

Gentium S.p.A.  
Form 20-F  
March 30, 2012

**As filed with the Securities and Exchange Commission on March 30, 2012**

**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**

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

**For the Fiscal Year Ended: December 31, 2011**

**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 385111**  
(Address, including zip code, and telephone number,  
including area code, of Registrant's principal executive offices)

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

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

(Title of Class)

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

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

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

**14,969,150 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

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

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  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

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  Non-accelerated filer

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

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

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

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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-stranded 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 has been given “orphan” status by the U.S. Food and Drug Agency, or FDA, and the European Medicines Agency, or EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide has also been granted “fast-track product” designation by the FDA for the treatment of severe VOD prior to stem cell transplantation. Currently, to the best of our knowledge, there are no FDA or EMA approved treatments for this life-threatening disease. While we have not yet obtained regulatory approval to market defibrotide, we are permitted to distribute defibrotide on a pre-approval basis under a treatment Investigational New Drug, or IND, protocol, which we call our cost recovery program, in the U.S., and through a named-patient program, or NPP, throughout the rest of the world.



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 marketing authorization application, or MAA, for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 List of Questions, or LoQs, from the EMA's Committee for Medical Products for Human Use, or CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a List of Outstanding Issues, or LoOIs, requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

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 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of contract research organizations (CROs) and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

We 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 Americas. We have entered into a supply and distribution agreement with IDIS Limited, in which IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in certain European countries and in certain territories in other parts of the world. Since December 31, 2010, we have entered into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient supply basis in the following territories: Turkey, Israel, Palestinian Authority, Australia, New Zealand, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia; and some of these 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.

In accordance with our overall strategy, we have appointed our commercial leadership team, which is currently responsible for, among other things, market research and pharmacoeconomics analysis, and will be responsible for marketing defibrotide in the major European countries upon regulatory approval, if any. In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, or APIs, such as the defibrotide compound, 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, which we refer to as defibrotide. 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 €92.85 million since our inception. We have been cash flow positive since 2010, primarily due to an upfront 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. As a result, we have been able to finance the establishment of our European commercial team, repay the current portion of our long-term debt and fund our working capital. 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 are required to fund additional clinical trials or 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, 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, 2010 and December 31, 2011 and for the three years ended December 31, 2011 are derived from our audited consolidated financial statements, which are included in this annual report. The selected financial data as of December 31, 2007, December 31, 2008 and December 31, 2009 and for the years ended December 31, 2007 and December 31, 2008 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:<br>(000s omitted except per share data) | For the Years Ended December 31, |          |         |        |        |                     |
|---|----------------------------------|----------|---------|--------|--------|---------------------|
|   | 2007                             | 2008     | 2009    | 2010   | 2011   | 2011 <sup>(1)</sup> |
| Revenues:   |                                  |          |         |        |        |                     |
| Product sales to related party  | €2,704                           | €651     | €195    | €      | €      | \$-                 |
| API product sales   | 2,390                            | 4,792    | 4,603   | 6,533  | 4,848  | 6,289               |
| NPP product sales   | -                                | -        | 4,904   | 13,182 | 16,886 | 21,906              |
| Total product sales   | 5,094                            | 5,443    | 9,702   | 19,715 | 21,734 | 28,195              |
| Other revenues  | 15                               | 25       | 129     | 289    | 123    | 160                 |
| Other revenues from related party                                     | 2,500                            | 1,970    | 337     | 4,547  | 2,026  | 2,628               |
| Total revenues  | 7,609                            | 7,438    | 10,168  | 24,551 | 23,883 | 30,983              |
| Operating costs and expenses:   |                                  |          |         |        |        |                     |
| Cost of goods sold  | 4,584                            | 5,596    | 4,002   | 5,786  | 6,035  | 7,829               |
| Research and development  | 14,497                           | 9,569    | 3,512   | 6,104  | 5,533  | 7,178               |
| General and administrative  | 6,279                            | 7,668    | 6,036   | 5,835  | 5,490  | 7,122               |
| Sales and marketing   | -                                | -        | -       | -      | 2,237  | 2,902               |
| Charges from related parties  | 748                              | 537      | 279     | 346    | 222    | 288                 |
| Restructuring charges   | -                                | -        | -       | 1,101  | -      | 0                   |
| Depreciation and amortization   | 725                              | 998      | 916     | 908    | 870    | 1,129               |
| Write-down of assets  | 13,740                           | 3,403    | -       | -      | -      | -                   |
|   | 40,573                           | 27,771   | 14,745  | 20,080 | 20,387 | 26,448              |
| Operating income/(loss)   | (32,964)                         | (20,333) | (4,577) | 4,471  | 3,496  | 4,535               |
| Foreign currency exchange gain (loss), net                            | (4,001)                          | 173      | 162     | 90     | 46     | 60                  |
| Interest income/(expense), net  | 1,357                            | 256      | (110)   | (87)   | (21)   | (27)                |
| Pre-tax income/(loss)   | (35,608)                         | (19,904) | (4,525) | 4,474  | 3,521  | 4,568               |

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|                              |           |           |           |        |        |          |
|------------------------------|-----------|-----------|-----------|--------|--------|----------|
| Income tax expense:          |           |           |           |        |        |          |
| Total income tax expense     | -         | -         | -         | (397 ) | (811 ) | (1,052 ) |
| Net income/(loss)            | €(35,608) | €(19,904) | €(4,525 ) | €4,077 | €2,710 | \$3,516  |
| Net income/(loss) per share: |           |           |           |        |        |          |
| Basic                        | €(2.52 )  | €(1.33 )  | €(0.30 )  | €0.27  | €0.18  | \$0.23   |
| Diluted                      | (2.52 )   | (1.33 )   | (0.30 )   | 0.27   | 0.18   | 0.23     |

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

| (000s omitted except shares)              | 2007       | 2008       | 2009       | 2010       | 2011       | 2011 <sup>(1)</sup> |
|---|------------|------------|------------|------------|------------|---------------------|
| <b>Balance Sheet Data:</b>                |            |            |            |            |            |                     |
| Cash and cash equivalent                  | €25,964    | €11,491    | €1,392     | €8,742     | €9,990     | \$12,960            |
| Working capital                           | 19,002     | 3,152      | 1,041      | 6,555      | 10,730     | 13,920              |
| Property, net                             | 11,544     | 10,751     | 9,717      | 8,598      | 8,508      | 11,037              |
| Total assets                              | 51,959     | 26,901     | 18,167     | 24,674     | 27,412     | 35,562              |
| Long-term debt, net of current maturities | 4,421      | 3,268      | 3,098      | 1,759      | 1,545      | 2,004               |
| Shareholders' equity                      | 28,359     | 10,451     | 7,330      | 12,930     | 17,383     | 22,551              |
| Capital stock                             | €14,946    | €14,956    | €106,962   | €108,485   | €110,228   | \$142,999           |
| Number of shares                          | 14,946,317 | 14,956,317 | 14,956,317 | 14,956,317 | 14,969,150 | 14,969,150          |

(1) Euro amounts are translated into U.S. dollars using the Noon Buying Rate for the Euro on December 30, 2011, of U.S. 1.2973 per Euro. No representation is made that the Euro amounts referred to in this annual report could have been or could be converted into U.S. dollars at any particular rate or at all.

### Exchange Rate Information

Fluctuations in the exchange rates between the Euro and the U.S. dollar will affect the U.S. dollar amounts received by owners of ADSs on conversion by the depository 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.

| Year | U.S. Dollar per Euro |            |
|------|----------------------|------------|
|      | Average              | Period End |
| 2007 | 1.3797               | 1.4603     |
| 2008 | 1.4726               | 1.3919     |
| 2009 | 1.3935               | 1.4332     |
| 2010 | 1.3261               | 1.3269     |
| 2011 | 1.3931               | 1.2973     |

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.

| Month                               | U.S. Dollar per Euro |        |
|-------------------------------------|----------------------|--------|
|                                     | High                 | Low    |
| September 2011                      | 1.4283               | 1.3446 |
| October 2011                        | 1.4172               | 1.3281 |
| November 2011                       | 1.3803               | 1.3244 |
| December 2011                       | 1.3487               | 1.2926 |
| January 2012                        | 1.3192               | 1.2682 |
| February 2012                       | 1.3463               | 1.3087 |
| March 2012 (through March 23, 2012) | 1.3320               | 1.3025 |

Source: Federal Reserve Statistical Release H.10

On March 23, 2012, the noon buying rate was €1.00 to \$1.3263.

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 sell 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.

We do not currently have regulatory approval to market and sell defibrotide anywhere in the world. 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-approved basis. If we are unable to obtain regulatory approval to commercialize defibrotide or unable to distribute defibrotide on a pre-approved 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 severe VOD or prevent VOD and/or collect additional data, which may delay or prevent approval and commercialization of our product candidate.**

Our current Phase III clinical trial of defibrotide to treat severe VOD uses a separate historical control group of untreated patients. We designed our study this way because our clinical investigators believed it was unethical to refuse treatment to patients when such treatment could potentially save their lives. In addition, the committee of clinical investigators who sponsored a Phase II/III clinical trial of defibrotide to treat VOD in Europe conducted by Consorzio Mario Negri Sud, which had a concurrent control group of untreated patients, cancelled the trial in October 2005 due to a lack of patient enrollment. We believe that patients were reluctant to enroll in the clinical trial due to the possibility of being placed into the control group and not receiving treatment. The FDA may require us to conduct a new clinical trial of defibrotide to treat VOD using a concurrent control group of untreated patients, which may not be possible if patients are unwilling to enroll and/or investigators refuse to participate in such a study.

Conducting clinical trials is a complex, time-consuming and expensive process. Our ability to complete our clinical trials in a timely fashion depends 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. We have opened clinical sites and are enrolling patients in a number of new countries where our experience is more limited, and we are in many cases using the services of third party clinical trial providers. If we fail to adequately manage the design, execution and regulatory aspects of our large, complex and diverse clinical trials, our studies and ultimately our regulatory approvals may be delayed or we may fail to gain approval for our product candidates altogether.

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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of CROs and several outside consultants to assist us in addressing the issues raised by the FDA. We may never be able to correct the datasets and databases, and, even if we are able to correct these datasets and databases, the data may still be insufficient for the FDA to grant us approval.

We may lack sufficient capital to commence and complete a new clinical trial of defibrotide, to start over in the enrollment of the historical control arm, or to enroll additional patients in the historical control arm. To the extent that we are required to obtain additional capital through equity and/or debt financings, loans or collaborative arrangements with corporate partners, such funding may not be available to us on favorable terms, if at all. Therefore, we may never be able to obtain regulatory approval of defibrotide to treat or prevent VOD.

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

As of December 31, 2011, we had approximately €9.99 million in cash and cash equivalents. We have generated a significant portion of our revenue through the distribution of our primary product candidate, defibrotide, on a pre-approval basis under a treatment IND protocol, which we call our cost recovery program, in the U.S, and through a named-patient program throughout the rest of the world. Prior to the initiation of these compassionate use programs in 2009, we were cash-flow negative and had only generated net losses. We do not know how much longer we will be able to distribute defibrotide through these compassionate use programs.

We expect that existing cash and cash equivalents with respect to the anticipated cash flow from product sales will be sufficient to support our current operations for at least the next twelve months. We will need additional funds if our cash requirements exceed our current expectation or if we generate less revenue than we expect. In addition, if we are required or decide to run any additional clinical trials, our existing cash and cash equivalents with respect to the anticipated cash flow from product sales may be insufficient to support our current operations, and if we are not able to secure additional capital through external sources, we may not be able to continue as a going concern.

Historically, we have financed our operations primarily through the sale of equity and convertible notes, interest income earned on cash and cash equivalents, and debt provided through secured lines of credit. If we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly-issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations. To the extent that we are required to obtain additional capital through equity and/or debt financings, loans or collaborative arrangements with corporate partners, such funding may not be available to us on favorable terms, if at all.

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

The development of defibrotide 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 future 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 or the timing and cost to address issues raised by the FDA upon submission of our NDA;
- 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.

**While we have started to generate limited revenues from sales of defibrotide on a pre-approval basis, we have had significant losses to date and we do not know whether we will ever generate significant revenues.**

We have generated net losses and been profitable since 2010. While we have generated revenues through commercial sales of our active pharmaceutical ingredients and, recently, through sales of defibrotide on a pre-approval basis through our named-patient and cost recovery programs, we may revert to incurring significant losses and may become cash-flow negative, particularly if we are required to perform additional clinical trials and testing and regulatory compliance activities, or if we are unable to continue to distribute defibrotide on a pre-approval basis. If we incur operating losses and become cash-flow negative for longer than we expect to and/or we are unable to raise additional capital, we may become insolvent and unable to continue our operations.

Our current ability to continue as a going concern is largely dependent on the revenues being generated from the distribution of defibrotide on a pre-approval basis through our named-patient and cost recovery programs. If we fail to generate projected revenues from these compassionate use programs, we may be unable to reduce our expenses quickly enough to compensate for the shortfall, and we may then need to obtain additional capital through equity or debt financings, loans and collaborative agreements with corporate partners, which may not be available to us on favorable terms, if at all. In addition, our fluctuating operating results may fail to meet the expectations of investors, which may cause the price of our ADSs to decline.

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 and the EMA have designated defibrotide to treat severe VOD and defibrotide to prevent VOD, as “orphan drugs,” which generally means that fewer than 200,000 people are affected by the disease or condition. In addition, our long-term ability to generate cash from operations depends in part on the success of our current strategic partner, Sigma-Tau Pharmaceuticals, Inc., in commercializing defibrotide in North America, Central America and South America and also on our capacity to commercialize defibrotide in Europe.

**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.

**We expect to 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 us time to find a replacement processor. 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, manufacture and storage and handling and disposal of materials and waste products. 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 for an additional three-year period. 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.

**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.

Moreover, we may need to hire additional personnel and add corporate functions that we currently do not have. To effectively manage our operations and growth, we will be required to continue to improve our operational, financial and management controls and reporting system and procedures, or to contract with third parties to provide these capabilities for us.

**We currently depend on third parties to distribute defibrotide, and we may continue to depend on third parties to market and distribute defibrotide in certain territories upon regulatory approval, if any.**

We depend on US Oncology Clinical Development to distribute defibrotide on a cost recovery basis in the United States, and on IDIS and certain regional partners to distribute defibrotide on a named-patient basis throughout the rest of the world. Our current revenues are highly dependent on the distribution of defibrotide by US Oncology and IDIS. If these services are not adequately provided to us, our business would be seriously harmed and our ability to continue as a going concern would be dependent on alternative sources of funding, which may not be available to us on favorable terms, if at all.

Following regulatory approval for defibrotide, if any, we plan on marketing and distributing defibrotide in major countries throughout Europe on our own. However, we have entered into alliances with regional partners to assist with registration, pricing approval, marketing and 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.

