "Item 10, Additional Information, Memorandum and Articles of Association, Meetings of Shareholders."

If we cannot repay our creditors, and a court determines that our directors did not perform their duties regarding the preservation of our assets, the court may find our directors liable to our creditors.

Our board of directors may also appoint one or more senior managers (direttori generali) who report directly to the board. These senior managers may be employees, and the board may delegate certain powers to senior managers that the board has not already delegated to managing directors or an executive committee, subject to the limitations discussed below.

Under Italian law, our board of directors may not delegate certain responsibilities, including the preparation and approval of draft financial statements, the approval of merger and de-merger plans to be presented to shareholders' meetings, increases in the amount of our share capital or the issuance of convertible debentures (if any such power has been delegated to our board of directors by our shareholders at an extraordinary shareholders' meeting) and the fulfillment of the formalities required when our capital is required to be reduced as a result of accumulated losses that affect our stated capital by more than one third. See also, "Item 10, Additional Information, Memorandum and Articles of Association, Meetings of Shareholders."

Meetings of our board of directors are called three days in advance or, in case of urgency, at least one day in advance. Statutory auditors are normally required to attend our board meetings, but if a meeting has been duly called, the board can validly take action at the meeting even if the board of statutory auditors does not attend. If the meeting has not been duly called, the meeting is nevertheless validly constituted if all of the directors in office and all of the statutory auditors are in attendance. The chairman may call meetings on his own initiative and meetings must be called upon the request of two directors.

Meetings of our board of directors may be held in person, or by audio-conference or video-conference, in any member state of the European Union or in the United States. The quorum for meetings of our board of directors is the attendance of the majority of the directors in office. Resolutions are adopted by the vote of the majority of the directors in attendance at a meeting at which a quorum is met.

Under Italian law, directors having any interest in a proposed transaction must disclose their interest to the board and to the statutory auditors, even if such interest is not in conflict with our interest in the same transaction. The interested director is not required to abstain from voting on the resolution approving the transaction, but the resolution must state explicitly the reasons for, and the benefit to us of, the approved transaction. If these provisions are not complied with, or if the transaction would not have been approved without the vote of the interested director, the resolution may be challenged by a director or by our board of statutory auditors if the approved transaction may be prejudicial to us. A managing director, a member of the executive committee or any senior manager having any interest in a proposed transaction that he or she has authority to approve must solicit prior board approval of such transaction. The interested

director or senior manager may be held liable for damages to us resulting from a resolution adopted in breach of the above rules. Finally, directors may be held liable for damages to us if they illicitly profit from insider information or corporate opportunities.

Under Italian law, directors may be removed from office at any time by the vote of shareholders at an ordinary shareholders' meeting although, if removed in circumstances where there was no just cause, such directors 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. Directors may resign at any time by written notice to our board of directors and to the chairman of our board of statutory auditors. Our board of directors must appoint substitute directors to fill vacancies arising from removals or resignations, subject to the approval of the board of statutory auditors, to serve until the next ordinary shareholders' meeting. If, at any time, more than half of the members of our board of directors resign or otherwise cease to be directors, the board of directors in its entirety ceases to be in office and our board of statutory auditors must promptly call an ordinary shareholders' meeting to appoint new directors.

Our Compensation Committee recommends the compensation of our directors to our board of directors, which in turn makes recommendations to our shareholders. 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/or fees for attending board meetings. Our board of directors, after consultation with our board of statutory auditors, may determine the remuneration of directors that serve on the various board committees and/or perform management or other special services for us, such as managing directors. Our directors are entitled to reimbursement for expenses incurred in connection with their service as directors, such as expenses incurred in travel to attend board meetings. Our articles of association and bylaws do not contain any provisions with respect to borrowing powers exercisable by our directors.

Effective January 1, 2004, an Italian share corporation may adopt one of three different models of corporate governance structure. The three models are:

- a board of directors and a board of statutory auditors, which is the historical model that all companies had prior to January 1, 2004;

- a one-tier model with a single board of directors, including an audit committee composed of independent non-executive directors; or

- a two-tier model, including a management board, which is entrusted with management responsibilities, and a supervisory board which is entrusted mainly with control and supervisory responsibilities and, among other functions, appoints and removes the members of the management board and approves our annual financial statements.

Replacing the historical model with the new one-tier model or two-tier model requires an extraordinary shareholders meeting resolution. The amended bylaws approved by our shareholders on September 30, 2004 do not provide for a change in our governance structure. As a result, we continue to have a board of directors and a board of statutory auditors.

Statutory auditors

Under Italian law, at least one effective statutory auditor and one alternate statutory auditor of a company shall be chosen among those registered with the Register of Auditors established with the Ministry of Justice. The other statutory auditors shall be chosen among those registered with any register established by decree of the Ministry of Justice or among University professors in economic and law matters, if they are not registered with the Register of Auditors. The following persons may not be appointed as statutory auditors:

• one who is legally incapacitated, bankrupt, or disqualified from holding public or an executive office under Italian law;

• a spouse, parent or relative-in-law of someone who is a director of the company, a director of a company that controls the company, or a director of a company that is under common control with the company; and

• one whose independence may be jeopardized due to an employment or consultant relationship or any other economic relationship with the company, a company that controls the company, or a company that is under common control with the company.

In addition to electing our board of directors, our shareholders elect the board of statutory auditors (Collegio Sindacale) from individuals qualified to act in such capacity under Italian law. At our ordinary shareholders' meetings, the statutory auditors are elected for a term of three fiscal years, they may be re-elected for successive terms and may be removed only for cause and with the approval of a competent court. Each member of our board of statutory

auditors must provide evidence that such individual is qualified to act in such capacity under Italian law and meets certain professional standards.

Our bylaws currently provide that the board of statutory auditors shall consist of three effective statutory auditors and two alternate statutory auditors (who will automatically replace a statutory auditor who resigns or is otherwise unable to serve).

Our board of statutory auditors is required, among other things, to verify that we:

- comply with applicable laws and our bylaws;
- respect principles of good governance; and
- maintain adequate organizational structure, internal controls and administrative and accounting system.

Our board of statutory auditors is required to meet at least once every ninety days. In addition, our statutory auditors are supposed to attend meetings of our board of directors and meetings of our shareholders. In case a statutory auditor, without just cause, does not attend the shareholders' meetings or does not attend two consecutive meetings of the board of directors during the same fiscal year, such statutory auditor shall cease from his/her office. If the statutory auditors do not attend two consecutive meetings of the board of directors or shareholders, they may be terminated for cause by the shareholders. Our statutory auditors may decide to call a meeting of our shareholders, ask for information about our management from our directors, carry out inspections and verifications at our offices and exchange information with our external auditors. Any shareholder may submit a complaint to our board of statutory auditors regarding facts that the shareholder believes should be subject to scrutiny by our board of statutory auditors, which must take any complaint into account in its report to the shareholders' meeting. If shareholders collectively representing 5% of our share capital submit such a complaint, our board of statutory auditors must promptly undertake an investigation and present its findings and any recommendations to a shareholders' meeting (which must be convened immediately if the complaint appears to have a reasonable basis and there is an urgent need to take action). Our board of statutory auditors may report serious breaches of directors' duties to a competent court. The court may take such actions as it feels appropriate, including inspecting our company's operations, removing directors, appointing temporary administrators to manage our company and any other actions that the court feels is necessary to preserve the value of our company for our creditors and shareholders.

As mentioned in the preceding section, effective January 1, 2004, an Italian joint stock company may depart from the traditional Italian model of corporate governance structure and opt for two alternative models, neither of which includes a board of statutory auditors. Our amended bylaws do not provide for a change in our governance structure, although we do have an audit committee simply as an internal body of our board of directors.

External auditor

Italian law requires us to appoint an external auditor or a firm of external auditors ("revisore legale dei conti"), each of them qualified to act in such capacity under Italian law, that shall verify during the fiscal year that our accounting records are correctly kept and accurately reflect our activities, and that our consolidated financial statements correspond to the accounting records and the verifications conducted by the external auditors and comply with applicable rules. The external auditor or the firm of external auditors expresses its opinion on the consolidated financial statements in a report that may be reviewed by the shareholders at our offices prior to the annual shareholders' meeting. The report remains on file at our offices and may be reviewed after the annual shareholders' meeting as well; it is also published for review by the general public.

The external auditor or the firm of external auditors is appointed for a three-year term by the vote of our shareholders at an ordinary shareholders' meeting. At the ordinary shareholders' meeting, the shareholders may ask questions of the board of statutory auditors about its view of the auditors prior to voting on whether to appoint the auditors. Once appointed, the shareholders may remove the auditors only for cause and with the approval of the board of statutory auditors and of a competent court.

Meetings of shareholders

Shareholders are entitled to attend and vote at ordinary and extraordinary shareholders' meetings. Votes may be cast personally or by proxy. Shareholders' meetings may be called by our board of directors (or, in certain cases, by the board of statutory auditors) and must be called if requested by holders of at least 10% of the issued shares. Shareholders are not entitled to request that a meeting of shareholders be convened to vote on issues which as a matter of law shall be resolved upon the basis of a proposal, plan or report by our board of directors. If the shareholders' meeting is not called despite the shareholders' request and such refusal is unjustified, a competent court may call the meeting.

We may hold meetings of shareholders at our registered office in Villa Guardia, or elsewhere within Italy, the European Union or the United States following publication of notice of the meeting in the "Gazzetta Ufficiale della Republica Italiana" or in the newspaper "Il Sole 24 Ore" at least 15 days before the date fixed for the meeting. Our bylaws provide that we must mail written notice of meetings to our shareholders at least 10 days before the date fixed for the meeting. The depositary will mail to all record holders of ADSs a notice containing a summary of all information included in any notice of a shareholders' meeting received by the depositary. The notice of a shareholders' meeting must specify two meeting dates for an ordinary or extraordinary shareholders' meeting (first and second "calls"). The notice of the shareholders' meeting also specifies the dates for further calls. The notice must contain a list of the items to be dealt with and state the day, hour and place for the meeting for both the first and second calls. However, if the above procedures are not complied with, the shareholders' meeting will still be deemed validly held if all outstanding shares are represented, all other holders having the right to vote are present and a majority of the board of directors and the board of statutory auditors are in attendance.

We must convene an ordinary shareholders' meeting at least once a year within 120 days following the end of the fiscal year. Our annual consolidated financial statements must be approved by a vote of our shareholders at this annual ordinary shareholders' meeting. We may delay holding the shareholders' meeting up to 180 days following the end of the fiscal year if we are required to prepare consolidated financial statements or if particular circumstances concerning our structure or our purposes so require. At ordinary shareholders' meetings, our shareholders also appoint the external auditors, approve any distribution of dividends that have been proposed by our board of directors, elect our board of directors and statutory auditors, determine their remuneration and vote on any business matter for which resolution or authorization is entrusted to the shareholders by law.

We may call extraordinary shareholders' meetings to vote upon split-ups, dissolutions, appointment of receivers and similar extraordinary actions. We may also call extraordinary shareholders' meetings to vote upon proposed amendments to our bylaws, issuance of convertible debentures, mergers and de-mergers and capital increases and reductions, if the actions may not be authorized by the board of directors. The board of directors has the authority to transfer our registered office within Italy, authorize, on a non-exclusive basis, amendments to our bylaws that are required by law, authorize mergers by absorption to our subsidiaries in which we hold all or at least 90% of the issued share capital, authorize reductions of our share capital in case of withdrawal of a shareholder and indicate who among the directors is our legal representative. If the shareholders authorize the issuance of shares or other securities at an extraordinary meeting, they may delegate the power to make specific issuances to the board of directors.

Once our shareholders have authorized the issuance of securities, the securities that have been subscribed must be fully paid for before the shareholders may authorize the issuance of additional securities, unless the shareholders meet and vote to cancel those authorized but unsubscribed securities.

The quorum for an ordinary meeting of our shareholders on the first call is at least 50% of the outstanding ordinary shares, while on second call there is no quorum requirement. In either case, resolutions are adopted by the majority of ordinary shares in attendance or represented at the meeting. The quorum for an extraordinary shareholders' meeting is more than half of the outstanding ordinary shares on the first call and more than one-third of the outstanding shares on second call. Resolutions are adopted by the majority of the outstanding ordinary shares on first call and at least two-thirds of the holders of shares in attendance or represented at the meeting on second call. In addition, certain matters (such as, for example, a change in our purpose, the transfer of our registered office outside Italy or our liquidation prior to the date set forth in our bylaws) must be adopted by shareholders representing more than one-third of the outstanding ordinary shares (not just the ordinary shares in attendance or represented at the meeting).

Shareholders are entitled to one vote per ordinary share. Neither Italian law nor our bylaws limit the right of non-resident or foreign owners to hold or vote their shares. Shareholders do not need to "lodge" their share certificates (if any) or any communication from their broker in order to take part in the meeting. As a registered shareholder, the depositary (or its nominee) will be entitled to vote the ordinary shares underlying the ADSs. The deposit agreement requires the depositary (or its nominee) to accept voting instructions from owners of ADSs and to execute such instructions to the extent permitted by law.

Shareholders may appoint attorneys-in-fact by delivering in writing the proxies to represent them in an ordinary or extraordinary shareholders' meeting. Our directors, auditors and employees may not be proxies. Italian law provides that no proxy may represent more than 20 shareholders prior to the company "making recourse to the risk capital market." Italian scholars are undecided as to whether listing shares on an exchange outside of the European Union constitutes "making recourse to the risk capital market for the purpose of the application of the Italian Civil Code." If we are deemed to make recourse to the risk capital market by means of listing ADSs representing our ordinary shares on the Nasdaq Global Market System, no proxy may represent more than 50 shareholders if the capital is equal to €5 million or less, and no proxy may represent more than 100 shareholders if the capital is more than €5 million but less than or equal to €25 million. If the capital is more than €25 million, no proxy may represent more than 200 shareholders. At December 31, 2012, we had 15,038,483 shares outstanding and capital equal to Euro 38.97 million and so if we are

deemed to make recourse to the risk capital market, each proxy may not be granted to represent more than 100 shareholders.

Preemptive rights

Pursuant to Italian law, holders of outstanding ordinary shares and convertible debentures are entitled to subscribe for issuance of ordinary shares or convertible debentures in proportion to their holdings at the time that the shareholders authorize the capital increase for those issuances, unless those issuances are for non-cash considerations. The preemptive rights may be excluded or limited by resolution of the shareholders' adopted by the affirmative vote of holders of more than 50% of the ordinary shares at an extraordinary meeting of shareholders, or by a board of directors if the bylaws delegate such power to the board of directors (including the power to exclude or limit the preemptive right), and provided that such exclusion or limitation is in the interest of the company. There can be no assurance that the holders of ADSs will be able to fully exercise any preemptive rights to which our holders of ordinary shares may be entitled. If ADS holders are not able to exercise their preemptive rights, the depositary will, to the extent possible, dispose of such rights for their account.

F3F S.p.A. (formerly known as FinSirton S.p.A.) waived its preemptive right in connection with the authorization of our private placement of the Series A notes and warrants, the issuance of options under our Amended and Restated 2004 Equity Incentive Plan and Amended and Restated Nonstatutory Share Option Plan and Agreement and the issuance of 4,554,000 additional ordinary shares, which includes the shares underlying the ADSs offered in our initial public offering and the shares issued in our October 2005 private placement. Our shareholders waived their preemptive rights in connection with the authorization of 713,518 ordinary shares to be reserved for issuance upon exercise of the warrants we issued to the participants in our October 2005 private placement and the placement agent for that private placement.

Our board of directors excluded the shareholders' pre-emptive rights in connection with the authorization of 1,943,525 ordinary shares and 466,446 ordinary shares to be reserved for issuance of the warrants we issued to the participants in our June 2006 private placement. Our board of directors also excluded the shareholders' pre-emptive rights in connection with the authorization of 2,354,000 ordinary shares we issued to the participants in our February 2007 private placement. Our shareholders waived their pre-emptive rights in connection with the authorization of 1,000,000 ordinary shares to be reserved for issuance upon exercise of options available for grant under our 2007 Stock Option Plan.

Preference shares; other securities

Italian law permits us to issue preference shares with limited voting rights, other classes of equity securities with different economic and voting rights, "participation certificates" with limited economic and voting rights, as well as "tracking shares," if our bylaws permit such issuance. Our bylaws currently allow us to issue these securities. We may also issue convertible and non-convertible debt securities. In order to issue convertible debt securities, our board of directors would need to recommend to our shareholders that they approve the issuance of particular securities in connection with a capital increase, and the shareholders would need to vote to approve such an issuance and capital increase at an extraordinary meeting. The board of directors would also need to recommend, and the shareholders would need to approve by vote at the extraordinary meeting, specific terms of the securities. The shareholders may vote at the extraordinary shareholders' meeting to delegate authority to the board of directors to issue those securities from time to time, but not for more than five years from the date of the extraordinary shareholders' meeting.

Debt-equity ratio

Italian law provides that we may not issue debt securities for an amount exceeding twice the value of our capital, of our legal reserve and any other disposable reserves appearing on our latest Italian 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. Until our outstanding debt securities are repaid in full, we may not voluntarily reduce our capital or distribute our reserves (such as by declaring dividends) in the event the aggregate of the capital and reserves, following such reduction of capital and/or distribution of reserves, is less than half of the outstanding amount of the debt securities. 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, we cannot distribute profits to our shareholders until the ratio between the amount of our debt securities and our capital and reserves is restored. Moreover, some legal scholars are of the opinion that in such a case the ratio must be restored by a recapitalization of our company. If our equity is reduced, we could recapitalize by means of issuing new shares or having our current 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. These laws regarding the ratio of debt securities to capital and reserves do not apply to issuances of debt securities to professional investors (as defined by Italian law). However, in such a case, should the professional investors transfer such debt securities to third parties not qualified as professional investors, the former remain liable to us for the payment of such securities.

Reduction of equity by losses

Italian law requires us to reduce our shareholders' equity in certain situations. Our shareholders' equity has three main components: capital, legal reserves and other shareholders' equity (such as any share premium and any retained earnings). We first apply our losses from operations against our shareholders' equity other than legal reserves and capital. If additional losses remain, or if we have no shareholders' equity other than legal reserves and capital, and the additional losses are more than one-third of the amount of our legal reserves and capital, 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 reducing the legal reserves and capital by the amount of the remaining losses, or carrying the losses forward for up to one year. If the shareholders vote to elect to carry the losses forward up to one year, and the losses are still more than one-third of the amount of the capital at the end of the year, then we must reduce our capital by the amount of the losses. However, as an S.p.A., we must maintain capital of at least €120 thousand. If the amount of the losses would reduce our capital to less than €120 thousand, then:

- we would need to increase our capital, which we could do 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; or

- our shareholders would need to convert our company to an "S.r.l", which has a lower capital requirement of €10 thousand; or

    - if neither of these options were taken, our shareholders or, if they do not so resolve, a court of competent jurisdiction, could appoint a liquidator, not necessarily an Italian citizen, to liquidate our company.

Segregation of assets and proceeds

Pursuant to Italian law, our board of directors may resolve to segregate our assets into one or more separate pools. Such pools of assets may have an aggregate value not exceeding 10% of the net worth of the company. Each pool of assets must be used exclusively for the carrying out of a specific business and may not be attached by our general creditors. Similarly, creditors with respect to such specific business may only attach those assets that are included in the corresponding pool. Tort creditors, on the other hand, may always attach any of our assets. Our board of directors may authorize us to issue securities carrying economic and administrative rights relating to a pool. In addition, financing agreements relating to the funding of a specific business may provide that the proceeds of such business be used exclusively to repay the financing. Such proceeds may be attached only by the financing party and such financing party would have no recourse against other assets of ours.

We have no present intention to enter into any such transaction and no such transaction is currently in effect.

Liquidation rights

Pursuant to Italian law and subject to the satisfaction of the claims of all creditors, our shareholders are entitled to a distribution in liquidation that is equal to an amount resulting from the division of the positive liquidation balance by the number of shares (to the extent available out of our net assets). Preferred shareholders and holders of "participating certificates" typically do not participate in the distribution of assets of a dissolved corporation beyond their established contractual preferences. Once the rights of preferred shareholders and holders of participating certificates and the claims of all creditors have been fully satisfied, holders of ordinary shares are entitled to the distribution of any remaining assets.

Purchase of shares by us

We are permitted to purchase our outstanding shares, subject to certain conditions and limitations provided for by Italian law. We may only purchase the shares out of profits available for dividends or out of distributable reserves, in each case as appearing on the latest shareholder-approved consolidated financial statements. Further, we may only repurchase fully paid-in shares. Such purchases must be authorized by our shareholders by vote at an ordinary shareholders' meeting and the authorization may be issued for a period not exceed the term of eighteen (18) months.

A corresponding reserve equal to the purchase price of such shares must be created in the balance sheet, and such reserve is not available for distribution, unless such shares are sold or cancelled. Shares purchased and held by us may be resold only pursuant to a resolution of our shareholders adopted at an ordinary shareholders' meeting. The voting rights attaching to the shares held by us or our subsidiaries cannot be exercised, but the shares can be counted for quorum purposes in shareholders' meetings. Dividends and other rights, including pre-emptive rights, attaching to such shares will accrue to the benefit of other shareholders.