**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 €15 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.

**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.

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

Our industry is highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. Incidence of VOD may decrease with new technologies and conditioning regimens, which will negatively impact our sales opportunities. While we are unaware of any other products or product candidates that treat or prevent VOD, we believe that other companies have products or are currently developing products to treat some of the same disorders and diseases that defibrotide is designed to treat. These companies include Genzyme Corp., Millennium Pharmaceuticals, Inc., Otsuka Pharmaceutical Co., Ltd., Eisai Co., Ltd., and Celgene Corp.

Many of these competitors have substantially greater research and development capabilities and experience, and greater manufacturing, marketing and financial resources than we 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 severe 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, 2011, the closing price of our American Depositary Shares, or 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, 2011 of 55,465 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, 2011, our stockholders' equity was \$22.55 million (€17.38 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, FinSirton S.p.A., owned approximately 17% of our outstanding ordinary shares at December 31, 2011. 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 FinSirton.

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. Dr. Brughera was elected to our board following the resignation of Marco Codella, the former Chief Financial Officer of Sigma-Tau Finanziaria, who served as a member of our board of directors since 2005. Moreover, we have licensed our rights in defibrotide to treat and prevent VOD to Sigma-Tau Pharmaceuticals, Inc., a wholly-owned subsidiary of Sigma-Tau Finanziaria.

Both FinSirton and Sigma-Tau Finanziaria may substantially control the outcome of all matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other important corporate events. They may exercise this ability in a manner that advances their best interests, and not necessarily 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 FinSirton 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 may not have the same voting rights as the holders of our ordinary shares and may not receive voting materials in time to be able to exercise your right to vote.**

Except as described in this annual report and in the deposit agreement for the ADSs with our depository, 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 depository, as the holders’ representative, to exercise these voting rights. You may not receive voting materials in time to instruct the depository 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 distribute rights to our shareholders, including rights to acquire our securities. Under our deposit agreement for the ADSs, the depository 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 restricts the amount of debt securities that we may issue relative to our equity.**

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. 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, 2011, the sum of our capital, our legal reserves and other reserves on our unaudited Italian GAAP financial statements was €37.05 million. If we issue debt securities in the future, until such debt securities are repaid in full, we may not voluntarily reduce our capital or allocate our reserves (such as by declaring dividends) if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt. If our equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of our equity, some legal scholars are of the opinion that the ratio must be restored 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, 2011, our unaudited Italian GAAP capital was approximately €14.97 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-looking statements. You should read statements that contain these words carefully because they discuss our future expectations, contain projections of our future results of operations or of our financial condition or state other “forward-looking” information. We believe that it is important to communicate our future expectations to our investors. Although we believe that our expectations reflected in any forward-looking statements are reasonable, these expectations may not be achieved. The factors listed in the section captioned “Risk Factors,” as well as any cautionary language included in this 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 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.. FinSirton is one of our largest shareholders owning approximately 17% of our outstanding ordinary shares at December 31, 2011, 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 385111. Our website is located at [www.gentium.it](http://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-stranded 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 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, for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 LoQs from the EMA's CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a LoOIs requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

On July 6, 2011, we announced the filing of our 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 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of CROs and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

We 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 Americas. We have entered into a supply and distribution agreement with IDIS, whereby IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in certain European countries and in certain territories in other parts of the world. Since the period ended December 31, 2010, we have entered into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient supply basis in the following territories: Turkey, Israel, Palestinian Authority, Australia, New Zealand, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia; and some of these 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.

In accordance with our overall strategy, we have appointed our commercial leadership team, which is currently responsible for, among other things, market research and pharmacoeconomics analysis, and will be responsible for marketing defibrotide in the major European countries upon regulatory approval, if any. In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations.

We have a manufacturing plant in Italy where we produce APIs, such as the defibrotide compound, 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, which we refer to as defibrotide. 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," 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 and the EMA have designated defibrotide to treat severe VOD and defibrotide to 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, 2011.

| (in thousands)           | For the Year Ended December 31, |      |        |
|--------------------------|---------------------------------|------|--------|
|                          | 2009                            | 2010 | 2011   |
| Land and buildings       | €-                              | €-   | €8     |
| Plant and machinery      | 206                             | 129  | 84     |
| Industrial equipment     | 5                               | 7    | 4      |
| Other                    | 23                              | 9    | 213    |
| Leasehold improvements   | 3                               | 50   | 718    |
| Computer Software        | 12                              | -    | 23     |
| Construction in progress | 28                              | 10   | 228    |
| Total                    | €277                            | €205 | €1,278 |

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-stranded 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, for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 LoQs from the EMA's CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a LoOIs requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

On July 6, 2011, we announced the filing of our 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 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of CROs and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

In August 2011, we formed Gentium GmbH, a wholly-owned subsidiary organized under the laws of Switzerland, as the headquarters for our commercial operations. In 2011, we also appointed our commercial leadership team, which operates out of Gentium GmbH, and is currently responsible for, among other things, market research and pharmacoconomics analysis, and will be responsible for marketing defibrotide in the major European countries upon regulatory approval, if any.

We 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 Americas. We have entered into a supply and distribution agreement with IDIS, whereby IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in certain European countries and in certain territories in other parts of the world. Since the period ended December 31, 2010,

we have entered into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient supply basis in the following territories: Turkey, Israel, Palestinian Authority, Australia, New Zealand, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia; and some of these 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. Our revenues from our named-patient and cost recovery programs were approximately €4.90 million, €13.18 million and €16.89 million in net sales for the years ended December 31, 2009, 2010 and 2011, respectively.

We also manufacture sulglicotide at our manufacturing facility near Como, Italy, and we lease a facility from Sirton S.p.A. (no longer an affiliate), to manufacture urokinase. These APIs are used to make other drugs. Our revenues from the sales of these APIs to date totaled €4.80 million, €6.53 million, and €4.85 million in 2009, 2010 and 2011, respectively. The drop in revenue of our API business from the prior-year period is primarily attributable to a lower volume of sales of sulglicotide and a reduction in the price of sulglicotide to accommodate Samil, a commercial partner in South Korea, that experienced a 20% reimbursement cut from the South Korean government with respect to its finished drug product that utilizes sulglicotide as the API.

## **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 plan to commercialize defibrotide in the major European countries on our own, and we have developed and will continue to develop appropriate partnerships for the commercialization of defibrotide in other parts of the world.

- **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 has received orphan status from both the FDA and the EMA. In addition, we have received fast track designation for the use of defibrotide for the treatment of severe VOD prior to stem cell transplantation. We have filed an MAA with the EMA for defibrotide for the prevention and treatment of VOD, which is currently under review. We also filed a NDA with the FDA, which we voluntarily withdrew. We are working to refile a new NDA with the FDA.

- **Increase our marketing capacity, including the use of strategic partnerships.** Because we plan on distributing defibrotide in certain major European countries on our own upon regulatory approval, if any, we have appointed a commercial leadership team, and we have formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations. In addition, we have a strategic license agreement with Sigma-Tau Pharmaceuticals, Inc., under which we will work collaboratively to market

defibrotide to treat and prevent VOD in North America, Central America and South America once regulatory approval is obtained. We have also entered into partnerships license with specialized regional partners for the distribution of defibrotide in the following territories upon regulatory approval, if any: Turkey, Israel, Palestinian Authority, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia. We will continue to develop appropriate partnerships for commercialization of defibrotide in other parts of the world.

- **Compassionate use programs to maximize pre-approval data.** We distribute defibrotide on a pre-approval compassionate use basis through our named-patient and treatment IND programs. We obtain data on the efficacy and safety of defibrotide through these programs. We expect to utilize this data to supplement the data obtained from our completed clinical trials and any future clinical trials that may be conducted as necessary. In 2010 and 2011, approximately 800 and 1,000 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.

## Product Candidate

Defibrotide is an investigational drug based on a mixture of single-stranded 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. The FDA granted orphan status to defibrotide as a treatment for severe VOD in 2003, and as a method of prevention of VOD in 2007. The EMA granted a similar status to defibrotide as a VOD treatment and preventative measure in 2004. Orphan status provides us with limited market exclusivity upon regulatory approval. 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 a treatment 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. No mortalities from VOD or other toxicities related to the cancer treatment were observed beyond 134 days after treatment with defibrotide, with the most common cause of later death being a relapse.

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 historically controlled Phase III clinical trial in the United States, Canada and Israel for this use of defibrotide on patients with severe VOD. 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 a treatment IND (TIND) expanded access program for defibrotide under a FDA approved protocol. During the course of these years, results from the ongoing TIND have been presented at scientific conferences. We have also initiated an expanded access program, which gives patients diagnosed with VOD in the United States access to defibrotide under a treatment IND. Under an expanded access program, the FDA allows early access to investigational drugs that are 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. 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 a TIND 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 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of contract research organizations (CROs) and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

On December 12, 2011, we announced the updated results on the ongoing treatment IND 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.

#### 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. The European Group for Blood and Marrow Transplantation, a not-for-profit scientific society, conducted a Phase II/III clinical trial in Europe and Israel involving defibrotide to prevent VOD in children. Unlike our Phase III treatment trial in the United States, 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 May 10, 2011, we announced the filing of our MAA for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 LoQs, from the EMA's CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a LoOIs requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

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% 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.

#### Defibrotide Pre-Approval

On March 6, 2009, we entered into a supply and distribution agreement with IDIS, under which IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in all countries except Italy and the United States. This agreement has been amended and will continue to be amended to exclude countries in which we have entered into distribution agreements with specialized regional partners.

We have also initiated an expanded access program, which gives patients diagnosed with VOD in the United States access to defibrotide under a treatment IND. Under an expanded access program, the FDA allows early access to investigational drugs that are 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. On September 29, 2009, we entered into an agreement with US Oncology, under which U.S 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 New Drug Application for the treatment of Severe VOD and/or the prevention of VOD.

We received €4.90 million, €13.18 million, and €16.89 million through our named-patient and cost recovery programs for 2009, 2010 and 2011, 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 Samil, which uses this API to finish a drug that it markets in South Korea. In 2011, we reduced the price of sulglicotide to accommodate Samil, which experienced a 20% reimbursement cut from the South Korean government for this finished drug. In addition, this reimbursement cut caused Samil to purchase smaller volumes of sulglicotide compared to the prior-year period.

##### 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 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, 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 patients.

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

### Phase III

If and when one or more Phase II trials demonstrate that a specific dose or range of doses of a product candidate is likely to be effective and has an acceptable safety profile, 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.





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

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

### *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, 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 to market a drug 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 severe 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 FDCA, 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 FDCA 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

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

## Foreign Regulatory Approval

Outside of the United States, our ability to market our product candidates will also be contingent upon our 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. We filed our MAA for defibrotide under the centralized procedure.

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.

#### 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, such as Genzyme Corp., Millennium Pharmaceuticals, Inc., Otsuka Pharmaceutical Co., Ltd., Eisai Co., Ltd., and Celgene Corp, as well as academic and research organizations and government agencies, 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 capital resources than we have, and greater capabilities and resources to conduct basic research, preclinical studies and clinical trials, regulatory affairs, manufacturing, marketing and sales. As a result, our competitors may develop or license products or other novel technologies that are more effective, 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 FinSirton 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. FinSirton 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, in connection with the establishment our European commercial team, through which we intend to commercialize defibrotide in certain European countries on our own, we formed a wholly-owned subsidiary, Gentium GbmH, organized under the laws of Switzerland.

## PROPERTY, PLANT AND EQUIPMENT

### Manufacturing and Facilities

We own a manufacturing facility near Como, Italy which, at December 31, 2011, is subject to a mortgage securing repayment of an aggregate of €1.56 million of debt owed to Banca Nazionale del Lavoro. The manufacturing facility is 2,350 square meters in size. In order to obtain FDA approval for the sale of any of our product candidates, the FDA must determine that this facility meets 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. In 2006, we replaced a principal reactor in the defibrotide production line and separated the defibrotide production line from the sulglicotide line by installing an additional reactor. These improvements allow us to produce defibrotide or sodium heparin and sulglicotide simultaneously and to double our potential capacity to manufacture defibrotide and sulglicotide.

We typically operate our manufacturing facility on two eight hour shifts per day. Our estimated current production, maximum production capacity, and percentage of utilization for defibrotide for the fiscal year 2012 are set forth below:

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

Our estimated current production, production capacity, and percentage of utilization for sulglicotide for the fiscal year 2012 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 | 4,400   | 8,626   | 51                        | % |

Our estimated current production, production capacity, and percentage of utilization for urokinase for the fiscal year 2012 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 for an additional three-year period. 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 FinSirton. 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.



## 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-stranded 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 has been given “orphan” status by the FDA and the EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide has also been granted “fast-track product” designation by the FDA for the treatment of severe VOD prior to stem cell transplantation. Currently, to the best of our knowledge, there are no FDA or EMA approved treatments for this life-threatening disease. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approval basis under a treatment IND protocol, which we call our cost recovery program, in the U.S., and through a named-patient program throughout the rest of the world.

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, for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 LoQs from the EMA’s CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a LoOIs requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

On July 6, 2011, we announced the filing of our 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 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of CROs and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

We 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 Americas. We have entered into a supply and distribution agreement with IDIS, whereby IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in certain European countries and in certain territories in other parts of the world. Since the period ended December 31, 2010, we have entered into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient supply basis in the following territories: Turkey, Israel, Palestinian Authority, Australia, New Zealand, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia; and some of these 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.

In accordance with our overall strategy, we have appointed our commercial leadership team, which is currently responsible for, among other things, market research and pharmacoeconomics analysis, and will be responsible for marketing defibrotide in the major European countries upon regulatory approval, if any. In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations.

We have generated a significant portion of our revenue through the distribution of our primary product candidate, defibrotide, on a pre-approval basis under a treatment IND protocol, which we call our cost recovery program, in the U.S., and through a named-patient program throughout the rest of the world. For the years ended December 31, 2009, 2010 and 2011, sales of defibrotide through these programs amounted to approximately 51%, 67% and 78% of our total product sales, respectively.

We have a manufacturing plant in Italy where we produce APIs, including 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, 2009, 2010 and 2011, sales of APIs amounted to approximately 49%, 33% and 22% 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.

Our revenue sources are detailed categorically below:

| (in thousands)                            | For The Years Ended December 31, |         |         |
|---|----------------------------------|---------|---------|
|   | 2009                             | 2010    | 2011    |
| Product sales:                            |                                  |         |         |
| API - Urokinase                           | €1,974                           | €1,893  | €1,612  |
| API - Sulglicotide                        | 2,789                            | 4,640   | 3,236   |
| API – Other                               | 35                               | -       | -       |
| Named-patient/cost recovery program sales | 4,904                            | 13,182  | 16,886  |
| Total product sales                       | 9,702                            | 19,715  | 21,734  |
| Other revenues                            | 466                              | 4,836   | 2,149   |
| Total revenue                             | €10,168                          | €24,551 | €23,883 |

Product sales made outside Italy during the periods shown in the table above amounted to 85.9% during the year ended December 31, 2009, which were primarily sales of sulglicotide in South Korea, and 94.5% and 97.2% for the years ended December 31, 2010 and 2011, respectively, which include sales of sulglicotide in South Korea, urokinase in Spain and defibrotide sold in the US and Ex-US through the named-patient and cost recovery programs.

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 entered into with Sigma-Tau Pharmaceuticals, Inc., as amended, to include the prevention indication of defibrotide for distribution in the Americas.

In 2011, 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 we are required to fund additional clinical trials, 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, 2011, 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, 2011, we held a cash balance of \$2.30 million, receivables of \$1.07 million and payables of \$0.41 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 have entered into interest rate cap agreements to manage exposure interest rate movement. Interest rate cap agreements lock in a maximum interest rate, enabling us to benefit from lower interest rates in the event that the variable rates rise.

#### 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 treatment IND programs. We state inventories at the lower of cost or market, determining cost on an average cost basis. We periodically review inventories and reduce items 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 a research and development expense. 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 configuration. Upon receipt of an approval letter from the FDA or EMA for a new product or product configuration, we will begin to capitalize the subsequent inventory costs relating to that product configuration.

#### Impairment of Long-lived Assets

Our long-lived assets consist primarily of property and equipment. We evaluate our ability to recover the carrying value of long-lived assets used in our business, considering changes in the business environment or other facts and circumstances that suggest their value may be impaired.

If, based on the preceding discussion, our management has concluded that impairment indicators exist, we will initially review 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 any 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, 2011, we had €0.81 million of future

payables under outstanding contracts that are not revocable. Most of these contracts are on a cost plus or actual cost basis.

### Stock-Based Compensation

Employee stock-based compensation is estimated 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. Historically, the fair value of all option grants were estimated on the grant date using the Black-Scholes option-pricing model. For all stock options granted after December 31, 2009, the fair value of the award is estimated on the date of grant 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:           | <b>Results in a fair value estimate that is:</b> |
|-------------------------------|--|
| 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 2011, we have used a 92.82% 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.

#### *Tax Loss Carryforwards*

As of December 31, 2011 and 2010, we had net operating loss (NOL) carryforwards of approximately €51.32 million.

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 it is unlikely that we will recognize the benefits of deferred tax assets and, as a result, a valuation allowance of approximately €22.37 million has been established at December 31, 2011.

#### 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, |            |            |   |
|---|----------------------------------|------------|------------|---|
|   | 2009                             | 2010       | 2011       |   |
| <b>Revenues:</b>  |                                  |            |            |   |
| Product sales to related party  | €195                             | €          | €          |   |
| API product sales   | 4,603                            | 6,533      | 4,848      |   |
| NPP product sales   | 4,904                            | 13,182     | 16,886     |   |
| Total product sales   | 9,702                            | 19,715     | 21,734     |   |
| Other revenues  | 129                              | 289        | 123        |   |
| Other revenues from related party   | 337                              | 4,547      | 2,026      |   |
| Total Revenues  | 10,168                           | 24,551     | 23,883     |   |
| <b>Operating costs and expenses:</b>  |                                  |            |            |   |
| Cost of goods sold  | 4,002                            | 5,786      | 6,035      |   |
| Research and development  | 3,512                            | 6,104      | 5,533      |   |
| General and administrative  | 6,036                            | 5,835      | 5,490      |   |
| Sales and Marketing   | -                                | -          | 2,237      |   |
| Charges from related parties  | 279                              | 346        | 222        |   |
| Restructuring charges   | -                                | 1,101      | -          |   |
| Depreciation and amortization   | 916                              | 908        | 870        |   |
| Total operating costs and expenses:   | 14,745                           | 20,080     | 20,387     |   |
| Operating income/(loss)   | (4,577                           | ) 4,471    | 3,496      |   |
| Foreign currency exchange gain, net   | 162                              | 90         | 46         |   |
| Interest income/(expense), net  | (110                             | ) (87      | ) (21      | ) |
| Income/(loss) before income tax expense                                     | (4,525                           | ) 4,474    | 3,521      |   |
| <b>Income tax expense:</b>  |                                  |            |            |   |
| Total income tax expense  | -                                | (397       | ) (811     | ) |
| Net income/(loss)   | €(4,525                          | ) €4,077   | €2,710     |   |
| <b>Net income/(loss) per share:</b>   |                                  |            |            |   |
| Basic   | €(0.30                           | ) €0.27    | €0.18      |   |
| Diluted   | €(0.30                           | ) €0.27    | €0.18      |   |
| <b>Weighted average shares used to compute net income/(loss) per share:</b> |                                  |            |            |   |
| Basic   | 14,956,317                       | 14,956,317 | 14,964,021 |   |
| Diluted   | 14,956,317                       | 14,956,317 | 15,340,859 |   |

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

*Product sales*

Total product sales, which include sales of defibrotide and APIs, 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 2011 compared 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 mainly refer to our licensing, supply and distribution and cost sharing agreements with Sigma Tau. 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 2011 compared 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-down 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. Research and development expenses were primarily for the development of defibrotide to treat and prevent VOD. 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 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.

#### *Sales and marketing*

Sales and marketing expenses were €2.24 million for 2011 compared to none for 2010. Sales and marketing expenses relate to costs incurred in connection with the establishment of our European commercial team. Sales and marketing expenses refer mainly to recruiting, payroll, health economic and marketing analysis and stock based compensation costs.

#### *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 expenses*

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.

Year Ended December 31, 2010 Compared to Year Ended December 31, 2009

*Product sales.*

Product sales were €19.72 million for 2010 compared to €9.70 million for 2009, an increase of €10.02 million or 103%. The increase was primarily due to the distribution of defibrotide through the named-patient and cost recovery programs initiated in April and October 2009, respectively. For the years ended December 31, 2010 and 2009, named-patient and cost recovery program sales amounted to €13.18 million and €4.90 million, respectively, which are net of €2.13 million and €0.79 million in service fees, respectively.

Sales to a related party, Sirton, for the years ended December 31, 2010 and 2009 represented none and 2% of the total product sales, respectively. The decrease in sales to a related party was primarily due to the fact that, in the second quarter of 2009, we terminated our supply agreement with Sirton and entered into direct sales agreements with Sirton's customers in order to mitigate the risk associated with Sirton's poor financial situation.

Sales to third parties increased from €9.51 million in 2009 to €19.72 million in 2010, an increase of €10.21 million or 107%. The increase was primarily due to the launch of the named-patient and cost recovery programs in 2009, through which sales amounted to €13.18 million for 2010 compared to €4.90 million for 2009. Excluding such sales, sales to third parties for active pharmaceutical ingredients would have been €6.54 million and €4.61 million in 2010 and 2009, respectively, an increase of €1.93 million or 42%, primarily due to the increase in volume for sulglicotide.

#### *Other revenues*

Other revenues were €4.84 million for 2010 compared to €0.47 million for 2009. The increase versus the prior year is primarily attributable to an increase in activities that were reimbursed from Sigma-Tau under a cost sharing arrangement with the Company, which amounted to €1.14 million, and a ratable recognition of €3.41 million (\$4.67 million) of the €5.11 million (\$7.0 million) up-front payment made by Sigma-Tau in connection with the amendment of the existing license and supply agreement with the Company.

#### *Cost of goods sold.*

Our cost of goods sold was €5.79 million in 2010 compared to €4.00 million in 2009. The cost of goods sold as a percentage of product sales, was 29% in 2010 compared to 41% in 2009. The percentage decrease is primarily due to the higher margin on defibrotide sold through the named-patient program and price increases in the active pharmaceutical ingredients business. We wrote-off €0.37 million of inventory of heparin that may not have met good manufacturing practices.

#### *Research and development expenses.*

We incurred research and development expenses of €6.10 million in 2010 compared to €3.51 million for 2009. 2009 research and development expenses were net of €0.85 million of government grants in the form of a tax credit, accrued as reduction of expenses. Excluding such grants, 2009 research and development expenses would have been €4.36 million. The increase from the comparable period in 2009 was primarily due to completion of a technology transfer and costs associated with pre-clinical and clinical studies such as reproductive toxicity, hERG channel, QT/QTc, pharmacokinetics of defibrotide in healthy volunteers as well as regulatory consulting services associated with the completion of the eCTD.



*General and administrative expenses.*

Our general and administrative expenses were €5.84 million for 2010 compared to €6.04 million for 2009. 2010 and 2009 general and administrative expenses include a release of a reserve for doubtful accounts for €0.27 million and for €0.68 million, respectively, due to the offset of accounts receivable against the same amount of account payables due to the counterparty. Excluding the effect of the release of the allowance, general and administrative expenses represent a slight decrease from the prior year mainly due to the closure of the New York office, decrease in payroll costs, and lower legal and public company expenses offset by an increase in stock based compensation costs.

*Restructuring charges.*

Our restructuring charges were €1.10 million for 2010 compared to none for 2009. Restructuring charges of €0.95 million include one-time employee termination benefits, cost to terminate lease contracts and others exit costs resulting from a strategic decision to close down the New York office and to consolidate our resources and operations into our headquarters in Como, Italy. Additionally, we implemented a workforce reduction and recorded €0.16 million in one-time employee termination benefits, outplacement costs, termination notice and legal contractual compensation due upon early termination of certain employments agreements.

*Income tax expense*

Income tax expenses primarily refers to the Italian Regional Tax on Productive Activities, or “IRAP,” and has a floating a statutory rate of 3.9%. The IRAP tax is not deductible for corporate tax purposes (subject to certain exceptions). The IRAP tax base is similar to the corporate tax base but does not permit a deduction for labor and interest.

*Net income/(loss)*

Our net income was €4.08 million in 2010 compared to a net loss of (€4.53) million in 2009. The difference was primarily due to higher sales and margins associated with the named-patient and cost recovery programs and API business, increase in other income and revenues (including the ratable recognition as revenue of a portion of the up-front payment made by Sigma-Tau in connection with the amendment of the existing license and supply agreement with us), and decrease in general and administrative expense offset by an increase in research and development expenses, restructuring charges and income tax expenses.

## LIQUIDITY AND CAPITAL RESOURCES

| (in thousands)                  | As of December 31, |        |
|---------------------------------|--------------------|--------|
|                                 | 2010               | 2011   |
| Cash and cash equivalents       | €8,742             | €9,990 |
| Available for sale securities   | 263                | -      |
| Total cash and cash equivalents | €9,005             | €9,990 |

| (in thousands)                                       | Years Ended December 31, |        |        |
|--|--------------------------|--------|--------|
|  | 2009                     | 2010   | 2011   |
| Net cash (used in) provided by operating activities  | €(5,156 )                | €8,237 | €2,401 |
| Net cash used in investing activities                | (3,986 )                 | (205 ) | (393 ) |
| Net cash used in financing activities                | (1,173 )                 | (716 ) | (801 ) |
| Effect of exchange rate on cash and cash equivalents | 216                      | 34     | 41     |
| Cash and cash equivalent, beginning of period        | 11,491                   | 1,392  | 8,742  |
| Cash and cash equivalents, end of period             | €1,392                   | €8,742 | €9,990 |

We require cash to fund our operating activities and our service debt. We have been cash flow positive since 2010, primarily due to an upfront 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. 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 are required to fund additional clinical trials and 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 2011, our primary sources of funding have been 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 of €1.32 million, stock-based compensation expenses of €1.66 million, a provision for income taxes of €0.58 million, and a write-down 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.

In 2009, the principal use of cash in our operations was to fund our €4.53 million net loss. Of this net loss, certain costs were non-cash charges, such as depreciation and amortization costs of €1.30 million, stock-based compensation expenses of €1.39 million, and non-cash income of €0.68 million due to the release of an allowance for doubtful accounts and €0.22 million in an unrealized foreign exchange gain on cash held in foreign currency. In addition to non-cash charges, we also had a net change in other operating assets and liabilities of €2.43 million, including an increase in accounts receivable of €2.60 million, an increase in inventory of €0.66 million, a decrease in prepaid expenses and other current assets of €0.52 million, an increase in accounts payable and other accrued expenses of €0.36 million and a decrease in termination indemnities of €0.05 million.

### *Investing Activities*

In 2011 we had capital expenditures of €1.23 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.

In 2009, we had capital expenditures of approximately €0.25 million, which were partially financed through the sale of marketable securities for €0.26 million. Additionally, we made a final installment payment of €4.0 million to Crinos for the acquisition of the Italian marketing authorization and a payment of €16.0 million to Crinos related to trademarks for Prociclide and Noravid. We entered into this transaction for long-term strategic purposes and, specifically, to enable us to manage defibrotide globally while maintaining control over its distribution and with the flexibility to market defibrotide on our own or through selected partners. These expenditures were financed through €11.49 million in cash available at December 31, 2008 and proceeds from product sales.

### *Financing Activities*

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.

In 2009, we used approximately €1.17 million to reimburse a portion of our long term debt and capital lease obligations.

At December 31, 2011, we had an aggregate of €2.05 million in debt outstanding and had €9.99 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, and we anticipate expanding 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 European regulatory marketing approval for, and begin selling, defibrotide to treat severe VOD and prevent VOD. We believe that some of the key factors that will affect our internal and external sources of cash are:

our ability to obtain FDA and European regulatory marketing approval for, and to commercially launch, defibrotide to treat 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.

Through December 31, 2011, we had accumulated losses of approximately €92.85 million. While we have been cash flow positive since 2010, 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, or if we are required to fund additional clinical trials, we may revert to operating on 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 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.”*

## *2012 Outlook*

In 2012 we intend 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 Americas. With respect to our NDA for defibrotide for the treatment of hepatic VOD in adults and children filed with the FDA, we expect to continue to work on a remediation plan, which includes an analysis of the issues raised by the FDA and the engagement of CROs and outside consultants to assist us in addressing these issues.

We intend to work closely with the EMA on our MAA for defibrotide for the treatment and prevention of hepatic VOD in adults and children, filed in May 2011. We have responded to the Day 120 LoQs from the EMA's CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA or submit a LoOIs requiring further clarification, the latter of which would stop the review clock to permit us time to respond.

We expect to continue to run our treatment IND expanded access protocol for defibrotide for patients diagnosed with severe VOD in the United States. Under an expanded access program, the FDA allows early access to investigational drugs that are being developed to treat serious diseases for which there is no satisfactory alternative therapy. We decided to implement this expanded access program due to the large number of requests received for the compassionate use of defibrotide, and the corresponding difficulty to obtain institutional review board and FDA approval for those compassionate use requests. We will collect usage tolerability and safety data from these patients to support our NDA for this use of defibrotide. Outside of the US, we expect to continue to grant access to defibrotide on a pre-approved compassionate use basis through our name-patient program.