Notification of the acquisition of shares

In accordance with Italian antitrust laws, the Italian Antitrust Authority is required to prohibit the acquisition of control in a company which would thereby create or strengthen a dominant position in the domestic market or a significant part thereof and which would result in the elimination or substantial reduction, on a lasting basis, of competition, provided that certain turnover thresholds are exceeded. However, if the turnover of the acquiring party and the company to be acquired exceed certain other monetary thresholds, the antitrust review of the acquisition falls within the exclusive jurisdiction of the European Commission.

Minority shareholders' rights; withdrawal rights

Shareholders' resolutions which are not adopted in conformity with applicable law or our bylaws may be challenged (with certain limitations and exceptions) within ninety days by absent, dissenting or abstaining shareholders representing individually or in the aggregate at least 5% of our share capital (as well as by our board of directors or our board of statutory auditors). Shareholders not reaching this threshold or shareholders not entitled to vote at our meetings may only claim damages arising from the resolution.

Dissenting or absent shareholders may withdraw from the company as a result of shareholders' resolutions approving, among others things, material modifications of our purpose or of the voting rights of our ordinary shares, our transformation from a share corporation into a different legal entity or the transfer of our registered seat outside Italy. In such a case, our other shareholders would have a pre-emptive right to purchase the shares of the withdrawing shareholder. Should no shareholder exercise that pre-emptive right, the shares must be offered to third parties or, in the absence of any third party wishing to buy them, they will be purchased by us by using the available reserves. In the event that no reserve is available, our capital must be reduced accordingly. Any repurchase of such shares by us must be on terms authorized by our board of directors, upon consultation with our board of statutory auditors and our external auditor, having regard to our net asset value, our prospective earnings and the market value of our ordinary shares, if any. Under Italian law, we may set forth different criteria in our bylaws for the consideration to be paid to withdrawing shareholders. We have not done so as of the date of this annual report.

Each shareholder may bring to the attention of the board of statutory auditors facts or acts which such shareholder deems wrongful. If such shareholders represent more than 5% of our share capital, our board of statutory auditors must investigate without delay and report its findings and recommendations at our shareholders' meeting. Shareholders representing more than 10% of our share capital have the right to report to the competent court serious breaches of the duties of the directors which may be prejudicial to us or to our subsidiaries. In addition, shareholders representing at least 20% of our share capital may commence derivative suits before the competent court against our directors, statutory auditors and general managers. We may waive or settle the suit unless shareholders holding at least 20% of the shares vote against such waiver or settlement. We will reimburse the legal costs of such action in the event that the claim of such shareholder is successful and the court does not award such costs against the relevant directors, statutory auditors or general managers.

Liability for mismanagement of subsidiaries

Pursuant to Italian law, if we, acting in our own interest or the interest of third parties, mismanage a company that we control, we are liable to that company's shareholders and creditors for ensuing damages. That liability is excluded if the ensuing damage is fully eliminated, including through subsequent transactions, or the damage is effectively offset by the global benefits to the company from the continued exercise of such direction and coordination powers. We are presumed to have control over, among other companies, any subsidiary whose financial statements are consolidated into ours. Since we currently have no subsidiaries in Italy, this law does not apply to us at this time.

LIMITATION OF LIABILITY AND INDEMNIFICATION MATTERS

Insofar as indemnification for liabilities arising under Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, officers or persons controlling our company under the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

THE NASDAQ GLOBAL MARKET

Our ADSs are listed on The Nasdaq Global Market under the trading symbol "GENT."

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COMPARISON OF ITALIAN AND DELAWARE CORPORATE LAWS

WE ARE GOVERNED BY THE CORPORATE LAWS OF ITALY, WHICH ARE OFTEN LESS FAVORABLE TO SHAREHOLDERS THAN THE CORPORATE LAWS OF DELAWARE, UNITED STATES.

The following is a summary of material differences between the Delaware General Corporate Law and the laws of Italy.

Mergers and other extraordinary corporate transactions

Under Delaware law, a merger or consolidation requires the approval of a majority of the votes cast by the holders of shares entitled to vote in person or by proxy and, if any class or series is entitled to vote thereon as a class, the affirmative vote of a majority of the shares within each class or series entitled to vote as a class in person or by proxy, unless the certificate of incorporation requires a greater vote. The sale, lease, exchange or other disposition of all, or substantially all, the property and assets, of a Delaware corporation requires a majority vote unless the certificate of incorporation requires a greater vote. Under Delaware law, the dissolution of a corporation requires a majority vote unless the certificate of incorporation requires a greater vote.

Under Italian law, a merger requires the approval of more than half of the share capital at an extraordinary shareholders' meeting. Our bylaws authorize the board of directors to approve mergers of wholly-owned subsidiaries and subsidiaries of which we own at least 90%, although our shareholders may overrule our board of directors.

Amendments to charter documents

Under Delaware law, charter documents consist of a certificate of incorporation and bylaws. An amendment to the certificate of incorporation ordinarily requires a majority vote (unless the certificate of incorporation requires a greater vote). If a class or series is separately entitled to vote on an amendment, then its majority vote (unless the certificate of incorporation requires a greater vote), separately calculated, is necessary to approve the amendment. In addition, under Delaware law, the holders of outstanding shares of a class or series are entitled to vote as a class on a proposed amendment, whether or not entitled to vote thereon by the provisions of a company's certificate of incorporation, if the amendment would have certain effects identified in Delaware law. In such a case, an amendment must be approved by a majority of the voting power of the class (unless the certificate of incorporation requires a greater vote).

Under Delaware law, directors of a corporation may adopt, amend or repeal the corporation's bylaws, unless the certificate of incorporation reserves the power exclusively for the shareholders, or the shareholders, in amending, repealing or adopting a particular bylaw, expressly provide that the board of directors may not amend or repeal that bylaw. Unless the certificate of incorporation or a bylaw adopted by the shareholders provides otherwise, a corporation's shareholders may amend, repeal or adopt the corporation's bylaws even though the bylaws may also be amended, repealed or adopted by the directors of the corporation.

Under Italian law, the charter documents consist of articles of association and bylaws. An amendment to these documents requires the approval of more than half of the share capital at an extraordinary shareholders' meeting, except that certain extraordinary actions, such as a change in purpose, an advanced liquidation or an issuance of preferred shares, among others, only require the approval of more than one-third of the outstanding shares for both first and second call.

Naming of companies

Under Delaware law, the legal name of a company must include a corporate identifier or name ending, such as "association", "company", "corporation", "club", "foundation", "fund", "incorporated," "institute", "society", "union", "synd

(or an abbreviation of any of the foregoing, with or without punctuation), or any word (or abbreviation, with or without punctuation) of like import in foreign countries or jurisdictions (provided that such word or abbreviation is written in roman characters or letters).

Under Italian law, the legal name of a corporation must end in “S.p.A.” or “Societá per Azioni.”

Capital

Delaware law permits companies to be incorporated with par value shares or no par value shares. If a Delaware company issues par value shares and receives an amount in excess of the par value, the directors may attribute a portion of the excess as “capital.” If a Delaware company issues no par value shares, the directors may attribute a portion of the amount paid as “capital.”

Italian law permits companies to be incorporated with par value shares or no par value shares. If an Italian company issues shares with par value and receives an amount in excess of the par value, the par value is attributed as “capital” and the excess is attributed to a “premium reserve,” which is part of shareholders’ equity.

Franchise tax

Delaware levies a franchise tax based on authorized capital. Italian law has no such tax.

Liability of shareholders

The liability of shareholders of a Delaware company is limited to the amount paid by the shareholders for their shares. The liability of shareholders of an Italian company is also limited to the amount paid by the shareholders for their shares.

Quorum of shareholders

Under Delaware law, no action may be taken at a meeting of the shareholders, with respect to any matter, unless a quorum is present. A quorum is present if the holders of a majority of the shares entitled to vote are represented at the meeting in person or by proxy, unless the certificate of incorporation provides for a greater percentage. Where a separate vote by a class or series or classes or series is required, a quorum shall be present at a meeting of shareholders if the holders of a majority of the shares entitled to vote are represented at the meeting in person or by proxy, unless the certificate of incorporation provides for a greater percentage.

Under Italian law, a quorum must be present at an ordinary meeting of shareholders on first call, and shall exist if the holders of at least 50% of the outstanding ordinary shares are represented at the meeting in person or by proxy. There is no quorum requirement on second call. A quorum must be present at an extraordinary meeting of shareholders on first call and second call. A quorum is present on first call if the holders of more than half of the share capital are represented at the meeting in person or by proxy, and on second call if the holders of more than one-third of the outstanding shares are represented at the meeting in person or by proxy.

Actions without a meeting-shareholders

Under Delaware law, shareholders may take an action without a meeting upon written consent, signed by the shareholders holding the minimum number of votes that would be necessary to take such action at a meeting, unless the certificate of incorporation provides otherwise.

Under Italian law, shareholders may not act without a meeting.

Special/extraordinary meetings

Under Delaware law, special meetings of shareholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or the bylaws.

Under Italian law, an extraordinary shareholders’ meeting may be called by our board of directors and must be called if requested by holders of at least 10% of the issued shares. Shareholders are not entitled to request that a meeting of shareholders be convened to vote on issues which as a matter of law shall be resolved upon the basis of a proposal, plan or report by our board of directors. If a request by the shareholders for an extraordinary meeting, or even an ordinary meeting, is refused by the board of directors, and such refusal is unjustified, the meeting may be called by a competent court.

Director qualifications

Under Delaware law, a director is not required to be a resident of Delaware or a shareholder of the corporation unless the certificate of incorporation or bylaws so require. The certificate of incorporation or bylaws may prescribe director qualifications.

Under Italian law, the only directorship requirement is that the individual has not been deemed “legally incompetent” to serve as a director under Italian law. “Legal incompetence” is determined by a competent court and may be declared by reason of lack of mental capacity, physical incapability, emotional instability, bankruptcy, certain criminal convictions or drug or alcohol addiction.

Election of directors

Under Delaware law, shareholders are not entitled to elect directors through cumulative voting, unless the certificate of incorporation provides otherwise. Absent a provision to the contrary, the directors of a corporation are elected by a plurality of the votes cast by the holders of shares entitled to vote in person or by proxy at a meeting of shareholders at which a quorum is present.

Under Italian law, shareholders are not entitled to elect directors through cumulative voting. The directors of a corporation are elected by a majority of the votes cast by the shareholders entitled to vote in person or by proxy at an ordinary meeting of shareholders at which the relevant quorum is met.