We intend to expand our presence into regional territories and enter into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide.

We are mindful of the fact that external conditions could affect our ability to achieve our goals, including healthcare policy changes, increasing concerns and scrutiny regarding potential or perceived safety issues associated with pharmaceuticals and biological products and continued government pricing pressures. We believe that remaining focused on the development of defibrotide and disciplined cost management will enable us to execute our operating objectives for 2012. 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 contract research organizations. The billings that we receive from contract research organizations 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 contract research organizations related services based on our estimate of management fees, site management and monitoring costs and data management costs. Differences between estimated trial costs and actual have not been material to date, and any changes have been made when they become known. Under this policy, research and development expense can vary due to accrual adjustments related to the underlying clinical trials and the expenses incurred by the contract research organizations. During the years ended December 31, 2009, 2010 and 2011, 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, 2009, 2010 and 2011.

| (in thousands)             | For The Years Ended December 31, |        |        |
|----------------------------|----------------------------------|--------|--------|
|                            | 2009                             | 2010   | 2011   |
| Defibrotide to treat VOD   | €641                             | €5,028 | €3,156 |
| Defibrotide to prevent VOD | 2,102                            | 521    | 1,583  |
| Others                     | 769                              | 555    | 794    |
| Total                      | €3,512                           | €6,104 | €5,533 |

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 and July 6, 2011, we announced the filing of our marketing authorization application, or MAA, for defibrotide with the EMA and new drug application, or NDA, for defibrotide with the FDA, respectively.

The successful development of defibrotide is uncertain. On August 17, 2011 we announced that we voluntarily withdrew our NDA for defibrotide for the treatment of VOD following correspondence from the FDA identifying



several potential “Refuse to File” issues regarding data in our NDA. In addition, we are not certain of the outcome following our response to the Day 120 LoQs presented by the CHMP regarding our MAA for defibrotide.

Therefore, we cannot estimate with certainty or know 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 are developing defibrotide or the date of completion of these development efforts. We cannot reasonably estimate when we may have material net cash inflows from commercial sales of defibrotide to treat or prevent VOD. We cannot estimate with certainty any of the foregoing 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, 2011, we had 2 U.S. patents issued with 7 U.S. patent applications pending, 26 foreign patents issued with 30 foreign patent applications pending, and 1 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.

## **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, 2011, 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                      | €1,560 | 240    | 240     | 240     | 240     | 240     | 360        |
| Finance loans                       | 200    | 77     | 81      | 42      | -       | -       |            |
| Equipment loans                     | 252    | 150    | 89      | 13      | -       | -       |            |
| Research loan                       | 37     | 37     | -       | -       | -       | -       |            |
|                                     | €2,049 | 504    | 410     | 295     | 240     | 240     | 360        |
| Operating leases                    | €1,280 | 300    | 240     | 185     | 185     | 185     | 185        |
| Capital lease obligation            | 21     | 21     | -       | -       | -       | -       |            |
| Research and Development Programs   | 810    | 791    | 6       | 6       | 4       | 3       |            |
| Sales and Marketing Programs        | 647    | 472    | 94      | 43      | 37      | 1       |            |
| General and Administration Programs | 509    | 385    | 83      | 38      | 2       | 1       |            |
|                                     | €3,267 | 1,969  | 423     | 272     | 228     | 190     | 185        |
| Total                               | €5,316 | 2,473  | 833     | 567     | 468     | 430     | 545        |

We received various loans from the Ministry for University and Research, made through San Paolo-IMI Bank (now Intesa SanPaolo) in September 2000 and December 2008. The loans are to finance the research and development of defibrotide to treat and prevent VOD and bear interest at 1.0% per annum. At December 31, 2011, the amount outstanding under the first loan was €37 thousand while the second loan was fully repaid in 2011.

On April 20, 2006, we obtained a financing facility from Banca Intesa Mediocredito S.p.A. of up to €1 million to finance the purchase and installation of two reactors in our manufacturing facility. The financing had a five-year term with an interest rate at the three-month Euribor rate plus 1.7%. The financing was secured by Banca Intesa debt securities in the aggregate amount of €263 thousand, and expired May 10, 2011. In April 2011 we made the final installment payment on the facility of €131 thousand.

On June 14, 2006, we obtained a loan in the amount of €2,800 thousand from Banca Nazionale Del Lavoro S.p.A. The loan is secured by a mortgage on certain of our land and buildings and bears interest at the six-month Euribor rate plus

1.00%. The principal is repayable in fourteen installments, every six months, from December 27, 2007 until final maturity in 2014, and interest is payable every six months from June 27, 2006. In December 2009, Banca Nazionale Del Lavoro S.p.A. agreed to defer payment of the loan principal for 12 months, extending the original term of the loan to 2015. In June 2011, Banca Nazionale Del Lavoro S.p.A. agreed to defer payment of the loan principal for an additional 36 months, extending the original term of the loan to 2018. At December 31, 2011, the principal amount outstanding under this loan was €1,560 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. In December 2009, San Paolo IMI S.p.A agreed to defer payment of the loan principal for 12 months, extending the original term of the loan to 2012. In June 2011, San Paolo IMI S.p.A. agreed to defer payment of the loan principal for an additional 12 months, extending the original term of the loan to 2013. 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, 2011. At December 31, 2011, the amount outstanding under this loan was €188 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 20 quarterly installments beginning on March 31, 2007. The loan bears interest at the three-month Euribor rate plus 1%. In December 2009, Banca Intesasanpaolo agreed to defer payment of the loan principal for 12 months, extending the original term of the loan to 2012. In June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal for an additional 12 months, extending the original term of the loan to 2013. At December 31, 2011, the amount outstanding under this loan was €63 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 60 monthly installments beginning on January 31, 2006. The loan bears interest at the three-month Euribor rate plus 1%. In December 2009, Banca Intesasanpaolo agreed to defer payment of the loan principal due for 12 months, extending the original term of the loan to 2012. In June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal due for further 12 months, extending the original term of the loan to 2013. At December 31, 2011, the amount outstanding under this loan was €137 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, Banca Intesasanpaolo agreed to defer payment of the loan principal for 12 months, extending the original term of the loan through 2012. In June 2011, Banca Intesasanpaolo agreed to defer payment of the loan principal for an additional 12 months, extending the original term of the loan through 2013. At December 31, 2011, the amount outstanding under this loan was €64 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 March 30, 2012. Our former Scientific Director, Massimo Iacobelli, left the Company in October 2011. In addition, Mr. Marco Codella resigned from the Board of Directors in November 2011 following his resignation from Sigma-Tau.

| Name                          | Age | Position   |
|-------------------------------|-----|--|
| Dr. Khalid Islam (1)          | 56  | President and Chief Executive Officer                      |
| Salvatore Calabrese           | 42  | Chief Financial Officer and Senior Vice President, Finance |
| Carin Heringa                 | 51  | Scientific Director and Senior Vice President              |
| Gigliola Bertoglio (2)        | 77  | Director   |
| Dr. Marco Brughera            | 56  | Director   |
| Dr. Glenn Cooper (3)          | 59  | Director   |
| Dr. Laura Ferro (1)           | 60  | Director   |
| Dr. Bobby W. Sandage, Jr. (4) | 58  | Director   |

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(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 (chairperson), nominating and corporate governance committee (chairperson) and audit committee.

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

**Dr. Khalid Islam** has served as our Chairman of our Board of Directors since December 2009, Chief Executive Officer since November 2009, and interim Scientific Director since October 2011. 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. He reported to the Chief Financial Officer of Cell Therapeutics, Inc. and was responsible for cost containment, budgeting, financial reporting and the implementation of Sarbanes-Oxley compliance. From September 1996 until November 2003, Mr. Calabrese was employed by PricewaterhouseCoopers as an accountant and was a Manager in Assurance Business Advisory Services at the time of departure. From October 2000 to June 2003, Mr. Calabrese worked in the Boston, MA office of PricewaterhouseCoopers. He earned a Bachelors' Degree in Economics at the University of Messina and a Masters' Degree in Accounting, Audit and Financial Control at the University of Pavia. He is also a chartered accountant in the Republic of Italy.

**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.

**Marco M. Brughera** was appointed to our Board of Directors on December 6, 2011 following the resignation of Marco Codella. Since January 2011, Dr. Brughera has held several positions for the Sigma-Tau Group, including Corporate R&D Managing Director of Sigma-Tau, S.p.A., President of Sigma-Tau Research CH, Chief Executive Officer of Prassis S.p.A., and the President and Chief Executive Officer of Tecnogen S.p.A. 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 Accelerera, Srl, an independent Contract Research Organization within the Nerviano Medical Sciences Group. From 1999 to 2004, Dr. Brughera held several senior-level positions at Pharmacia/Pfizer. Prior to 1999, 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. Glenn Cooper** has served as one of our directors since October 2009. Dr. Cooper is currently the Executive Chairman of Coronado Biosciences, Inc., a clinical stage biopharmaceutical company focused on cancer care, and has held that position since July 2010. Dr. Cooper was also Coronado's acting Chief Executive Officer from December 2010 to April 2011. From 1993 until 2009, Dr. Cooper served as Chairman and Chief Executive Officer of Nasdaq-listed Indevus Pharmaceutical, a specialty pharmaceutical company focused on urology and endocrinology. Prior to joining Indevus in 1993, Dr. Cooper held numerous executive level positions, including President and Chief Executive Officer of Progenitor, Inc., Executive Vice President and Chief Operating Officer of Sphinx Pharmaceuticals Corporation, and various clinical and regulatory positions with NYSE-listed Eli Lilly and Company. Dr. Cooper has participated in the development and commercialization of numerous drugs, including Prozac®, Axid®, Lorabid®, Ceclor®, SANCTURA®, SANCTURA XR®, Supprelin-LA®, and Vantas®. Dr. Cooper is currently a member of the Board of Directors of Repligen Corporation, listed on Nasdaq. Dr. Cooper received an M.D. from Tufts University School of Medicine, performed his postdoctoral training in Internal Medicine and Infectious Diseases at the New England Deaconess Hospital and the Massachusetts General Hospital and received a B.A. from Harvard University.

**Dr. Laura Ferro** is our former President and Chief Executive Officer (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. From 1991 to 2010, Dr. Ferro also held various positions at Sirton Pharmaceuticals S.p.A., a subsidiary of FinSirton that specializes in manufacturing pharmaceutical products. Prior to that, Dr. Ferro was a practicing physician for 15 years. Dr. Ferro is a member of the executive committee of Farindustria, 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 and Chief Executive Officer of Coronado Biosciences, Inc., a clinical stage biopharmaceutical company focused on cancer care, and has held these positions since April 2011. 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 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.

All of our directors' terms expire on the date of our ordinary shareholders' meeting approving our 2011 Italian GAAP financial statements, which will be held on April 27, 2012 (first call) and, if necessary, May 9, 2012 (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, 2009, compensation to our executive officers and directors was €1.18 million and €0.30 million, respectively. For the year ended December 31, 2010, compensation to our executive officers, excluding amounts due to termination of employment 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.

We did not grant any options to purchase ordinary shares to executive officers and directors during the year ended December 31, 2009 and 177,148 options previously granted to directors were forfeited with the resignation of those directors in August 2009. 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.

## 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, 2011, there were 1,135,067 shares underlying outstanding options, with a weighted average exercise price of \$7.35. 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, 2011, there were 1,063,008 shares underlying outstanding options, with a weighted average exercise price of \$6.17. 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. Cooper, Dr. Brughera, Dr. Ferro, Dr. Islam and Dr. Sandage. Ms. Bertoglio, Dr. Cooper and Dr. Sandage have never been employed by us or any of our subsidiaries and are independent directors. FinSirton also agreed to vote its shares in favor of electing one person designated by Sigma-Tau Finanziaria S.p.A. Dr. Brughera is the designee of Sigma-Tau. Dr. Brughera was elected as a director on December 6, 2011, following the resignation of 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 2011 Annual Ordinary Shareholders' Meeting to our 2012 Annual Ordinary Shareholders' Meeting:

· an annual cash retainer of \$45 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, Dr. Cooper and Dr. Sandage, each of whom is an independent director. Ms. Bertoglio is an audit committee financial expert. The audit committee is a standing committee of, and operates under a written charter adopted by, our board of directors. The audit committee:

establishes procedures for the receipt, retention and treatment of complaints 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 Dr. Cooper and Ms. Bertoglio, each of whom is an independent director. Under Nasdaq rules, the compensation of a U.S. domestic company's chief executive officer and all other officers must be determined, or recommended to the board of directors, either by a compensation committee comprised entirely of independent directors or by a majority vote of independent directors serving on the board. 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 Dr. Cooper and Ms. Bertoglio, each of whom is an independent director. Under Nasdaq rules, the directors of a U.S. domestic company must be 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 two alternate statutory auditors, as of the date of this annual report. The current board of statutory auditors was elected on June 30, 2009 for a term that ends at the date of the ordinary shareholders' meeting to approve our 2011 Italian GAAP financial statements.

| Name             | Position  |
|------------------|-----------|
| Giorgio Iacobone | Chairman  |
| Carlo Ciardiello | Member    |
| Augusto Belloni  | Member    |
| Domenico Ferrari | Alternate |
| Romano Chiapponi | Alternate |

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

In 2009, the board of statutory auditors met thirteen times and attended ten board of directors' meetings and one shareholders' meeting. 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 2011, we accrued €78 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, 2009, 2010 and 2011. As of December 31, 2011, all of our employees are in Italy, except for eleven individuals, one based in the United States and ten throughout Europe, outside of Italy.

|   | As of December 31, |      |      |
|---|--------------------|------|------|
|   | 2009               | 2010 | 2011 |
| Administration, accounting, finance, business development | 18                 | 13   | 15   |
| R&D, clinical, regulatory                                 | 14                 | 15   | 14   |
| Sales and marketing                                       | -                  | -    | 9    |
| Production, quality assurance control                     | 35                 | 33   | 30   |
| Total   | 67                 | 61   | 68   |

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 are subject to a collective bargaining agreement that was renewed on December 18, 2009 and expires on December 31, 2012. 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, 2011 was €376. 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 March 30, 2012. Dr. Ferro also holds options that, within 60 days of March 30, 2012 are vested as to 64,000 ordinary shares. Dr. Ferro and members of her family control FinSirton. Accordingly, Dr. Ferro may also be deemed to beneficially own FinSirton's shares of our company. 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 March 30, 2012, are vested as to 410,767 and 227,715, respectively.