Actions without a meeting - directors

Under Delaware law, any action required or permitted to be taken at any meeting of the board of directors may be taken without a meeting if all members of the board consent to the action in writing or by electronic transmission, and the writing or electronic transmission is filed with the minutes of proceedings of the board, unless otherwise restricted by the certificate of incorporation or bylaws.

Under Italian law, directors of a joint stock company may not act without a meeting.

Removal of directors

Under Delaware law, one or more directors of a corporation may be removed by the shareholders for cause or, unless the certificate of incorporation provides otherwise, without cause, upon the affirmative vote of the majority of votes cast by the holders of shares entitled to vote thereon, subject to certain exceptions.

Under Italian law, a director may be removed from office at any time by the vote of shareholders at an ordinary shareholders' meeting although, if the removal of a director was without just cause, such director 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. Subject to the approval of the board of statutory auditors, our board of directors appoints substitute directors to fill any vacancies caused by removal, who will serve until the next ordinary shareholders' meeting. If, at any time, more than half of the members of our board of directors are removed or otherwise cease to be directors, the board of directors will, in its entirety, cease to be in office, and our board of statutory auditors must promptly call an ordinary shareholders' meeting to appoint new directors.

Location of directors meetings

Delaware law provides that the board may hold its meetings outside of the State of Delaware, unless otherwise restricted by the certificate of incorporation or bylaws. Under Italian law and our bylaws, meetings of our board of directors may be held in person, or by audio-conference or video-conference, in any member state of the European Union or in the United States.

Limitation of liability and indemnification

Delaware law requires that directors and members of any committee designated by the board of directors perform their duties in good faith and with the degree of diligence, care and skill that an ordinary prudent person would exercise under similar circumstances. Delaware law permits a corporation to impose limitations on director liability. Italian law requires directors and members of any committee designated by the board of directors to perform their duties in good faith and with that degree of diligence that is required by the nature of their office and under their specific level of competence. If we cannot repay our creditors, and a court determines that our directors did not adequately perform their duties relating to the preservation of our assets, the court may find our directors liable to our creditors.

Dividends

Delaware law provides that the board of directors of a corporation may authorize and the corporation may make distributions subject to any restrictions in its certificate of incorporation. However, Delaware law provides that

distributions may not be made if, after making the distribution, the corporation would not be able to pay its debts as they become due in the usual course of its business or the total assets would be less than total liabilities.

Under Italian law, our payment of any annual dividend must be proposed by our board of directors to the shareholders and is subject to the approval of our shareholders at the annual ordinary shareholders' meeting. Before dividends may be paid out of our profits in any year, we must allocate an amount equal to 5% of the net profit to our legal reserve until such reserve is at least equal to 20% of our capital. If our capital is reduced as a result of accumulated losses, we may not pay dividends until the capital is reconstituted or reduced by the amount of such losses. We may distribute reserves derived from available earnings retained from prior years, provided that after such payment, we will have a legal reserve at least equal to the legally required minimum of 20% of the capital. We may not approve or pay dividends until this minimum (i.e., 20% of the capital) is met. If the minimum is met, the board of directors could propose the issuance of a dividend and the shareholders' resolution might approve that issuance. The shareholders' resolution will specify the manner and the date of dividend payment. Any dividends which shareholders do not collect within five years of the date on which they become payable will be forfeited by those shareholders and the money will come back to us. The board of directors may not approve interim dividends at times between our annual ordinary shareholders' meetings.

Return of capital

Delaware law provides that corporations may return capital by dividend, redemption or repurchase subject to certain solvency tests. Shareholder approval is not required for these transactions so long as the corporation meets the solvency tests.

Under Italian law, we are permitted to purchase our outstanding shares, subject to certain conditions and limitations. We may only purchase the shares out of profits available for dividends or out of distributable reserves, in each case as appearing on the latest shareholder-approved financial statements. Further, we may only repurchase fully paid-in shares. Such purchases must be authorized by shareholder vote at an ordinary shareholders' meeting and the authorization may be issued for a period not to exceed eighteen (18) months. A corresponding reserve equal to the purchase price of such shares must be created in the balance sheet, and such reserve is not available for distribution, unless such shares are sold or cancelled. Shares purchased and held by us may be resold only pursuant to a resolution of our shareholders adopted at an ordinary shareholders' meeting. The voting rights attaching to the shares held by us or our subsidiaries cannot be exercised, but the shares can be counted for quorum purposes in shareholders' meetings. Dividends and other rights, including pre-emptive rights, attaching to such shares, will accrue to the benefit of other shareholders.

Officers

Under Delaware law, a corporation is required to have at least two officers vested with the authority sign stock certificates and instruments to be filed with the Secretary of State. The corporation has complete freedom to designate any name to its executive positions and to allocate managerial power to its executives as it wishes. Any number of offices may be held by the same person, unless otherwise provided in the certificate of incorporation or the bylaws. Officers may be selected by any person or body and in any way specified in the bylaws or in a resolution of the governing body.

Under Italian law, there are no requirements with respect to the number, title or election of officers.

Share certificates

Under Delaware law, the shares of a corporation shall be represented by certificates, provided that the board of directors may resolve that some or all of any or all classes or series of its stock shall be uncertified stock. However, existing shareholders and future shareholders may, if they desire, obtain a stock certificate signed in the name of the corporation by the chairman or vice-chairman of the board of directors or the president or vice-president, and by the treasurer or an assistant treasurer, or the secretary or an assistant secretary of such corporation. The terms governing preferred stock, if any, must be expressed "in clear language" in the certificate of incorporation (or by a separate resolution authorized by the charter).

Under Italian law, the shares of a corporation may be issued in either registered or certificated form. Our bylaws provide that our ordinary shares are not certificated. Rather, they are held through various participants, primarily institutions, on Monte Titoli's system and registered by book-entry form on our shareholders book.

Preemptive rights

Under Delaware law, shareholders do not possess preemptive rights with respect to the issuance of additional securities by the corporation, unless the certificate of incorporation provides otherwise.

Under Italian law, shareholders and holders of convertible debentures are entitled to subscribe for issuance of ordinary shares or convertible debentures in proportion to their holdings at the time of authorization of the capital increase for

those issuances, except in the case of contributions in kind. The preemptive rights may be excluded or limited by a shareholders' resolution adopted by the affirmative vote of holders of more than 50% of the ordinary shares at an extraordinary meeting of the shareholders, in first and second call, and if such exclusion or limitation is in the interest of our company.

Liquidation rights generally

Under Delaware law, shareholders are entitled to share ratably in the distribution of assets upon the dissolution of a corporation. Asset distribution to preferred shareholders upon corporate dissolution is typically limited to established contractual preferences. Once the rights of preferred shareholders have been fully satisfied, holders of common stock are entitled to any remaining assets.

Under Italian law, and subject to the satisfaction of the claims of all creditors, upon liquidation our shareholders are entitled to a distribution that is equal to an amount resulting from the division of the positive liquidation balance by the number of shares or shareholders (to the extent available out of our net assets). Asset distribution to preferred shareholders and holders of "participating certificates" upon corporate dissolution is typically limited to established contractual preferences. Once the rights of preferred shareholders and holders of participating certificates have been fully satisfied, holders of ordinary shares are entitled to any remaining assets.

Shareholder derivative suits

Under Delaware law, a derivative suit may be brought only if the plaintiff was a record or beneficial owner of shares on the date of the transaction that gave rise to the suit, and the initial pleading in the suit states that the ownership requirement is satisfied, and also states with particularity, plaintiff's efforts to first obtain the action desired from the board of directors, or the reasons for not making such efforts. The court may require the plaintiff to give security for the expenses incurred or expected to be incurred by the defendants. The court may also require the plaintiff to pay expenses to the defendants if the court finds, upon a final judgment in favor of the defendants, that the suit was brought without reasonable cause.

Under Italian law, a shareholder's name must be entered in the shareholder's register in order to establish his shareholder rights against us. Shareholders may bring to the attention of the board of statutory auditors, facts or acts which such shareholder deems wrongful. If such shareholders represent more than 5% of our share capital, our board of statutory auditors must investigate without delay and report its findings and recommendations at our shareholders' meeting. Shareholders representing more than 10% of our share capital have the right to report to a competent court, serious breaches by directors of their director duties, which may be prejudicial to us or to our subsidiaries. In addition, shareholders representing at least 20% of our share capital may commence a derivative suit before a competent court against our directors, statutory auditors and general managers. We may waive or settle the suit unless shareholders holding at least 20% of the shares vote against such waiver or settlement. We will reimburse the legal costs of such action in the event that the claim of such shareholders is successful and the court does not award such costs against the relevant directors, statutory auditors or general managers.

Dissenters' rights

Any shareholder of a Delaware corporation has the right to dissent from any plan of merger or consolidation to which the corporation is a party, except that, unless the certificate of incorporation provides otherwise, a shareholder shall not have the right to dissent from any plan of merger or consolidation, with respect to shares of a class or series that are listed on a national securities exchange or held of record, by not less than 2,000 holders on the record date fixed to determine the shareholders entitled to vote upon the plan of merger or consolidation. A dissenting shareholder has a right to appraisal of its shares.

Under Italian law, shareholders' resolutions which are not adopted in conformity with applicable law or our bylaws may be challenged (with certain limitations and exceptions) within ninety days of such resolution by any absent, dissenting or abstaining shareholders representing in the aggregate at least 5% of our share capital (or by our board of directors or our board of statutory auditors). Shareholders who do not meet the threshold or are not otherwise entitled to vote at our meetings may only claim damages arising from the resolution.

Dissenting or absent shareholders may withdraw from the company as a result of shareholders' resolutions approving, among others things, material modifications to our purpose, the voting rights of our ordinary shares, our conversion from a share corporation into a different legal entity or a transfer of our registered office outside of Italy. Under any such circumstances, our other shareholders would have pre-emptive rights to purchase the shares of the withdrawing shareholders. Should no shareholder exercise its pre-emptive right, the shares must be offered to third parties. In no third party desires to purchase the shares, we will purchase them with our available reserves. In the event that there are no reserves available, we must reduce our capital accordingly. According to Italian law, our repurchase of any such shares must be on terms authorized by our board of directors, after consultation with our board of statutory auditors and our external auditor, and careful consideration of our net asset value, our prospective earnings and the market value of our ordinary shares, if any. Under Italian law, we may include provisions in our bylaws governing the payment of consideration to shareholders in the event of withdrawal. We have not done so as of the date of this annual report.