To our knowledge, none of our other directors and officers listed herein owned one percent or more of our ordinary shares at March 30, 2012. 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 March 30, 2012 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 March 30, 2012, we had 15,018,150 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 March 30, 2012 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<br>Beneficially Owned | <b>Percent</b> |
|---|--|----------------|
| <b>Principal Shareholders</b>                                   |  |                |
| Laura Ferro (1)   | 2,714,000                              | 18.13 %        |
| Paolo Cavazza (2)   | 2,611,995                              | 17.45 %        |
| FinSirton S.p.A.(3)   | 2,550,000                              | 17.04 %        |
| Claudio Cavazza's estate (4)                                    | 2,474,943                              | 16.53 %        |
| Sigma-Tau Finanziaria S.p.A. (5)                                | 2,311,011                              | 15.44 %        |
| Defiante Farmaceutica, S.A. (6)                                 | 1,011,001                              | 6.75 %         |
| All directors and executive officers as a group (9 persons) (7) | 3,444,720                              | 23.01 %        |

Dr. Laura Ferro, who is our former Chief Executive Officer and President and one of our current directors, may be (1) deemed to share voting or dispositive control with FinSirton over the ordinary shares in Gentium that FinSirton beneficially owns. Dr. Ferro disclaims beneficial ownership of such shares.

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 FinSirton in April 2005, FinSirton 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, FinSirton 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).

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

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 FinSirton in April 2005, FinSirton 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, FinSirton 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 FinSirton in April 2005, FinSirton 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, FinSirton 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, as amended. Address is Rua dos Ferreiros, 260, Funchal-Madeira (Portugal) 9000-082.

Assumes that Dr. Laura Ferro is deemed to beneficially own the ordinary shares beneficially owned by FinSirton (7) and includes 894,720 ordinary shares issuable upon exercise of options currently exercisable and exercisable within 60 days of March 30, 2012.

Other than our depositary, the Bank of New York Mellon, as of March 30, 2012, 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 30, 2012, 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 30, 2012.

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 FinSirton, which beneficially owned approximately 17.04% of our outstanding ordinary shares at March 30, 2012.

Change of Control Arrangements

We are not aware of any arrangements that could result in a change of control, other than FinSirton'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, between January 1, 2011 and the date of this report, 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 FinSirton. As a result, Dr. Ferro and her family may be deemed to indirectly control approximately 17.03% of our outstanding ordinary shares as of March 30, 2012.

### Agreements with Various Entities

We had two commercial leases with FinSirton. The first lease contract was entered in 2005. The area leased was approximately 1,750 square meters in size for offices, laboratories and storage facilities. The contract provided for an annual fee of €156 thousand which was updated each year on the basis of the variation of the cost of living index. The second lease contract was entered in 2007. The area leased was approximately 600 square meters in size for offices, manufacturing, laboratories and storage facilities. The contract provided for an annual fee of €30 thousand which was updated each year on the basis of variation of the cost of living index. In July 2009, the agreement was amended to reduce space rented and the annual fee was decreased to €15 thousand.

These two leases were terminated on December 31, 2011 and, as of January 1, 2012, we entered into a new commercial lease with FinSirton. 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, Gentium received an initial payment of \$7,000 and will receive an additional payment of \$6,000 following approval from the FDA to market defibrotide in the U.S. and a further \$2,000 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.

### **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 profit 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 depository, 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

No significant changes have occurred since the date of the most recent annual financial statements.

## 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 depository 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<br>ADSs |          |
|--------------------|------------------------|----------|
|                    | High                   | Low      |
| 2007               | \$24.40                | \$13.51  |
| 2008               | \$13.98                | \$0.44   |
| 2009               | \$3.87                 | \$0.33   |
| 2010               |                        |          |
| First Quarter      | \$3.23                 | \$1.32   |
| Second Quarter     | \$5.49                 | \$3.57   |
| Third Quarter      | \$7.19                 | \$3.82   |
| Fourth Quarter     | \$7.20                 | \$5.27   |
| Full Year          | \$7.20                 | \$1.32   |
| <b><u>2011</u></b> |                        |          |
| First Quarter      | \$6.88                 | \$12.125 |
| Second Quarter     | \$9.05                 | \$10.38  |
| Third Quarter      | \$6.00                 | \$9.99   |
| Fourth Quarter     | \$5.65                 | \$6.32   |
| Full Year          | \$5.65                 | \$12.125 |
| Month Ended        |                        |          |
| October 31, 2011   | \$6.32                 | \$5.68   |
| November 30, 2011  | \$6.10                 | \$6.65   |
| December 31, 2011  | \$6.25                 | \$5.71   |
| January 31, 2012   | \$7.75                 | \$5.51   |

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|   |        |        |
|---|--------|--------|
| February 29, 2012                       | \$9.20 | \$7.88 |
| March 30, 2012 (through March 28, 2012) | \$8.74 | \$7.98 |

The closing price of the ADSs on NASDAQ on March 28, 2012 was \$8.60.

Sources: American Stock Exchange and the 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 28, 2012 was \$8.60. 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 30, 2012, our issued and outstanding share capital consisted of 14,966,317 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 Repubblica 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 depository 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 depository. 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, 2011, we had 14,969,150 shares outstanding and capital equal to Euro 37.05 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 depository will, to the extent possible, dispose of such rights for their account.

FinSirton 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."

## 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", "syndicate" (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 "Società 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 since March 30, 2010 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 development, filing and relevant funding of defibrotide for any therapeutic indication in the territory licensed to Sigma-Tau.

On March 6, 2009, we entered into a supply and distribution agreement with IDIS Limited, pursuant to which IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in all countries other than Europe and the Americas. Gentium will supply the finished and labeled product to IDIS, which will in turn provide the product directly to hospitals in countries outside Europe and the Americas. IDIS will maintain all relevant importation and regulatory licenses necessary to perform this service. IDIS will also assist Gentium with various clinical and regulatory obligations such as adverse event reporting. Gentium will instruct IDIS on the pricing for defibrotide, and in some cases, whether defibrotide will be distributed free of charge. IDIS will invoice the hospitals directly and will compensate Gentium once the receivables are collected. Gentium will pay a fee to IDIS for each unit shipped and will also pay IDIS a monthly service fee. This agreement has been amended and will continue to be amended to exclude countries in which we have entered into distribution agreements with specialized regional partners.

## 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 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](http://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 material 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, 2011, 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, 2011 we held a cash balance of €2.30 million, accounts receivable of €1.07 million and accounts payable of €0.41 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, 2011, our foreign currency transactions are minimal and changes to the exchange rate between the US dollar and Euro would have an immaterial affect on our earnings. If the US dollar were 10% stronger against the Euro, our net assets balance would increase by approximately €0.33 million as of December 31, 2011.

As of December 31, 2011, we had floating debts in the principal amount of €2.05 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 2.02% to 3.06 %. Each 100 basis point increase in interest rates will cause interest payments in 2012 to increase by approximately €0.02 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.

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:

\$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)

For:

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

As necessary



for servicing the deposited securities

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, 2011. 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, 2011, 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, 2011, 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.

March 30, 2012

### **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, 2011, 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, 2011, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the 2011 consolidated financial statements of Gentium S.p.A. and our report dated March 30, 2012 expressed an unqualified opinion thereon.

Reconta Ernst & Young S.p.A.

Milan, Italy

March 30, 2012

**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](http://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, 2010 and 2011:

| (in thousands of Euros) | Year ended   |      |
|-------------------------|--------------|------|
|                         | December 31, |      |
|                         | 2010         | 2011 |
| Audit Fees              | €121         | €150 |
| Audit-Related Fees      | -            | -    |
| Tax Fees                | -            | -    |
| All Other Fees          | -            | -    |
| Total fees              | €121         | €150 |

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, 2010 and 2011.

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.

#### 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 Practice:* 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 Practice:* 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

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| Report of Independent Registered Public Accounting Firm  | F-1 |
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| Consolidated Statements of Operations for the years ended December 31, 2009, 2010 and 2011           | F-3 |
| Consolidated Statements of Shareholders' Equity for the years ended December 31, 2009, 2010 and 2011 | F-4 |
| Consolidated Statements of Cash Flows for the years ended December 31, 2009, 2010 and 2011           | F-5 |
| Notes to Consolidated Financial Statements   | F-6 |

Item 19. Exhibits

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.

- 2.8.2 Form of Ordinary Share Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.

Investor Rights and Registration Rights Agreements

- 2.9.1 Form of Investors' Rights Agreement between Gentium S.p.A. and holders of the Series A senior convertible promissory notes and warrants dated October 15, 2004, incorporated by reference to Exhibit 4.2.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.

Exhibit Description

- 2.9.2 Amendment No. 1 to Gentium S.p.A. Series A Senior Convertible Promissory Notes, Warrants, Subscription Agreements and Investor Rights Agreements among Gentium S.p.A. and the other parties thereto dated May 27, 2005, incorporated by reference to Exhibit 4.2.6 to Amendment No. 4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 31, 2005.
- 2.10 Investors' Rights Agreement by and among Gentium S.p.A., Alexandra Global Master Fund Ltd. and Generation Capital Associates made as of January 10, 2005, incorporated by reference to Exhibit 4.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 2.11 Investors' Rights Agreement by and among Gentium S.p.A. and Sigma-Tau Finanziaria S.p.A. made as of April 4, 2005, incorporated by reference to Exhibit 4.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on April 7, 2005.
- 2.12 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of October 14, 2005, incorporated by reference to Exhibit 4.8.3 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
- 2.13 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of June 6, 2006, incorporated by reference to Exhibit 4.9.4 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 2.14 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of February 9, 2007, incorporated by reference to Exhibit 4.10.3 to the Registration Statement on Form F-3, Registration No. 333-141198, previously filed with the SEC on March 9, 2007.

Equity Incentive and Stock Option Plans

- 4.1.1 Amended and Restated 2004 Equity Incentive Plan, incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-8, Registration No. 333-137534, previously filed with the SEC on September 22, 2006.
- 4.1.2 Amendment No. 1 to Amended and Restated 2004 Equity Incentive Plan, made as of March 26, 2007, incorporated by reference to Exhibit 4.1.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.2.1 Amended and Restated Nonstatutory Share Option Plan and Agreement dated March 23, 2006, incorporated by reference to Exhibit 4.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.2.2 Amendment No. 1 to Amended and Restated Nonstatutory Share Option Plan and Agreement, made as of March 26, 2007, incorporated by reference to Exhibit 4.2.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.3 Amended 2007 Stock Option Plan dated May 9, 2011.



Loan Agreements

4.4 Ministry for Universities, Scientific and Technological Research Loan granted to Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., by Sanpaolo Imi S.p.A., dated September 27, 2000, incorporated by reference to Exhibit 10.6 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.

4.5 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A. dated June 14, 2006 incorporated by reference to Exhibit 10.7.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.

4.6 Loan Agreement for €230,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.

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| Exhibit | Description   |
|---------|---|
| 4.7     | Loan Agreement for €500,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.   |
| 4.8     | Loan Agreement for €225,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.   |
| 4.9     | Financing Contract between Banca Intesa Mediocredito S.p.A. and Gentium S.p.A. dated April 20, 2006, incorporated by reference to Exhibit 4.36.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006. |
| 4.10    | Loan Agreement, dated June 30, 2006, between San Paolo IMI S.p.A. and Gentium S.p.A. , incorporated by reference to Exhibit 4.43 to the Annual Report on Form 20-F for the year ended December 31, 2006, previously filed with the SEC on April 30, 2007.               |

#### Clinical Trial Agreements

|        |  |
|--------|--|
| 4.11.1 | Master Services Agreement, dated March 14, 2007, between MDS Pharma Services (US), Inc. and Gentium S.p.A., incorporated by reference to Exhibit 1 to the report on Form 6-K, previously filed with the SEC on March 20, 2007.           |
| 4.11.2 | Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (prospective arm), incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on August 22, 2007. |
| 4.11.3 | Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (historical arm), incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.  |

#### License and Distribution Agreements

|         |   |
|---------|---|
| 4.12.1  | License and Supply Agreement by and between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc. (assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.) dated December 7, 2001, incorporated by reference to Exhibit 10.15 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005. |
| 4.12.2  | Letter Agreement, dated October 12, 2007, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 99.4 to the report on Form 6-K, previously filed with the SEC on December 12, 2007.  |
| 4.12.3* | Amendments to License and Supply Agreement and Letter Agreement, dated December 7, 2001 and October 12, 2007, respectively, effective January 7, 2010, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 2 to the Form 6-K, previously filed with the SEC on January 11, 2010.                               |

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- 4.13.1 Contract to Supply Active Ingredients between Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 4.24.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.13.2 Amendment No. 1 to Contract to Supply Active Ingredients, effective as of December 7, 2007, by and between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.).
- 4.14.1 Master Agreement, dated December 28, 2006, among Gentium S.p.A., Crinos S.p.A., SFI Stada Financial Investments Ltd. and SFS Stada Financial Services International Ltd., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
- 4.14.2 Distribution Agreement, dated December 28, 2006, between Gentium S.p.A. and Crinos S.p.A., incorporated by reference to Exhibit 6 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
- 4.15\* Technical Transfer Services Agreement, dated February 2, 2009, between Gentium S.p.A. and Patheon Italia S.p.A, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.

#### Exhibit Description

- 4.16.1 Technical Agreement, dated February 26, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.22.1 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.16.2\* Supply and Distribution Agreement, dated March 6, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.22.2 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.17\* Master Contract Clinical Research Agreement, dated September 29, 2009, between US Oncology Clinical Development and Gentium S.p.A., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on December 8, 2009.

#### Management Services Agreements

- 4.18 Service Agreement between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.25.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.19 Service Agreement between Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.26.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.

#### Leases

- 4.20 Commercial Lease Contract between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) dated January 1, 2005, incorporated by reference to Exhibit 10.33 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.
- 4.21 Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2012

#### Miscellaneous

- 4.22 Form of indemnification agreement between Gentium S.p.A. and each officer and director, incorporated by reference to Exhibit 10.34 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.

#### Certifications and Consents

- 12.1 Chief Executive Officer Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- 12.2 Chief Financial Officer Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- 13.1 Chief Executive Officer Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
- 13.2 Chief Financial Officer Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

15(a) Consent of Reconta Ernst & Young S.p.A. dated March 30, 2012.

\*Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.

## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Shareholders of Gentium S.p.A.

We have audited the accompanying consolidated balance sheets of Gentium S.p.A. (the “Company”) as of December 31, 2011 and 2010, and the related consolidated statements of operations, shareholders’ equity, and cash flows for each of the three years in the period ended December 31, 2011. These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits 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 the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Gentium S.p.A. at December 31, 2011 and 2010, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2011, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Gentium S.p.A.’s internal control over financial reporting as of December 31, 2011, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 30, 2012 expressed an unqualified opinion thereon.

Reconta Ernst & Young S.p.A.

Milan, Italy

March 30, 2012

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**GENTIUM S.p.A.****CONSOLIDATED BALANCE SHEETS**

| In thousands, except share   | As of December 31, |                |
|--|--------------------|----------------|
|  | 2010               | 2011           |
| <b>Current assets:</b>   |                    |                |
| Cash and cash equivalents  | €8,742             | €9,990         |
| Available for sale securities  | 263                | -              |
| Accounts receivable, net of allowance of €27 as of December 31, 2010 and 2011  | 3,442              | 5,128          |
| Accounts receivable from related parties, net of allowance of €850 as of December 31, 2010 and 2011  | 657                | 286            |
| Inventories, net of allowance of €451 and €789 as of December 31, 2010 and 2011, respectively  | 2,364              | 2,946          |
| Prepaid expenses and other current assets  | 541                | 488            |
| <b>Total Current Assets</b>  | <b>16,009</b>      | <b>18,838</b>  |
| <br>   |                    |                |
| Property, manufacturing facility and equipment, net  | 8,598              | 8,508          |
| Intangible and other non-current assets  | 67                 | 66             |
| <b>Total Assets</b>  | <b>€24,674</b>     | <b>€27,412</b> |
| <br>   |                    |                |
| <b>LIABILITIES AND SHAREHOLDERS' EQUITY</b>  |                    |                |
| <b>Current Liabilities</b>   |                    |                |
| Accounts payable   | €4,308             | €5,089         |
| Accounts payable to related parties  | 372                | 290            |
| Accrued expenses and other current liabilities   | 1,902              | 1,710          |
| Deferred Revenues  | 1,704              | 494            |
| Current portion of capital lease obligations   | 70                 | 21             |
| Current maturities of long-term debt   | 1,098              | 504            |
| <b>Total Current Liabilities</b>   | <b>9,454</b>       | <b>8,108</b>   |
| <br>   |                    |                |
| Long-term debt, net of current maturities  | 1,759              | 1,545          |
| Capital lease obligations  | 21                 | -              |
| Termination indemnities  | 510                | 376            |
| <b>Total Liabilities</b>   | <b>11,744</b>      | <b>10,029</b>  |
| <br>   |                    |                |
| Share capital (no par value as of December 31, 2010 and 2011; 18,302,617 and 19,656,317 shares authorized as of December 31, 2010 and 2011; 14,956,317 and 14,969,150 shares issued and outstanding at December 31, 2010 and 2011) | 108,485            | 110,228        |
| Accumulated deficit  | (95,555 )          | (92,845 )      |
| <b>Total Shareholders' Equity</b>  | <b>12,930</b>      | <b>17,383</b>  |
| <b>Total Liabilities and Shareholders' Equity</b>  | <b>€24,674</b>     | <b>€27,412</b> |

The accompanying notes are an integral part of these consolidated financial statements.





**GENTIUM S.p.A.****CONSOLIDATED STATEMENTS OF OPERATIONS**

| In thousands, except share and per share amounts                     | For the Year Ended December 31, |            |            |
|--|---------------------------------|------------|------------|
|  | 2009                            | 2010       | 2011       |
| Revenues:  |                                 |            |            |
| Product sales to related party                                       | €195                            | €          | €          |
| API product sales  | 4,603                           | 6,533      | 4,848      |
| NPP product sales  | 4,904                           | 13,182     | 16,886     |
| Total product sales  | 9,702                           | 19,715     | 21,734     |
| Other revenues   | 129                             | 289        | 123        |
| Other revenues from related party                                    | 337                             | 4,547      | 2,026      |
| Total Revenues   | 10,168                          | 24,551     | 23,883     |
| Operating costs and expenses:  |                                 |            |            |
| Cost of goods sold   | 4,002                           | 5,786      | 6,035      |
| Research and development   | 3,512                           | 6,104      | 5,533      |
| General and administrative   | 6,036                           | 5,835      | 5,490      |
| Sales and Marketing  | -                               | -          | 2,237      |
| Charges from related parties   | 279                             | 346        | 222        |
| Restructuring charges  | -                               | 1,101      | -          |
| Depreciation and amortization  | 916                             | 908        | 870        |
|  | 14,745                          | 20,080     | 20,387     |
| Operating income/(loss)  | (4,577)                         | ) 4,471    | 3,496      |
| Foreign currency exchange gain, net                                  | 162                             | 90         | 46         |
| Interest expense, net  | (110)                           | ) (87)     | ) (21)     |
| Pre-tax income/(loss)  | €(4,525)                        | ) €4,474   | €3,521     |
| Income tax expense:  |                                 |            |            |
| Total income tax expense   | -                               | (397)      | ) (811)    |
| Net income/(loss)  | €(4,525)                        | ) €4,077   | €2,710     |
| Net income/(loss) per share:   |                                 |            |            |
| Basic  | €(0.30)                         | ) €0.27    | €0.18      |
| Diluted  | €(0.30)                         | ) €0.27    | €0.18      |
| Weighted average shares used to compute net income/(loss) per share: |                                 |            |            |
| Basic  | 14,956,317                      | 14,956,317 | 14,964,021 |
| Diluted  | 14,956,317                      | 14,956,317 | 15,340,859 |

The accompanying notes are an integral part of these consolidated financial statements.

**GENTIUM S.p.A.****CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY****FOR THE YEARS ENDED DECEMBER 31, 2009, 2010 AND 2011***In thousands*

|  | Shares | Amount   | Additional<br>Paid-in<br>Capital | Accumulated<br>Deficit | Accumulated<br>Other<br>Comprehensive<br>Income | Total<br>Shareholders'<br>Equity |
|--|--------|----------|----------------------------------|------------------------|---|----------------------------------|
| Balance at December 31, 2008                                   | 14,956 | €14,956  | €0,619                           | €(95,107)              | (17)  | €10,451                          |
| Unrealized gain on marketable securities                       |        |          |                                  |                        | 17  | 17                               |
| Stock-based compensation prior to no par value resolution      |        |          | 717                              |                        |   | 717                              |
| Resolution of no par value                                     |        | 91,336   | (91,336)                         |                        |   | -                                |
| Stock-based compensation subsequent to no par value resolution |        | 670      |                                  |                        |   | 670                              |
| Net loss for 2009  |        |          |                                  | (4,525 )               |   | (4,525 )                         |
| Balance at December 31, 2009                                   | 14,956 | €106,962 | €                                | €(99,632)              | -   | €7,330                           |
| Stock-based compensation                                       |        | 1,523    |                                  |                        |   | 1,523                            |
| Net income for 2010  |        |          |                                  | 4,077                  |   | 4,077                            |
| Balance at December 31, 2010                                   | 14,956 | €108,485 | €                                | €(95,555)              | -   | €12,930                          |
| Stock based compensation                                       |        | 1,666    |                                  |                        |   | 1,666                            |
| Issuance of common stock upon exercise of stock options        | 13     | 77       | €                                |                        |   | 77                               |
| Net income for 2011  |        |          |                                  | 2,710                  |   | 2,710                            |
| Balance at December 31, 2011                                   | 14,969 | €110,228 | €                                | €(92,845)              | -   | €17,383                          |

The accompanying notes are an integral part of these consolidated financial statements.

**GENTIUM S.p.A.****CONSOLIDATED STATEMENTS OF CASH FLOWS**

| Amounts in thousands   | For the Year Ended December 31, |          |          |
|--|---------------------------------|----------|----------|
|  | 2009                            | 2010     | 2011     |
| Net income/(loss)  | €(4,525 )                       | €4,077   | €2,710   |
| Adjustments to reconcile net income/(loss) to net cash provided by/(used in) operating activities: |                                 |          |          |
| Write-down of inventory  | 19                              | 375      | 337      |
| Unrealized foreign exchange gain/(loss)  | (223 )                          | 8        | (48 )    |
| Depreciation and amortization  | 1,300                           | 1,323    | 1,320    |
| Stock based compensation   | 1,386                           | 1,523    | 1,666    |
| (Gain)/loss on fixed asset disposal  | 2                               | 24       | (14 )    |
| Allowance for doubtful accounts  | -                               | 27       | -        |
| Release of allowance for doubtful accounts   | (684 )                          | (251 )   | -        |
| Provision for income taxes   | -                               | 397      | 580      |
| Loss on marketable securities  | 2                               | -        | -        |
| Changes in operating assets and liabilities:   |                                 |          |          |
| Accounts receivable  | (2,603 )                        | (499 )   | (1,281 ) |
| Inventories  | (663 )                          | (1,188 ) | (919 )   |
| Prepaid expenses and other current and noncurrent assets   | 524                             | 890      | 42       |
| Accounts payable and other accrued expenses and deferred revenues                                  | 363                             | (82 )    | (648 )   |
| Termination indemnities  | (54 )                           | (91 )    | (134 )   |
| Deferred Revenues  | -                               | 1,704    | (1,210 ) |
| Net cash provided by/(used in) operating activities  | (5,156 )                        | 8,237    | 2,401    |
| Cash Flows From Investing Activities:  |                                 |          |          |
| Capital expenditures   | (245 )                          | (205 )   | (718 )   |
| Proceeds from sale of equipment  | -                               | -        | 62       |
| Intangible assets expenditures   | (3 )                            | -        | -        |
| Sales of marketable securities   | 262                             | -        | 263      |
| Acquisition of Crinos assets   | (4,000 )                        | -        | -        |
| Net cash used in investing activities  | (3,986 )                        | (205 )   | (393 )   |
| Cash Flows From Financing Activities:  |                                 |          |          |
| Proceeds from stock option exercises, net  | -                               | -        | 77       |
| Repayments of long-term debt   | (1,108 )                        | (649 )   | (808 )   |
| Principal payment of capital lease obligation  | (65 )                           | (67 )    | (70 )    |
| Net cash used in financing activities  | (1,173 )                        | (716 )   | (801 )   |
| Increase/(Decrease) in cash and cash equivalents   | (10,315 )                       | 7,316    | 1,207    |
| Effect of exchange rate on cash and cash equivalents   | 216                             | 34       | 41       |
| Cash and cash equivalents, beginning of period   | 11,491                          | 1,392    | 8,742    |
| Cash and cash equivalents, end of period   | €1,392                          | €8,742   | €9,990   |

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Supplemental disclosure of cash flow information:

|   |      |      |     |
|---|------|------|-----|
| Cash paid for interest  | €143 | €78  | €66 |
| Cash paid for income taxes  | -    | -    | 375 |
| Supplemental disclosure of non cash investing and financing activities: |      |      |     |
| Offset noncash assets and liabilities with Crinos and Sirton            | €744 | €332 | €-  |

The accompanying notes are an integral part of these consolidated financial statements.

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**GENTIUM S.p.A.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**December 31, 2011**

**(In thousands of Euro or U.S. dollars unless specified otherwise)**

**1. BUSINESS AND BASIS OF PRESENTATION**

*Basis of Presentation:* Gentium S.p.A. (“**Gentium**,” the “**Company**,” “**we**,” or “**our**”) is a biopharmaceutical company focused on the development and manufacture of our primary product candidate, defibrotide, an investigational drug based on a mixture of single-stranded and double-stranded DNA extracted from pig intestines. Our development of defibrotide has been focused on the treatment and prevention of a disease called 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 has been given “orphan” status by the FDA and the EMA, which means that we will have limited market exclusivity upon regulatory approval. Defibrotide has also been granted “fast-track product” designation by the FDA for the treatment of severe VOD prior to stem cell transplantation. Currently, to the best of our knowledge, there are no FDA or EMA approved treatments for this life-threatening disease. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approval basis under a treatment IND, protocol, which we call our cost recovery program, in the U.S., and through a named-patient program (“NPP”) throughout the rest of the world.

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 for defibrotide for the treatment and prevention of hepatic VOD in adults and children, with the EMA under a centralized procedure. We have responded to the Day 120 LoQs from the EMA’s CHMP. The CHMP will continue its review of the MAA and will either issue an opinion on the MAA

or submit a LoOIs requiring further clarification, the latter of which will stop the review clock to permit us time to respond.

On July 6, 2011, we announced the filing of our 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 the 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 begun implementing a remediation plan, which includes an analysis of the issues raised by the FDA, and the engagement of CROs and several outside consultants to assist us in addressing the issues raised by the FDA. Currently, we are working with these CROs and consultants to conduct additional quality reviews of the original datasets and databases.

We 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 North America, Central America and South America (collectively, the “Americas”). We have entered into a supply and distribution agreement with IDIS, whereby IDIS agreed to be the exclusive supplier of defibrotide on a named-patient supply basis in certain European countries and in certain territories in other parts of the world. We have entered into license and/or supply and distribution agreements with specialized regional partners for the distribution of defibrotide on a named-patient supply basis in the following territories: Turkey, Israel, Palestinian Authority, Australia, New Zealand, Sweden, Denmark, Norway, Iceland, Finland, Latvia, Lithuania and Estonia; and some of these 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.

In accordance with our overall strategy, we have appointed our commercial leadership team, which is currently responsible for, among other things, market research and pharmacoeconomics analysis, and will be responsible for marketing defibrotide in the major European countries upon regulatory approval, if any. In August 2011, we formed a wholly-owned subsidiary, Gentium GmbH, organized under the laws of Switzerland, as the headquarters for our commercial operations.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, or APIs, such as the defibrotide compound, 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, defibrotide, at Patheon's manufacturing facility. We believe that we are the sole worldwide producer of defibrotide. Our operating assets are located in Italy.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America. These consolidated financial statements are denominated in the currency of the European Monetary Union (the Euro or €). Unless otherwise indicated, all amounts are reported in thousands of Euro or US\$, except share and per share data.

The accompanying consolidated financial statements have been prepared on the assumption that we will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business for the twelve-month period following the date of the balance sheet. Through December 31, 2011, the Company had accumulated losses of approximately €92.85 million. We have been cash flow positive since 2010, primarily due to an upfront 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. As a result, we have been able to finance the establishment of our European commercial team, repay the current portion of our long-term debt and fund our working capital. 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 are required to fund additional clinical trials and 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. Management performed an evaluation of the Company's activities through the date of filing of this annual report on Form 20-F, and has concluded that there are no subsequent events requiring disclosure through that date.

## **2.SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

*Consolidation:* Our consolidated financial statements reflect the financials of the Company and its wholly-owned subsidiary, Gentium GmbH. All intercompany balances and transactions have been eliminated upon consolidation.

*Use of Estimates:* The preparation of our consolidated financial statements in accordance with U.S. GAAP requires management to make judgments, estimates and assumptions that may affect the reported amounts of assets and liabilities, and related disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ from these estimates under different assumptions or conditions.



*Segment Information:* The Company is managed and operated as one business. The entire business is managed by a single management team that reports to the chief executive officer. The Company does not operate separate lines of business or separate business entities with respect to any of its products or product candidates. The Company's chief operating decision makers review the profits and losses and manage the operations of the Company on an aggregate basis. Accordingly, the Company operates in one segment, which is the biopharmaceutical industry.

*Cash and Cash Equivalents:* Cash and cash equivalents include highly liquid, temporary cash investments having original maturity dates of three months or less.