Interested shareholder transactions

Delaware corporations are subject to the State of Delaware's "business combination" statute. In general, that statute prohibits a publicly-traded corporation from engaging in various "business combination" transactions with any "interested stockholder" for a period of three years after the time that the shareholder became an interested stockholder, unless the business combination is approved by the board prior to the time the shareholder became an interested stockholder, the interested stockholder acquired 85% or more of the outstanding shares in a transaction in which it became an interested stockholder, or the business combination is approved by the board and by holders of two-thirds of the shares, excluding any shares held by the interested stockholder. A "business combination" includes a merger, assets sale or other transaction resulting in a financial benefit to a shareholder. An "interested stockholder" is a person who, together with affiliates and associates, owns 15% or more of a corporation's voting stock.

Under Italian law, a director having any interest in a proposed transaction must disclose his or her interest to the board of directors and to the board of statutory auditors, even if such interest does not conflict with our interest in the transaction. The interested director is not required to abstain from voting on the resolution approving the transaction, but the resolution must explicitly state the reasons for the approved transaction and the benefit of the transaction to us. If these provisions are not complied with, or if the transaction would not have been approved without the vote of the interested director, the resolution may be challenged by any director or by our board of statutory auditors on grounds that the approved transaction would be prejudicial to us. A legal representative of our company having any interest in a proposed transaction that he or she has authority to approve must solicit prior board approval before consenting to such transaction. The interested director may be held liable for damages to us resulting from a resolution adopted in breach of the above rules. Finally, a director may be held liable for illicitly profiting from insider information or a corporate opportunity.

Inspection of books and records

Under Delaware law, upon the written request of any shareholder, the corporation shall mail to such shareholder its balance sheet as of the end of the preceding fiscal year, and its profits, losses and surplus statements for such fiscal year. Inspection rights are extended to any person who beneficially owns stock through either a voting trustee or a nominee who holds the stock of record on behalf of such person. If the shareholder is not a holder of record, such person must state under oath the person's status as a shareholder and produce documentary evidence of beneficial ownership. Any shareholder is entitled to examine the relevant books and records of a corporation for any proper purpose, namely, a purpose reasonably related to such person's interest as a shareholder, upon written demand stating the purpose thereof.

Under Italian law, our shareholders may review the report of the board of directors on the management of our company and the report of our statutory auditors and accounting firm on our consolidated financial statements during the fifteen days prior to the ordinary shareholders' meeting to approve those consolidated financial statements. The report remains on file at our offices and may be reviewed after the annual shareholders' meeting. The report is also filed with the Companies' Registry of Como and made publicly available. Moreover, any shareholder is entitled to examine the shareholders' ledger and the ledger of the minutes of the shareholders' meeting, at any time.

Registered office

Delaware law requires that a corporation have a "registered office" in Delaware. Italian law requires that a corporation have a registered office in Italy.

Issuance of shares

Under Delaware law, directors have the authority to issue shares of common stock. If the certificate of incorporation so provides, the directors may also designate the terms of preferred stock and issue shares of preferred stock.

Under Italian law, the issuance of any shares, ordinary or otherwise, requires an amendment to our bylaws to increase our capital, which must be recommended to our shareholders by our board of directors and approved by a vote of our shareholders at an extraordinary meeting of the shareholders. Once our shareholders have authorized the issuance of securities and the same have been subscribed, those securities must be paid for before the newly issued shares may be purchased. The board would also need to recommend, and the shareholders would need to approve by vote at the extraordinary meeting, specific terms of the securities. Alternatively, our shareholders can delegate the power to increase our capital to the board of directors, but the board's right to exercise such power, if delegated, will expire after five years. If the board does not approve a capital increase by the end of those five years, our board and shareholders would need to meet again to re-delegate this authority. Our shareholders authorized our board of directors to increase our capital by up to €90 million of ordinary shares and €10 million for ordinary shares issuable upon conversion of convertible bonds on May 9, 2011. In addition, on June 30, 2009, our shareholders resolved to grant the board of directors with the power to increase our capital in cash up to an amount equal to €100 million on a separable basis, in one or more transactions, with the faculty to reserve all or part of such amount to the exercise of warrants issued by means of the same resolution of the Board of Directors approving the relevant capital increase, and with the faculty to reserve 1/4 of any such capital increase to employees as equity incentive under the Company's equity incentive plans. With respect to shareholders' resolutions approving capital increases, Italian law provides that in the absence of meeting minutes, any interested person may challenge such resolution for a period of 180 days following the filing of the shareholders' resolution with the Register of Companies. 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 consolidated financial statements referring to the year during which the shareholders' resolution has been, also partially, executed. Finally, once our shareholders authorize a capital increase, all those authorized shares that have been subscribed must be paid-up entirely before the

shareholders may authorize a new capital increase.

Debt-equity ratio

Under Delaware law, there are no restrictions on the amount of debt securities that a corporation may issue.

Under Italian law, we may issue debt securities in an amount not to exceed twice the sum of our capital, our legal reserve and any other disposable reserves appearing on our latest Italian balance sheet approved by our shareholders. The legal reserve is a reserve to which we allocate 5% of our net income each year until it equals at least 20% of our capital. One of the other reserves that we maintain on our balance sheet is a “share premium reserve”, which reflects the amount paid for our ordinary shares in excess of the amount of such ordinary shares allocated to our capital. We may not voluntarily reduce our capital or distribute our reserves (such as by declaring dividends) until our outstanding debt securities are repaid in full. In the event the aggregate of the capital and reserves, following such reduction of capital and/or distribution of reserves, is less than half of the outstanding amount of the debt securities. 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, we cannot distribute profits to our shareholders until the ratio between the amount of our debt securities and our capital and reserves is restored. 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 means of issuing new shares by or having our current 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. These laws regarding the ratio of debt securities to capital and reserves do not apply to the issuance of debt securities to professional investors (as defined by Italian law). However, professional investors who transfer such debt securities issued by us to third parties not qualified as professional investors would remain liable to us for the payment of such securities.

Reduction of equity by losses

Under Delaware law, shareholder equity in a corporation is reduced by losses and may become negative.

Italian law requires us to reduce our shareholders' equity in certain situations. Our shareholders' equity has three main components: capital, legal reserves and other shareholders' equity (such as any premium paid for the shares over the par value and any retained earnings). We apply our losses from operations against our legal reserves and capital. If our capital is reduced by 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, reducing the legal reserves and capital by the amount of the remaining losses, or carrying the losses forward up to one year. If the shareholders vote to carry the losses forward up to one year, and the losses are still more than one-third of the amount of the capital at the end of that year, then we must reduce our capital by the amount of the losses suffered. However, as an S.p.A., we must maintain capital of at least €120 thousand. If the amount of the losses would reduce our capital to less than €120 thousand, then:

- we would need to increase our capital, which we could do 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; or
    - our shareholders would need to convert our company to an "S.r.l", a private limited liability company, which has a lower capital requirement of €10 thousand; or
- if neither of these options is pursued, our shareholders or, if they do not so resolve, a court of competent jurisdiction, could appoint a liquidator, who need not be an Italian citizen, to liquidate our company.

MATERIAL CONTRACTS

The contracts described below have been in existence during the last two years and, as of the date of this report, contain provisions under which we have an obligation or right that is or may be material to us. This discussion is not complete and should be read in conjunction with the agreements described below, each of which has been filed with the SEC as an exhibit to this annual report.

On January 7, 2010, we amended our existing license with Sigma-Tau Pharmaceuticals, Inc. to encompass a license for the intravenous formulation of defibrotide for the prevention of veno-occlusive disease in the Americas and to transfer the New Drug Application post-approval in the United States. In addition, we agreed to establish a joint steering committee with Sigma-Tau to engage in good faith negotiations regarding the funding of certain additional costs that may be required to obtain regulatory approval in the U.S., and we further agreed that $1.0 million in costs reimbursed by Sigma-Tau will be deductible from royalty payments owed to us in the future under the license agreement. In 2012, Sigma-Tau agreed to reimburse us approximately $2.9 million over the next two years.

EXCHANGE CONTROLS

No exchange control consent is required in Italy for the transfer of dividends or other distributions with respect to shares of an Italian company or proceeds from the sale thereof to persons outside of Italy.

TAXATION

Tax Consequences Applicable to US Holders

The following section contains a description of the principal United States federal and Italian tax consequences of the purchase, ownership and disposition of ADSs or ordinary shares by a US holder, as defined below. This summary does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a decision to purchase ADSs representing our ordinary shares and each potential purchaser is therefore urged to consult an independent tax advisor.

In particular, this summary deals only with US holders who will hold ADSs as capital assets and does not address the tax treatment of a US holder:

- who owns ADSs representing 10% or more of our voting shares (either directly or through attribution);
- who holds ADSs in connection with a permanent establishment or fixed base of business located in Italy;
- who holds ADSs in the ordinary course or as an integral part of the holder's trade or business or as part of a hedging, straddle, integrated or conversion transaction;
- who is subject to special treatment under the US income tax laws (such as securities dealers, brokers, traders that elect to market, insurance companies, banks, tax-exempt organizations, partnerships and other pass-through entities);
- whose functional currency is not the US dollar; or
- who is a resident of Italy for purposes of Italian domestic law or the Income Tax Convention, as defined above, or acts through an Italian permanent establishment or fixed base to which the ADSs are connected.

In addition, the following discussion does not address any aspect of state, local or non-US tax laws (other than certain Italian tax laws) or any alternative minimum tax consequences.

The summary is based upon tax laws of the United States and the Republic of Italy and on the provisions of the Income Tax Convention in each case as in effect on the date hereof, all of which are subject to change (possibly with retroactive effect). We will not update this summary to reflect changes in laws and if such a change occurs, this summary could become inaccurate. For purposes of these laws and Income Tax Conventions, beneficial owners of ADRs representing ADSs should be treated as the beneficial owners of the ordinary shares represented by the ADSs. Prospective purchasers of the ADSs are advised to consult an independent tax advisor as to the tax consequences of the purchase, ownership and disposition of the ADSs including, in particular, state and local tax consequences.

For purposes of this section, a US holder means:

- an individual citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) organized in or under the laws of the US or any political subdivision thereof;
- an estate, the income of which is includible in gross income for US federal income tax purposes regardless of its source;
- a trust, if a US court is able to exercise primary jurisdiction over the administration of the trust and one or more US persons have the authority to control all substantial decisions of the trust; and

- any other person subject to US federal income taxation on a net income basis in respect of income attributable to its ownership of the ADSs. A US owner means a US holder that is considered a resident of the United States for purposes of the Income Tax Convention and who is not subject to an anti-treaty shopping provision.