*Concentration of Credit Risk and Other Risks and Uncertainties:* Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash, cash equivalents, marketable securities and trade receivables. The Company limits its investments to short-term low risk instruments. Trade receivables from one foreign customer are guaranteed by a letter of credit from a primary banking institution. The Company is exposed to credit risk with respect to its trade accounts receivable, from sales of defibrotide through its named-patient and cost recovery programs, which are typically unsecured. As of December 31, 2011, top two customers accounted for approximately 49% and 18% of our accounts receivable, respectively. As of December 31, 2010, two customers accounted for approximately 70% and 19% of our accounts receivable, respectively. We are exposed to risks associated with foreign currency transactions in which we use U.S. dollars to make contract payments denominated in euros and vice versa. As the net positions of our unhedged foreign currency transactions fluctuate, our earnings might be affected. We currently do not utilize forward exchange contracts or any type of hedging instruments to hedge foreign exchange risk, as we believe our overall exposure is relatively limited. For the year ended December 31, 2011, three customers accounted for 56%, 14% and 12% of our product sales, respectively. For the year ended December 31, 2010, three customers accounted for 55%, 23% and 12% of our product sales, respectively. For the year ended December 31, 2009, three customers accounted for 47%, 28% and 12% of our product sales to third parties, respectively.

The Company is subject to a number of risks common to companies in the biotechnology industry including, but not limited to, its ability to successfully obtain regulatory approval for defibrotide, the uncertainty as to whether defibrotide will become a successful commercial product, its ability to generate projected revenue through its named-patient and cost recovery programs, its dependence on corporate partners and key personnel, protection of proprietary technology, compliance with FDA and other governmental regulations and approval requirements, its ability to obtain financing, if necessary, and potential changes in the health care industry.

*Accounts Receivable:* Accounts receivable are primarily comprised of amounts due from our wholesale distributors and pharmaceutical companies. Account receivables are recorded net of allowances for distributors' fees where we are not invoiced directly and doubtful accounts. Estimates for distributors' fees are based on contractual terms. Estimates for our allowance for doubtful accounts are determined based on existing contractual payment terms, historical payment patterns of our customers and individual customer circumstances. Amounts determined to be uncollectible are charged or written-off against the reserve.

*Inventories:* Inventories consist of raw materials, semi-finished and finished active pharmaceutical ingredients and defibrotide distributed through the named-patient and treatment IND programs. Inventories are stated at the lower of cost or market, with cost being determined on an average cost basis, which approximates the first-in-first-out method. 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. Since signing the agreements associated with the named-patient and cost recovery programs, we capitalized the subsequent costs of manufacturing defibrotide as inventory, including costs to convert existing active pharmaceutical ingredients to ampoules and vials and costs to package and label previously manufactured inventory which costs had previously been expensed as research and development expenses. Until we sell the inventory, the carrying values of our inventories and our cost of sales will reflect only incremental costs incurred subsequent to the signing of these agreements.

The Company periodically reviews its inventories and items that are considered outdated or obsolete which are reduced to their estimated net realizable values. The Company estimates reserves for excess and obsolete inventories based on inventory levels on hand, future purchase commitments, and current and forecast product demand. If an estimate of future product demand suggests that inventory levels will become obsolete, then inventories are reduced to their estimated net realizable values. We also review our inventory for quality assurance and quality control issues identified in the manufacturing process and determine whether a write-down is necessary.

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

*Property, Manufacturing Facility and Equipment:* Property and equipment are carried at cost, subject to review for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. The cost of normal, recurring, or periodic repairs and maintenance activities related to property and equipment are expensed as incurred, and the cost for major expenditures for additions and improvements are capitalized if they extend the useful life or capacity of the asset.

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The cost of our property, manufacturing facility and equipment also includes a proportionate share of the Company's financing costs. The amount of interest cost to be capitalized for qualifying assets is that portion of the interest cost incurred during the assets' acquisition period that could have been avoided if expenditures for the assets had not been made. Capitalized interest expense is amortized over the same life as the underlying constructed asset.

We depreciate or amortize the cost of our property and equipment using the straight-line method over the estimated useful lives of the respective assets, which are summarized as follows:

| <b>Asset Category</b>         | <b>Useful Lives</b>   |
|-------------------------------|---|
| Land                          | Not depreciated   |
| Buildings                     | 20 years  |
| Plant and Machinery           | 10 to 15 years  |
| Industrial Equipments         | 10 years  |
| Furniture and Fixtures        | 5 to 10 years   |
| Leasehold Improvements        | Lesser of the useful life or the term of the respective lease |
| Internally Developed Software | 15 years  |

When we dispose of property, plant and equipment, we remove the associated cost and accumulated depreciation from the related accounts on our consolidated balance sheet and include any resulting gain or loss in our consolidated statement of operations.

*Computer Software* We capitalize costs of computer software obtained for internal use. Such costs are included in property, manufacturing facility and equipment and are amortized over the estimated useful life of the software.

*Intangibles:* Intangible assets are stated at cost and amortized on a straight-line basis over the expected useful life of such assets, which is estimated to be five to ten years for licenses and trademarks.

*Impairment of Long-lived Assets, including Intangibles:* The Company's long-lived assets consist primarily of property and equipment. The Company evaluates its ability to recover the carrying values of long-lived assets used in its business, considering changes in the business environment or other facts and circumstances that suggest the value of such assets may be impaired. If this evaluation indicates the carrying value will not be recoverable, based on the undiscounted expected future cash flows estimated to be generated by these assets, the Company reduces the carrying amount to the estimated fair value.

*Marketable Securities:* The Company's marketable securities, which consist of debt securities due on May 2011, are classified as securities available for sale in current assets and are carried at fair value based on market prices. Unrealized gains and losses (which are deemed to be temporary), if any, are reported in other comprehensive income or loss as a separate component of shareholders' equity.

A decline in the market value of any available for sale securities below cost are deemed to be other than a temporary result in a reduction in the carrying amount to fair value. In this case, impairment is charged to earnings and a new cost basis for the securities is established. Factors evaluated to determine whether an impairment is other than temporary include significant deterioration in the credit rating, asset quality, or business prospects of the issuer; adverse changes in the condition of the general market in which the issuer operates; the intent and ability to retain the investment for a sufficient period of time to allow for recovery in the market value of the investment; and any concerns about the issuer's ability to continue as a going concern.

*Revenue Recognition:* We recognize revenues 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. Product revenues are recorded net of applicable reserves for discounts, distributors' fees and allowances.

Items deducted from Total Product Sales:

*Distributor fees:* We have entered into an agreement with distributors to manage defibrotide as an investigational drug on a named-patient and cost recovery basis. We recognize a fee to distributors based on a contractually determined fixed percentage of sales. These fees are accrued at the time of the sale and offset against product sales and are typically paid within 60 days after the issuance of a sales report. Distributor fees are recorded as accrued expenses and other current liabilities on our balance sheets

*Cash discounts:* We may offer a price discount to a customer if a minimum number of purchase quantities are purchased in a calendar year. We establish a reserve based on estimates of the amounts earned or to be claimed on the related sales, which is classified under accrued expenses and other current liabilities on our balance sheets, and as a reduction of product sales.

*Product returns:* We do not provide our customers with a general right of product return, although we do permit returns if the product is damaged or defective when received by the customer.

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 item. The consideration received from these arrangements is allocated among the separate units based on their respective selling prices, and the applicable revenue recognition criteria are applied to each separate unit. Revenues from collaborative arrangements generally include manufacturing fee arrangements if the research and development efforts ever reach the commercialization phase.

Revenue from non-refundable up-front license fees and milestone payments is recognized as performance occurs and our obligations are completed. In accordance with the specific terms of the Company's obligations under these arrangements, revenue is recognized as the obligation is fulfilled or ratably over the development or manufacturing period. Revenue associated with substantive at-risk milestones is recognized based upon the achievement of the milestones as defined in the respective agreements. Revenue from the reimbursement of research costs under collaborative arrangements is recognized as the related research and development costs are incurred, as provided under the terms of these arrangements.

Advance payments received in excess of amounts earned are classified as deferred revenue until earned on the balance sheets. Costs incurred by the Company for shipping and handling are included in cost of goods sold.

*Research and Development:* Research and development expenditures are charged to operations as incurred. Research and development expenses consist of costs incurred for proprietary and collaborative research and development, including activities such as product registration and investigator-sponsored trials. Research and development expenses include salaries, benefits and other personnel related costs, clinical trial and related clinical manufacturing expenses, fees paid to clinical research organizations (CROs), contract and other outside service fees, employee stock based compensation expenses and allocated facility and overhead costs, offset by research and development tax credits due from the Italian Tax Authorities. Payments we make for research and development services prior to the services being rendered are recorded as prepaid assets on our consolidated balance sheets and are expensed as the services are provided.

*Clinical Trial Accruals:* The Company accounts for the costs of clinical studies conducted by contract research organizations based on the estimated costs and contractual progress over the life of the individual study. These costs can be a significant component of research and development expenses.

*Income Taxes:* The Company uses the liability method of accounting for income taxes. Deferred tax assets and liabilities are recognized for the estimated future tax consequences of temporary differences between the financial

statements carrying amounts and the respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the year in which the temporary differences are expected to be recovered or settled. We evaluate the realizability of our deferred tax assets and establish a valuation allowance when it is more likely than not that all or a portion of deferred tax assets will not be realized. We account for uncertain tax positions using a “more-likely-than-not” threshold for recognizing and resolving uncertain tax positions. We evaluate uncertain tax positions and consider various factors, including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position.

*Foreign Currency Transactions:* The functional currency of the Company’s foreign subsidiary is the Euro and, therefore, there are no translation adjustments in the consolidated financial statements. However, net realized and unrealized gains and losses resulting from foreign currency transactions that are denominated in a currency other than the Company’s functional currency, the Euro, are included in the statements of operations.

*Share-Based Compensation:* The Company has always recognized stock-based compensation at fair value. Compensation expenses for awards that are ultimately expected to vest are recognized as expenses on a straight-line basis over the requisite service period of the equity compensation award, which is generally the vesting period.

Historically, the fair value of all option grants was estimated on the grant date using the Black-Scholes option-pricing model. For all stock options granted after December 31, 2009, the fair value of the award is estimated on the date of grant 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, the Company believes that the binomial model provides a fair value that is more representative of actual experience and future expected experience than that value calculated using the Black-Scholes model.

*Fair Value of Financial Instruments:* The carrying amounts of cash and cash equivalents, accounts receivable, prepaid expenses, other current assets, accounts payable and accrued expenses approximate fair values due to the short-term maturities of these instruments. Marketable securities are carried at market price.

*Comprehensive Income:* Comprehensive income (loss) consists of net income (loss) and other comprehensive income (loss), or OCI. OCI includes certain changes in stockholders' equity that are excluded from net loss. Specifically, we include only unrealized gains or losses on our available for sale securities in OCI. Other comprehensive income (loss), net of tax, for the years ended December 31, 2009, 2010 and 2011, was €(4,508), €4,077, and €2,710 respectively.

*Earnings per Share:* Basic net earnings per share is based upon the weighted average number of common shares outstanding and excludes the effect of dilutive common stock issuable from stock options and warrants. In computing diluted earnings per share, only potential common shares that are dilutive, or those that reduce earnings per share, are included. The issuance of common stock from stock options and warrants is not assumed if the result is anti-dilutive, such as when a loss is reported.

#### *Recent Accounting Pronouncements*

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (FASB) or other standard setting bodies, which are adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.



In December 2011, the FASB issued ASU 2011-11, *Balance Sheet (Topic 210): Disclosures about Offsetting Assets and Liabilities* (ASU 2011-11). This newly issued accounting standard requires an entity to disclose both gross and net information about instruments and transactions eligible for offset in the statement of its financial position as well as instruments and transactions executed under a master netting or similar arrangement. The standard was issued to enable users of financial statements to understand the effects or potential effects of those arrangements on its financial position. This ASU is required to be applied retrospectively and is effective for fiscal years, and interim periods within those years, beginning on or after January 1, 2013. As this accounting standard only requires enhanced disclosure, the adoption of this standard is not expected to have an impact on our financial position or results of operations.

### **3. RELATED PARTIES**

Historically, the Company had significant relationships with two privately owned Italian companies: FinSirton and its wholly owned subsidiary, Sirton (now Vifarma S.p.A.). FinSirton, the parent company of several businesses, remains one of the Company's largest shareholders (with approximately 17% ownership at December 31, 2011) and was originally the Company's sole shareholder. The Company's former Chief Executive Officer and Chairman, Dr. Laura Ferro may be deemed to control FinSirton. In addition, Dr. Ferro previously served as a member of Sirton's Board of Directors.

In 2010, Sirton (now Vifarma S.p.A.) was put into liquidation and, on June 28, 2010, Sirton was admitted by the Court of Como to a composition with creditors' proceedings ("concordato preventivo"). The composition with creditors was approved on February 3, 2011. At that time, Sirton's assets were acquired by a third party, as approved by the Court of Como. A liquidator has been appointed to manage the liquidation process and the distribution of proceeds received from the sale of Sirton's assets to Sirton's creditors. Although the distribution allocation has not yet been finalized, we understand that the liquidator may propose to satisfy the amounts due to secured creditors in full, with a payout distribution of 18.26% to all unsecured creditors. Our net exposure to Sirton at the date of the admission to the composition with creditors (June 28, 2010) was €850. If the preliminary indication from the liquidator is confirmed we may collect 18.26% or €155 of the receivables outstanding on the date of the admission to the composition with creditors (June 28, 2010) which amounts to €850 thousand. Due to the uncertainty of the final distribution to creditors from the sales of Sirton's assets, we established an allowance for doubtful accounts of €850, which represents our exposure against Sirton.

The Company had a lease agreement with Sirton (now Vifarma S.p.A.) that expired on December 31, 2010, but was renewed for an additional six-year term. In connection with Sirton's (now Vifarma S.p.A.) liquidation proceeding, the lease agreement with Sirton (now Vifarma S.p.A.) along with the premises to which such lease pertains were transferred to an unrelated third party that has also acquired the rights to Sirton's name.

We had two commercial leases with FinSirton. The first lease contract was entered into 2005. The area leased was approximately 1,750 square meters in size for offices, laboratories and storage facilities. The contract provided for an annual fee of €156 thousand which was updated each year on the basis of the variation of the cost of living index. The second lease contract was entered into 2007. The area leased was approximately 600 square meters in size for offices, manufacturing, laboratories and storage facilities. The contract provided for an annual fee of €30 thousand which is updated each year on the basis of variation of the cost of living index. In July 2009, the agreement was amended to reduce space rented and the annual fee was decreased to €15 thousand.

These two leases were terminated on December 31, 2011 and, as of January 1, 2012, we entered into a new commercial lease with FinSirton. 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.

Expenses under these operating leases for the years ended December 31, 2009, 2010 and 2011 amounted to €198, €192 and €212, respectively. See Note 17 for the commitments under these leases.