Italian Taxation of US Holders

General. Under Italian law, financial instruments issued by an Italian company are subject to the same tax regime as are shares, provided that their remuneration is entirely represented by participation in the economic results of the issuer. Pursuant to Article 10(3) of the Income Tax Convention, the tax regime of dividends applies to income from corporate rights of an Italian company, which is subject to the same taxation treatment as income from shares under the laws of Italy. One interpretation of these laws is that a beneficial owner of an ADS should be subject to the same tax regime as a beneficial owner of a share for purposes of both Italian law and the Income Tax Convention. However, no official interpretation has been issued by the Italian tax authorities on this subject matter to date.

Income Tax Withholding on Dividends. We do not anticipate making any distributions on our ordinary shares in the foreseeable future. However, if we were to make distributions on our ordinary shares, we would generally be required under Italian law, except as otherwise discussed below, to apply a 20% final withholding tax on payments made to holders of ADSs who are not residents of Italy for tax purposes. Under Italian law, US owners can claim a refund of up to one-fourth of the Italian withholding tax withheld on dividends (effectively reducing the rate of withholding to 15%) upon presenting evidence to the Italian tax authorities that income taxes have been fully paid on the dividends in the country of residence of the US owners in an amount at least equal to the total refund claimed. US holders should consult an independent tax advisor concerning the availability of this refund, which has traditionally become payable only after extensive delays.

Under the Income Tax Convention, dividends paid to US owners will be subject to Italian withholding tax at a reduced rate of 15% for individuals not engaged in entrepreneurial activities. However, the amount that we will initially make available to the depositary for payment to US owners will reflect withholding at the 20% rate. US owners who comply with the certification procedures described below may claim a refund of the difference between the 20% rate and the 15% rate (referred to herein as a "treaty refund"). The certification procedure will require the US owner to:

• obtain from the US Internal Revenue Service (generally, by filing Form 8802) a form of certification required by the Italian tax authorities with respect to each dividend payment (Form 6166, printed on U.S. Department of Treasury stationary), unless a previously filed certification is effective with respect to the payment,

• produce a statement whereby the US owner represents that it is a US owner that does not maintain a permanent establishment in Italy, and

• set forth certain other required information. The time for processing requests for certification by the Internal Revenue Service can be lengthy. Accordingly, US owners should begin the process of obtaining a certification from the Internal Revenue Service as soon as possible after receiving instructions from the depositary.

The depositary's instructions will specify certain deadlines for delivering the documentation required to obtain a treaty refund, including the certification that the US owners must obtain from the US Internal Revenue Service. In the case of ADSs held by US owners through a broker or other financial intermediary, the required documentation should be delivered to such financial intermediary for transmission to the depositary. In all other cases, US owners should deliver the required documentation directly to the depositary. We have agreed with the depositary that if the required documentation is received by the depositary on or within 30 days after the dividend payment date and, in our reasonable judgment, such documentation satisfies the requirements for a refund of Italian withholding taxes under the Income Tax Convention then in effect between the United States and Italy, we will (within 45 days after that period) pay an amount equal to the treaty refund to the depositary for the benefit of the US owners entitled thereto.

If the depositary does not receive a US owner's required documentation within 30 days after the dividend payment date, the US owner may, for a short grace period (specified in the depositary's instructions), continue to claim an amount equal to the treaty refund by delivering the required documentation (either through the US owner's financial intermediary or directly, as the case may be) to the depositary. However, after this grace period, the treaty refund must be claimed directly from the Italian tax authorities rather than through the depositary. US owners seeking refunds from the Italian tax authorities have encountered expensive and extensive delays.

Income Tax on Capital Gains. Under Italian law, capital gains realized by a person who is not a resident of Italy (meaning that such person does not have a permanent establishment or fixed base in Italy to which the ADSs are connected) on the disposal of a "qualified" shareholding, contribute to determine the overall taxable income for income tax purposes. Ministerial Decree April 2, 2008 – issued pursuant to Article 1, paragraph 38 of the Law December 24, 2007 (Budget Law 2008) – sets out that 49.72% (it was 40% until 2008) of the capital gains would contribute to

determine the overall taxable income. This rate applies to capital gains realized from January 1, 2009. The 40% previously in effect still applies to capital gains realized in connection with disposal deeds executed before January 1, 2009. Losses can be offset against taxable gains for a corresponding amount and, if in excess, can be carried forward up to four years. A "qualified" shareholding is defined as ordinary shares and/or rights (including ADSs) that represent more than 20% of share capital voting in the ordinary shareholders' meeting or 25% of the company's total share capital. A "disposal" of a qualified shareholding occurs if, in any 12-month period following the date when a shareholding meets one of the thresholds illustrated above, a shareholder disposes of shares or ADSs that, individually or in the aggregate, constitute a "qualified" shareholding. Generally, Italian capital gain tax, levied at a rate of 20%, is imposed on gains realized upon the transfer or sale of "non-qualified" shareholdings whether held within or outside Italy. A "non-qualified" shareholding is defined as an interest in ordinary shares and/or rights (including ADSs) which does not reach the thresholds described above for a qualified shareholding.

Furthermore, save for any applicable anti-avoidance provision, pursuant to the Income Tax Convention, a US owner will not be subject to Italian capital gain tax or to Italian individual or corporate income tax unless such US owner has a permanent establishment or fixed base in Italy to which the owner's ADSs is effectively connected. To this end, US owners selling ADSs and claiming benefits under the Income Tax Convention may be required to produce appropriate documentation establishing that the above-mentioned conditions have been met.

Estate and Gift Tax. Inheritance and gift taxes, which were abolished in 2001, have been re-introduced in the Italian system by Law Decree No. 262 of October 3, 2006 (converted into law, with amendments, by Law Decree No. 286 of November 24, 2006), as amended. Such taxes will apply to the overall net value of the relevant assets, at the following rates, depending on the relationship between the testate (or donor) and the beneficiary (or donee): (a) 4%, if the beneficiary (or donee) is the spouse or a direct ascendant or descendant (such rate only applying on the net asset value exceeding, for each person, €1 million); (b) 6%, if the beneficiary (or donee) is a brother or sister (such rate only applying on the net asset value exceeding, for each person, €100 thousand); (c) 6% if the beneficiary (or donee) is another relative within the fourth degree or a direct relative-in-law as well as an indirect relative-in-law within the third degree; and (d) 8% if the beneficiary is a person other than those mentioned under (a), (b) and (c), above. If the beneficiary has a serious disability recognized under applicable law, inheritance and gift taxes will apply to its portion of the net asset value exceeding €1.5 million.

Transfer tax. In connection with the Italian stamp duty tax on the transfer of shares and ADSs, according to article 37 of Law No. 248 of December 31, 2007, converted with amendments into Law No. 31 of February 28, 2008, the stamp duty has been abolished with regard to contracts having as their object the transfer of shares. In certain cases the relevant transfer acts would be subject to the registration tax at a flat amount equal to €168.

New Stamp Duty. A stamp duty has been introduced under article 19 of Law Decree No. 201 of December 6, 2011, converted into Law No. 214 of December 22, 2011, to be imposed on communications (issued by banks and financial intermediaries) to clients relating to securities, even where the deposit of such securities is not mandatory (although certain entities are excluded). The amount of the stamp duty is based on the market value of the securities or, in the absence of a market value, on the nominal amount or the amount payable on redemption. The following rates apply:

0.1% for 2012; and

0.15% for 2013,

subject to a minimum amount of €34.20 and, for the year 2012, a maximum amount of €1,200. The communication is deemed to be sent to clients at least once a year, even where there is no obligation to issue any such communication.

United States Taxation of US Holders

Taxation of Distributions Made on ADSs. As previously indicated, we do not anticipate making any distributions on our ordinary shares in the foreseeable future. However, if we were to make distributions with respect to our ordinary shares, the amount of any such distribution (including the amount of any Italian taxes withheld therefrom) would generally be includible in the gross income of a US holder of an ADS (on the date of receipt by the depositary) as foreign source dividend income to the extent that such distributions are paid out of our current or accumulated earnings and profits, as determined for United States federal income tax purposes. If the amount of any distribution paid on our ordinary shares exceeds our current and accumulated earnings and profits, that excess will first reduce a holder's basis in its ADSs and, to the extent the distribution is in excess of the holder's basis, the excess amount will be treated as a capital gain. Dividends paid to US holders that are corporations will not be eligible for the dividends-received deduction (which is generally applicable only to dividends paid by US corporations).

The US dollar amount of dividends received by individuals prior to January 1, 2013 with respect to our shares or ADSs will be subject to taxation at a maximum rate, 15% subject to exceptions for certain short-term and hedged stock positions. Dividends received from a "qualified foreign corporation" generally qualify for the reduced rate. In this regard, a foreign corporation that is not a passive foreign investment company (PFIC) in the year that the dividends are paid or in the preceding taxable year will generally constitute a qualified foreign corporation with respect to any dividends paid by it on its stock if the stock is readily tradable on an established securities market in the United States. Because the ADSs are readily tradable on an established securities market in the United States, we should constitute a

qualified foreign corporation and dividends paid on our ordinary shares prior to January 1, 2013 and received by US holders of ADSs that are individuals should qualify for the reduced rate, subject to above-mentioned exception for certain short-term and hedged stock positions, so long as we are not a PFIC in the year the dividends are paid or in the preceding taxable year (and so long as the ADSs continue to be readily tradable on an established securities market). While we do not believe that we qualify as a PFIC at present, no assurances can be provided that we will not constitute a PFIC in any year during which we make a distribution on our ordinary shares (or in the taxable year preceding the year of distribution).

The amount of any cash distribution received in Euro with respect to the ADSs will equal the US dollar value of the distribution, including the amount of any Italian taxes withheld therefrom, determined on the basis of the spot exchange rate in effect on the date that the distribution is received by the depositary (regardless of whether or not the distribution is in fact converted into US dollars), and a US holder will have a tax basis in the Euro equal to that same value. Upon a subsequent sale or other disposition of the Euro, any gain or loss recognized by the US holder will be ordinary income or loss for US federal income tax purposes.

Subject to general foreign tax credit limitations, a US holder may elect to credit any Italian income taxes withheld on dividends paid with respect to the ADSs against the holder's US federal income tax liability (provided, inter alia, that the US holder satisfies certain holding requirements with respect to the ADSs). Amounts withheld in excess of the applicable rate under the Income Tax Convention in effect between the United States and Italy in respect of a US holder who qualifies for the benefits of the convention will not be eligible for this credit, but the US holder may claim a refund for this excess from the Italian tax authorities. See "Item 10, Additional Information, Taxation, Italian Taxation of US Holders, Income Tax Withholding on Dividends." As an alternative to claiming a foreign tax credit, a US holder may claim a deduction for any Italian income taxes withheld, but only with respect to a year from which the US holder elects to do so with respect to all of its foreign income taxes. There are complex rules that limit the amount of foreign income taxes that may be credited against a US holder's federal income tax liability, and US holders are strongly urged to consult an independent tax advisor as to the applicability of these limitations.

Sales or other Disposition of the ADSs. Subject to the discussion set forth below regarding PFICs, a US holder will recognize capital gain or loss for US federal income tax purposes on the sale or other disposition of the ADSs equal to the difference between the amounts realized on the disposition and the holder's basis in the ADSs. Such gain or loss will generally be long-term capital gain or loss if the US holder has owned the ADSs for more than one year at the time of the sale or other disposition.

Back-up Withholding. A US holder may be subject to back-up withholding at the applicable rate with respect to dividends paid on or proceeds from the sale or other disposition of the ADSs unless the US holder (a) is an exempt recipient or (b) provides a taxpayer identification number, certifies as to no loss of exemption from back-up withholding and otherwise complies with all applicable back-up withholding requirements.

Special Rules Applicable to PFICs. Special federal income tax rules apply to US holders who own stock in a PFIC. In this regard, a foreign corporation is generally considered for PFIC for any taxable year in which 75% or more of its gross income is passive income or in which 50% or more of the average value of its assets are considered "passive assets" (generally assets that generate passive income or assets held for the production of passive income). We believe that we do not qualify as a PFIC at present and we do not anticipate that we will become a PFIC in the future.

However, if we were to be classified as a PFIC, a US holder would generally be subject to a special tax at ordinary income tax rates on so-called "excess distributions"—which include certain distributions received on the ADSs and gain recognized on any sale or other disposition of the ADSs. To compensate for any tax deferral, the amount of income tax on these excess distributions will be increased by an interest charge, calculated as if the excess distributions were earned ratably over the period during which the US holder held the ADSs. In addition, the tax on excess distributions treated as earned in prior years will be subject to tax at the maximum rate applicable in the year in which such income is deemed to have been earned. The harsh consequences of these rules may be avoided if the US holder properly elects to include such holder's pro rata share of our ordinary earnings in its ordinary income each year and to include such holder's pro rata share of our net capital gain, whether or not distributed, in its long-term capital gain income each year. However, we do not intend to provide US holders with the information that they would need in order to make this election. Alternatively, a holder of ADSs may avoid the tax consequences detailed above by making a mark-to-market election, but only if the ADSs are "regularly traded" for purposes of Section 1296 of the Code. No assurances can be made that the ADSs will be regularly traded and, in any event, a US holder should consult an independent tax advisor before making any election under Section 1296 of the Code.

In addition, if we were to be classified as a PFIC, US holders would not qualify for the benefit of the reduced US federal tax rate applicable to certain dividends received by individuals through the end of 2013, as described above in "United States Taxation of US Holders—Taxation of Distributions Made on the ADSs."

DIVIDENDS AND PAYING AGENTS

Not applicable.

STATEMENTS BY EXPERTS

Not applicable.

DOCUMENTS ON DISPLAY

We are subject to the periodic reporting and other informational requirements of the Exchange Act applicable to a foreign private issuer. Under the Exchange Act, we are required to file annual reports on Form 20-F within six months of our fiscal year end, and we submit other reports and information under cover on Form 6-K with the SEC. Copies of the registration statements, their accompanying exhibits, as well as such reports and other information, when so filed, may be inspected without charge and may be obtained at prescribed rates at the SEC's Public Reference Room located at 450 Fifth Street, N.W., Room 1200, Washington, D.C. 20549. You may obtain information regarding the Washington, D.C. Public Reference Room by calling the SEC at 1-800-SEC-0330 or by contacting the SEC at its website at www.sec.gov.

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and consolidated financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act.

SUBSIDIARY INFORMATION

In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations. Our consolidated financial statements reflect the financials of the Company and Gentium GmbH. All intercompany balances and transactions are eliminated in consolidation.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

As of December 31, 2012, substantially all of our cash and cash equivalents were held in accounts at financial institutions located in the Republic of Italy and in the United States, which we believe are of acceptable credit quality. The goals of our investment policy are liquidity and capital preservation. To achieve this objective, we invest our cash in liquid instruments that meet high credit quality standards and generally have a maturity of less than three months from the date of purchase. We are exposed to exchange rate risk with respect to certain of our cash balances, accounts receivable and accounts payable that are denominated in the U.S. dollar. As of December 31, 2012 we held a cash balance of $2.06 million, accounts receivable of $0.83 million and accounts payable of $0.84 million that were denominated in U.S. dollars. As the net positions of our unhedged foreign currency transactions fluctuate, our earnings might be negatively affected. As of December 31, 2012, our foreign currency transactions are minimal and changes to the exchange rate between the US dollar and euro would have an immaterial effect on our earnings. If the US dollar were 10% stronger against the euro, our net assets balance would increase by approximately €0.31 million as of December 31, 2012.

As of December 31, 2012, we had floating debts in the principal amount of €1.54 million. Our exposure includes changes in interest rates, as borrowing under our debts bears interest at floating rates based on Euribor plus an applicable margin. The rate is currently variable based on Euribor interest rates, subject to certain minimums, that range from 0.99% to 1.89%. Each 100 basis point increase in interest rates will cause interest payments in 2013 to increase by approximately €0.01 million. Substantially all of our current revenue generating transactions and substantially all of our assets and liabilities are denominated in the euro. In the future, we expect to transact business in U.S. dollars and other currencies. The value of the euro against the United States dollar and other currencies may fluctuate and is affected by, among other things, changes in political and economic conditions. Any change in the value of the euro relative to other currencies in which we transact business in the future could materially and adversely affect our cash flow, revenues and financial condition. To the extent that we hold assets denominated in United States dollars, any appreciation of the euro against the United States dollar could result in a charge to our operating results and a reduction in the value of our United States dollar denominated assets upon re-measurement.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES.

The Bank of New York Mellon serves as the depositary for our ADR program and collects fees for depositing shares or surrendering ADSs. The Bank of New York Mellon is headquartered at One Wall Street, New York, New York, 10286.

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Each ADS represents one ordinary share. Holders of ADSs will not be able to independently exercise voting rights attaching to the ordinary shares evidenced by the ADSs. Holders of ADSs will only have the right to instruct the depositary, as the holders' representative, to exercise these voting rights. The depositary will mail to all ADS record holders a notice containing a summary of all information included in any notice of a shareholders' meeting received by the depositary, and will solicit proxies from ADS holders for instructions on how to vote its ordinary shares at our shareholder meetings. Additional limitations are imposed on the rights of owners of ADSs representing our ordinary shares, as explained in our risk factors entitled Risks Related to Ownership of the American Depositary Shares "–You may not be able to participate in rights offerings and may experience dilution of your holdings as a result" and "–You may be subject to limitations on transfer of your ADSs."

The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deducting from cash distributions, directly billing investors or charging the book-entry system accounts of participants acting for them. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

Persons depositing or withdrawing shares must pay:	For:
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of shares or rights; or Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$0.02 (or less) per ADS	Any cash distribution to ADS holders For depositary services accrued on the last day of each calendar year to the extent no fee was charged for any cash distribution
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities which are distributed by the depositary to ADS holders
Registration or transfer fees	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	Cable, telex and facsimile transmissions (when expressly provided in the deposit agreement), or Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian have to pay on any ADS or share underlying an ADS, for example, stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The deposit arrangement, including the fees listed above, may be amended from time to time by agreement between the Bank of New York Mellon and the Company, and without consent from holders of the ADSs. In addition, both the Company and Bank of New York have the ability to terminate the agreement upon proper notice given to the other party.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

None.

ITEM 15. CONTROLS AND PROCEDURES

Management's Report on Internal Control Over Financial Reporting

(a) We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports filed under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) of the Exchange Act, an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act) as of the end of the period covered by this annual report was carried out under the supervision and with the participation of our management, including our chief executive officer and chief financial officer. Based on that evaluation, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures are effective to provide reasonable assurance that information required to be disclosed in the reports the Company files and submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's applicable rules and forms and that it is accumulated and communicated to the Company's management, including the Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

(b) Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published consolidated financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to consolidated financial statement preparation and presentation.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2012. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework. Based on our assessment, management has concluded that, as of December 31, 2012, our internal control over financial reporting is effective.

(c) There has not been any change in our internal control over financial reporting identified in the evaluation required by Rule 13a-15 or Rule 15d-15 of the Exchange Act that occurred during the period covered by this annual report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

(d) As of December 31, 2012, the effectiveness of internal controls over Financial Reporting has been audited by Reconta Ernst & Young S.p.A., an independent registered public accounting firm, in their report on the Company's internal controls over financial reporting, which follows below.

Gentium S.p.A.
April 1, 2013

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Gentium S.p.A.

We have audited Gentium S.p.A.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Gentium's S.p.A. management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's report on internal control over financial reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Gentium S.p.A. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the 2012 consolidated financial statements of Gentium S.p.A. and our report dated April 1, 2013 expressed an unqualified opinion thereon.

/s/ Reconta Ernst & Young S.p.A.
Milan, Italy
April 1, 2013

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

We have both a board of statutory auditors and an audit committee. Our board of directors has determined that Gigliola Bertoglio qualifies as an "audit committee financial expert" within the meaning of this Item 16A.

ITEM 16B. CODE OF ETHICS

We have adopted a code of ethics, as defined in Item 16B of Form 20-F under the Securities Exchange Act of 1934, as amended, that is applicable to, among others, our Chief Executive Officer and Chief Financial Officer. Copies of this code of ethics are available upon request by writing to us at the address on the cover page of this annual report; we have also posted the code of ethics on our website at www.gentium.it. Material appearing on this website is not incorporated by reference into this annual report. If we amend the provisions of this code of ethics, or if we grant any waiver of such provisions, we will disclose such amendment or waiver on our website at the same address.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The following table sets forth the fees contractually agreed to with our independent auditors, Reconta Ernst & Young S.p.A. for the fiscal years ended December 31, 2011 and 2012:

(in thousands of Euros)	Year ended December 31,	
	2011	2012
Audit Fees	€ 150	€ 180

In the above table, in accordance with the SEC's definitions and rules, "audit fees" are fees for professional services the audit of a company's consolidated financial statements, and for services that are normally provided by the accountant in connection with statutory and regulatory filings or engagements. Reconta Ernst & Young S.p.A. did not provide any tax compliance services or advice on specific changes in tax regulations for the years ended December 31, 2011 and 2012.

To help ensure the independence of our independent registered public accounting firm, the Audit Committee is required to pre-approve all audit and non-audit services to be performed for us by our independent registered public accounting firm. All audit and permitted non-audit services, including the fees and terms thereof, to be performed by our independent registered public accounting firm must be approved in advance by the Audit Committee.

ITEM 16D. EXEMPTION FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Under Italian law, our shareholders, not the audit committee, 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. As a result, our audit committee is not able to perform all of the duties required by Rule 10A-3 of the Securities Exchange Act of 1934, as amended. Our audit committee has established procedures for the receipt, retention and treatment of complaints regarding accounting, internal accounting controls and auditing matters, and has authority to engage independent counsel and other advisors and to determine the compensation of such advisors, as well as its ordinary administrative expenses, and together with the board of statutory auditors, oversees our independent accountants (including resolution of disagreements between management and the independent accountants regarding financial reporting). Rule 10A-3 provides that foreign private issuers with a board of statutory auditors established in accordance with local law or listing requirements and which meets specified requirements with regard to independence and responsibilities (including the performance of most of the specific tasks assigned to audit committees by the rule, to the extent prohibited by local law) ("Statutory Auditor Requirements") are exempt from the audit committee requirements established by the rule. Our board of directors has determined that, because of the existence and nature of our board of statutory auditors, together with the performance of other duties under Rule 10A-3 by our shareholders and the performance of the remaining duties by our audit committee, we either satisfy Rule 10A-3 or qualify for an exemption from the audit committee requirements of Rule 10A-3, as provided in the Rule.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Not applicable.

ITEM 16F. CHANGE IN CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

The Nasdaq Listing Rules set forth the corporate governance requirements of companies listed on The Nasdaq Stock Market. Subsection (a)(3) of Listing Rule 5615 provides that a foreign private issuer may follow its home country practices in lieu of the corporate governance requirements of the Nasdaq Stock Market under certain circumstances. Pursuant to this Listing Rule 5615(a)(3), we follow Italian practices in lieu of six of the Nasdaq Stock Market's corporate governance requirements pertaining to: (1) independent directors, (2) our audit committee, (3) solicitation of proxies and provision of proxy statements, (4) quorum requirements, (5) shareholder approval requirements, and (6) executive sessions. In addition, while we are currently in compliance with Nasdaq's requirement that either a majority of our independent directors or a committee comprised solely of independent directors shall determine or recommend compensation for our executive officers and select or recommend director nominees, we are

not required to follow these rules, nor does Italian law provide for such requirements.

Majority of Independent Directors

The Nasdaq Stock Market: Listing Rule 5605(b)(1) requires that a majority of the board of directors be "independent." In order for a director to be considered "independent," a director may not be an employee of the company or have a relationship with the company which, in the opinion of the company's board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

Italian practices: The presence of a prescribed number of independent directors on the company's board is neither mandated by any Italian law applicable to the company nor required by the company's bylaws.

However, Italian law sets forth certain independence requirements applicable to the company's statutory auditors. The following persons may not be appointed as statutory auditors: (i) one who is legally incapacitated, bankrupt, or disqualified from holding public or executive offices under Italian law (ii) a spouse, parent or relative-in-law of a director of the company, a director of a company controls the company, or a director of a company under common control of the company, or (iii) one whose independence may be jeopardized due to an employment or consultant relationship or any other economic relationship with the company, a company that controls the company, or a company that is under common control of the company. The Italian Civil Code mandates that at least one effective statutory auditor be a chartered public accountant. Each of the current members of the board of statutory auditors is a chartered public accountant.

Audit Committee

The Nasdaq Stock Market: Listing Rule 5605(c)(3) requires compliance with Rule 10A-3 of the Securities Exchange Act of 1934, as amended, which requires that:

- a company's audit committee be directly responsible for the appointment, compensation, retention and oversight of the work of any registered public accounting firm engaged (including resolution of disagreements between management and the auditor regarding financial reporting) for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the company;
    - each such registered public accounting firm must report directly to the audit committee;
- the audit committee establish procedures for the receipt, retention and treatment of complaints regarding accounting, internal accounting controls or auditing matters;
    - the audit committee have the authority to engage independent counsel and other advisors;
        - the audit committee determine compensation for the independent accountants; and
- the audit committee determine compensation for any advisors to the audit committee, as well as the ordinary administrative expenses of the committee.

Italian practices: Under Italian law, our shareholders, not the audit committee, 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. As a result, our audit committee is not able to perform all of the duties required by Rule 10A-3 of the Securities Exchange Act of 1934, as amended. Our audit committee directly oversees our independent accountants and the resolution of disagreements between management and the independent accountants. Under Italian law, our board of statutory auditors also oversees our independent accountants with respect to our Italian GAAP financial statements. Rule 10A-3 provides that foreign private issuers with a board of statutory auditors established in

accordance with local law or listing requirements and meeting specified requirements with regard to independence and responsibilities (including the performance of most of the specific tasks assigned to audit committees by the rule, to the extent prohibited by local law) ("Statutory Auditor Requirements") are exempt from the audit committee requirements established by the rule. Our board of directors has determined that we are in compliance with requirements of Rule 10A-3 or otherwise qualify for an exemption from the audit committee requirements of Rule 10A-3.

Compensation Committee

The Nasdaq Stock Market: Listing Rule 5205(d) requires the compensation of the chief executive officer and all other executive officers of U.S. domestic companies to be approved either by a compensation committee comprised solely of independent directors or by a majority of the independent directors serving on the board of directors.

Italian practices: Under Italian law, the compensation of executive officers is determined by a vote of the entire board of directors. Our compensation committee makes recommendations to the board of directors with regard to the compensation of executive officers, which recommendations are voted on by the independent directors serving on our board.

Proxy Solicitation and Proxy Statements

The Nasdaq Stock Market: Listing Rule 5620(b) requires issuers to solicit proxy statements for all meetings of shareholders and to provide copies of such proxy solicitation to Nasdaq.

Italian Practice: As a foreign private issuer, we are exempt from the proxy rules of the Securities Exchange Act of 1934, as amended. We do not solicit proxies from holders of our ordinary shares, nor are we required to do so under Italian law. Our depositary, the Bank of New York, does solicit proxies from ADS holders for instructions on how to vote its ordinary shares at our shareholder meetings. The Bank of New York also delivers reports from our board of directors regarding the agenda items for the shareholder meetings to the ADS holders. We file these board reports, the Bank of New York's proxy card and any related items with the SEC on Form 6-K.

Quorum requirements

The Nasdaq Stock Market: Listing Rule 5620(c) sets forth The Nasdaq Stock Market's quorum requirement for shareholder meetings, stating that "in no case shall such quorum be less than 33 1/3% of the outstanding shares of the company's common voting stock."

Italian Practices: In accordance with Italian law, our shareholders are entitled to attend and vote at ordinary and extraordinary shareholders' meetings. Shareholders are notified of two meeting dates for an ordinary and extraordinary shareholders' meeting (first and second "calls"). The quorum for an ordinary meeting of shareholders on the first call is at least 50% of the outstanding ordinary shares, while on a second call there is no quorum requirement. The quorum for an extraordinary meeting of shareholders is the majority of the capital on the first call and more than one-third of the outstanding capital on a second call.

Shareholder approval requirements

The Nasdaq Stock Market: Listing Rule 5635 sets forth certain Nasdaq Stock Market's shareholder approval requirements in connection with the acquisition of stock or assets of another company, equity based compensation of officers, directors, employees or consultants, a change of control, and private placements. Specifically, Listing Rule 5635(a) requires shareholder approval prior to the issuance of securities in connection with the acquisition of the stock or assets of another company, if the issuance of securities will have voting power equal to or greater than 20%, the number of shares to be issued will be equal to or in excess of 20% of the outstanding number of shares before the issuance of such securities, or any director, officer or "substantial shareholder" gains an increase in outstanding common shares or voting power of 5% or more in connection with such transaction. Listing Rule 5635(b) requires shareholder approval prior to the issuance of securities when such issuance or potential issuance will result in a change of control. Listing Rule 5635(c) requires shareholder approval when an equity incentive plan is established or materially amended or other equity compensation is made or materially amended. Listing Rule 5635(d) requires shareholder approval in connection with a private placement at a price less than the greater of book or market value which results in the issuance of 20% or more of the outstanding common stock prior to issuance or 20% or more of the outstanding voting power prior to issuance.

Italian Practices: Although the Company's shareholders must authorize the issuance of shares in connection with any capital increase, such power can be granted to the board of directors in advance of any of the above mentioned transactions, if necessary, and none of the Listing Rule 5635 requirements discussed above require specific shareholder approval under Italian law.

Executive Sessions

The Nasdaq Market: Listing Rule 5602(b)(2) requires that independent directors hold regularly scheduled meetings at which only independent directors are present.

Italian Practices: Under Italian law, neither non-executive directors nor independent directors are required to meet in executive sessions. The members of the Company's board of statutory auditors are required to meet at least every 90 days.

PART III

ITEM 17. CONSOLIDATED FINANCIAL STATEMENTS

Not applicable.

ITEM 18. CONSOLIDATED FINANCIAL STATEMENTS

GENTIUM S.p.A.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

ITEM 19. EXHIBITS

[INSERT 8.1 LIST OF SUBSIDARY AND AGREEMENTS WITH GMBH – ONCE UPDATED COPY EXHIBIT LIST TO THE END OF DOCUMENT]

Exhibit	Description
Charter documents	
1.1	Articles of Association of Gentium S.p.A., formerly known as Pharma Research S.r.l. dated November 11, 1993, incorporated by reference to Exhibit 3(i) to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
1.2	Amended and Restated Bylaws of Gentium S.p.A. dated May 9, 2011
American Depositary Share Documents	
2.1	Form of Deposit Agreement among Gentium S.p.A., The Bank of New York and the owners and beneficial owners from time to time of American Depositary Receipts (including as an exhibit the form of American Depositary Receipt), incorporated by reference to Exhibit 4.6 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on June 9, 2005.
2.2	Form of American Depositary Receipt (see Exhibit 2.1).
Security Subscription Agreements	
2.3	Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto dated as of May 31, 2006, incorporated by reference to Exhibit 4.9.1 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
2.4	Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto, dated as of February 6, 2007, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 7, 2007.
Warrants	
2.5	Form of warrant (regarding Series A financing), incorporated by reference to Exhibit 4.2.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
2.6	Form of Representatives' Purchase Option between Gentium S.p.A. and Maxim Group LLC and I-Bankers Securities Inc., incorporated

	by reference to Exhibit 1.2 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on June 9, 2005.
2.7	Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated October 14, 2005, incorporated by reference to Exhibit 4.8.2 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
2.8.1	Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.2 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.