For the years ended December 31, 2009, 2010 and 2011, the Company had the following transactions with FinSirton and Sirton (now Vifarma S.p.A.):

|                              | For the Year Ended<br>December 31, |            |            |
|------------------------------|------------------------------------|------------|------------|
|                              | 2009                               | 2010       | 2011       |
| <b>Revenues</b>              |                                    |            |            |
| Product sales                | €195                               | €-         | €-         |
| <b>Expenses</b>              |                                    |            |            |
| Cost of goods sold           | 296                                | 164        | -          |
| Charges from related parties | 279                                | 346        | 222        |
| <b>Total</b>                 | <b>575</b>                         | <b>510</b> | <b>222</b> |

As of December 31, 2010 and 2011 the Company had balances with FinSirton and Sirton (now Vifarma S.p.A.) as listed below. In 2011, transactions with the new Sirton Pharmaceuticals S.p.A were not classified as transactions with a related party since the new Sirton Pharmaceuticals S.p.A. is no longer a related party of the Company given the change of ownership.

|   | December 31, |       |
|---|--------------|-------|
|   | 2010         | 2011  |
| Accounts Receivable – Sirton (now Vifarma S.p.A.) | €1,050       | €850  |
| Accounts Receivable – FinSirton                   | 14           | 256   |
| Allowance of doubtful accounts                    | (850 )       | (850) |
| Accounts Receivable, net                          | 214          | 256   |
| <br>  |              |       |
| Accounts Payable Sirton                           | 308          | 5     |
| Accounts Payable FinSirton                        | 64           | 285   |
|   | 372          | 290   |

The Company and Sirton (now Vifarma S.p.A.) formally offset nil and €332 in payables due to Sirton (now Vifarma S.p.A.) against the same amount of receivables due from Sirton, for the years ended December 31, 2011 and 2010, respectively.

Due to the uncertainty of the final distribution to creditors from the sale of Sirton’s assets, we had established an allowance for doubtful accounts of €1,783, which was partially released in 2010 and 2009 for €251 and €684 respectively, as general and administrative expenses. We still maintain an allowance of €850 which represents our exposure against Sirton (now Vifarma S.p.A.).

The Company is a party to a License and Supply 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. and pursuant to which Sigma-Tau Pharmaceuticals, Inc. has agreed to purchase defibrotide from us for this use. Sigma-Tau Pharmaceuticals, Inc. is an affiliate of Sigma-Tau Finanziaria S.p.A. Dr. Marco Brughera, who holds various senior-level positions within the Sigma-Tau Group, serves as a member of our Board of Directors. Dr. Brughera was elected to our board following the resignation of Marco Codella, the former Chief Financial Officer of Sigma-Tau Finanziaria, who served as member of our board of directors since 2005. See Note 4 for further discussion of our relationship with Sigma-Tau.

The accounting policies applied in transactions with our affiliates are consistent with those policies applied in transactions with independent third parties and all related party agreements are negotiated on an arm’s length basis.

#### 4. COLLABORATIVE ARRANGEMENTS

In December 2001, the Company entered into a license and supply agreement with Sigma-Tau Pharmaceuticals, Inc. (as assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., hereinafter referred to as “Sigma-Tau”). Under the

agreement, Sigma-Tau obtained exclusive rights to distribute, market and sell defibrotide to treat VOD in the United States. This license expires 8 years after Company's launch of the product. In 2005, the Company expanded Sigma-Tau's current license territory to all of North America, Central America and South America (collectively, the "Americas"). In January 2010, the Company amended its existing license and supply agreement to encompass a license to Sigma-Tau for the intravenous formulation of defibrotide for the prevention of VOD in the Americas and to transfer the New Drug Application (NDA) post-approval in the United States. Pursuant to the amended terms, Gentium received an initial payment of \$7,000 and will receive an additional payment of \$6,000 following approval from the FDA to market defibrotide in the U.S. and a further \$2,000 following the transfer of the approved NDA to Sigma-Tau.

The agreement also envisages that the Company will produce and supply defibrotide to Sigma-Tau for marketing and distribution in the United States if and when the drug is approved by the FDA. Gentium will receive a 7% royalty on net sales and a supply margin equal to the greater of 31% of net sales of defibrotide or €0.050 per unit in the Americas. Gentium will reimburse \$1,000 of costs reimbursed by Sigma-Tau from its future royalty payments due to Gentium under the License and Supply Agreement.

If the Company unilaterally discontinues the development of defibrotide to treat VOD (after written notice to Sigma-Tau) and, within 36 months of the discontinuation, resumes the development of defibrotide, substantially availing itself of the stages previously completed, either independently or with a third party, then it will be required to promptly reimburse Sigma-Tau for the amounts received. The Company has no intention of discontinuing the development of the product.

If, during the drug development stage the Company realizes that the activities required to bring the product to completion will necessitate a material increase in expenditures, the parties will discuss the increased costs and possible revisions to the terms of the agreement; if the parties are unable to mutually agree on such revisions, either party can terminate the agreement. If the Company or Sigma-Tau terminates the agreement for that reason and the Company resumes the development within 36 months of the termination, substantially availing itself of the stages previously completed, either independently or with a third party, the Company will be required to promptly reimburse Sigma-Tau for the amounts received.

On October 12, 2007, the Company and Sigma-Tau entered into a cost sharing agreement to address the need for additional funding not included in the original license and supply agreement. Under this agreement Sigma-Tau will reimburse the Company for 50% of certain costs incurred in the Company's ongoing Phase III clinical trial of defibrotide to treat severe VOD. We recognize the reimbursement of research and development expenses as revenue when we incur the costs subject to reimbursement. For the years ended December 31, 2009, 2010 and 2011, the Company recorded contributions of €0.10 million, €1.14 million, and €0.32 million received from Sigma-Tau which has been recognized as other revenue.

The following table outlines the nature and amount of other revenue recognized under the cost sharing agreement in the accompanying consolidated financial statements:

|   | For the Year Ended<br>December 31, |        |        |
|---|------------------------------------|--------|--------|
|   | 2009                               | 2010   | 2011   |
| Research and development cost reimbursement | €103                               | €1,138 | €323   |
| Upfront payments recognized ratably         | -                                  | 3,409  | €1,703 |
| Milestone payments                          | 234                                | €-     | -      |
|   | €337                               | €4,547 | €2,026 |

The following table outlines the receivable that Sigma-Tau Pharmaceuticals, Inc. has agreed to pay as reimbursement for costs incurred on the Phase III trial for the treatment of severe VOD pursuant to a cost-sharing letter agreement between the Company and Sigma-Tau. The balance is classified as accounts receivable from related parties in the consolidated financial statements.

|                                    | December<br>31, |      |
|------------------------------------|-----------------|------|
|                                    | 2010            | 2011 |
| Accounts Receivable from Sigma-Tau | €43             | €0   |

## 5. INVENTORIES

The Company's inventories consist of:

|                     | December 31, |        |
|---------------------|--------------|--------|
|                     | 2010         | 2011   |
| Raw materials       | €310         | €271   |
| Semi-finished goods | 768          | 979    |
| Finished goods      | 1,286        | 1,696  |
| Total               | €2,364       | €2,946 |

At December 31, 2010 and 2011, the reserves for obsolescence were €451 and €789 respectively. The increase from 2010 is mainly due to an adjustment of the net realizable value of the heparin active pharmaceutical ingredient manufactured in connection with our costs associated with the heparin manufacturing process, for which there is doubt as to the Company's ability to recover the cost incurred.

Prior to signing the named-patient and cost recovery program agreements, all costs associated with the production of defibrotide were expensed as research and development expenses. In connection with completion of the technology transfer with a third party contractor, as of December, 31 2011 inventory included €487 for defibrotide commercial batches classified as finished goods, which are expected to be sold through the named patient and cost recovery programs.

## 6. PREPAID EXPENSES AND OTHER CURRENT ASSETS

The Company's prepaid expenses and other current assets consisted of:

|   | December<br>31, |      |
|---|-----------------|------|
|   | 2010            | 2011 |
| VAT receivables                           | €291            | €111 |
| Other prepaid expenses and current assets | 250             | 377  |
| Total prepaid expenses and current assets | €541            | €488 |

The "VAT" (value added tax) receivables represent the tax on the value of consumption. VAT has no effect on the Company's operating results, as payments and receipts may be offset against each other in periodic filings with the tax authorities. The VAT payment system is a "custodial" relationship. VAT liabilities are generated when the Company invoices customers, including the VAT amount, and VAT receivables are created when the Company purchases goods and services subject to VAT. The decrease in VAT receivables is due to the utilization of i) €285 to offset the payment of an equivalent amount of social charges and withholding taxes, ii) €133 to offset the payment of an equivalent amount of the 2011 Italian Regional Tax on Productive Activities and iii) €238 as an increase in VAT receivables which may be claimed back in 2012 to offset an equivalent amount of social security charges and withholding tax.

Other prepaid expenses and current assets refer mainly to advances to vendors and prepaid premiums to insurance companies.

## 7. PROPERTY, MANUFACTURING FACILITY AND EQUIPMENT



Property, plant and equipment are recorded at historical cost, net of accumulated depreciation. Components of property, plant and equipment, net are summarized as follows:

|                               | December 31,<br>2010 |                             |                   | 2011    |                             |                   |
|-------------------------------|----------------------|-----------------------------|-------------------|---------|-----------------------------|-------------------|
|                               | Cost                 | Accumulated<br>Depreciation | Net book<br>value | Cost    | Accumulated<br>Depreciation | Net book<br>value |
| Land and building             | €2,682               | 1,404                       | 1,278             | €2,643  | 1,480                       | 1,163             |
| Plant and machinery           | 15,363               | 9,439                       | 5,924             | 15,464  | 10,392                      | 5,072             |
| Industrial equipment          | 1,275                | 833                         | 442               | 1,280   | 904                         | 376               |
| Furniture and fixtures        | 1,088                | 653                         | 435               | 1,289   | 743                         | 546               |
| Leasehold improvements        | 325                  | 309                         | 16                | 1,126   | 379                         | 747               |
| Internally Developed Software | 685                  | 201                         | 484               | 708     | 249                         | 459               |
| Construction in progress      | 19                   | -                           | 19                | 145     | 0                           | 145               |
|                               | €21,437              | 12,839                      | 8,598             | €22,655 | 14,147                      | 8,508             |

As of December 31, 2009, 2010 and 2011, property, manufacturing facility and equipment include €460 attributed to lab instruments acquired under capital lease arrangements. The related accumulated depreciation at December 31, 2009, 2010 and 2011 was €138, €184, and €230 respectively.

## 8. FAIR VALUE MEASUREMENT

The table below presents information on assets and liabilities measured at fair value on a recurring basis at December 31, 2011 and 2010, and includes the valuation techniques the Company utilizes to determine such fair value.

Fair values determined on the basis of Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. The Company's Level 1 assets consist of cash and marketable debt securities. Fair values determined on the basis of Level 2 inputs utilize observable quoted prices for similar assets and liabilities in active markets and observable quoted prices for identical or similar assets in markets that are not very active. Fair values determined on the basis of Level 3 inputs utilize unobservable inputs and include valuations of assets or liabilities for which there is little, if any, market activity. Level 3 assets or liabilities include those for which fair value measurements are determined using pricing models, discounted cash flow methodologies or similar valuation techniques, as well as significant management judgment or estimation.

|                           | Total Carrying Value at December 31, 2011 | Fair Value Measurements at December 31, 2011 using |   |   |
|---------------------------|---|--|---|---|
|                           |   | Quoted prices in active markets (Level 1)          | Significant other observable inputs (Level 2) | Significant unobservable inputs (Level 3) |
| Cash and cash equivalents | €9,990                                    | €9,990   | -   | -   |
| Total                     | €9,990                                    | €9,990   | -   | -   |

|                               | Total Carrying Value at December 31, 2010 | Fair Value Measurements at December 31, 2010 using |   |   |
|-------------------------------|---|--|---|---|
|                               |   | Quoted prices in active markets (Level 1)          | Significant other observable inputs (Level 2) | Significant unobservable inputs (Level 3) |
| Cash and cash equivalents     | € 8,742                                   | € 8,742  | -   | -   |
| Available for sale securities | 263                                       | 263  | -   | -   |
| Total                         | € 9,005                                   | € 9,005  | -   | -   |

## 9. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of:

|  | December 31, |        |
|--|--------------|--------|
|  | 2010         | 2011   |
| Accrued compensation and employee benefits | €1,039       | €642   |
| Due to social security                     | 256          | 282    |
| Withholding tax due                        | 142          | 118    |
| Current taxes liabilities                  | 397          | 580    |
| Other payables                             | 68           | 88     |
| Total                                      | €1,902       | €1,710 |

Accrued compensation and employee benefits include bonuses, salaries, vacation and deferred compensation due to employees, directors and management. The decrease versus the prior year is mainly due to lower employee incentives.

Current tax liabilities represent amounts due to Italian tax authorities for the Italian Regional Tax on Productive Activities, (“IRAP”) and Corporate tax (“IRES”) and amount due to the Swiss tax authority as minimum tax.

The increase in current tax liabilities is mainly due to the new corporate tax legislation enacted in December 2011 by the Italian Parliament to raise funds for the country’s deficit. The recently enacted corporate tax legislation establishes that net operating losses (“NOLs”) can be carried forward without any time limit, as opposed to what was provided for under the previous regime, and can be offset up to 80% of the taxable income generated in each given fiscal year. We accrued €297 thousand for the 2011 fiscal year.

## 10. CREDIT FACILITIES AND LONG-TERM DEBT

Long term debt, net of current maturities consists of:

|   | December 31, |       |
|---|--------------|-------|
|   | 2010         | 2011  |
| a) Mortgage loan bearing interest at the Euribor 6 month rate plus 1.0% due June 2015 (2.23% and 2.62% at December 31, 2010 and 2011, respectively) | 1,800        | 1,560 |

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|    |  |         |        |
|----|--|---------|--------|
| b) | Equipment loan secured by marketable securities, bearing interest at the Euribor 3 months rate plus 1.70% due April 2012 (2.70% and 3.06% at December 31, 2010 and 2011, respectively) | 131     | -      |
| c) | Equipment loan bearing interest at the Euribor 3 months rate plus 1.20% due June 2012 (2.20% and 2.56% at December 31, 2010 and 2011, respectively)                                    | 375     | 188    |
| d) | Financing loan bearing interest at the Euribor 1 months rate plus 1.00% due December 2012 (1.78% and 2.02% at December 31, 2010 and 2011, respectively)                                | 214     | 137    |
| f) | Research loan from the Italian Ministry for University and Research, interest at 1% per annum, due January 2012  | 73      | 37     |
| g) | Financing loan bearing interest at the Euribor 3 months rate plus 1.00% due December 2012 (2% and 2.36% at December 31, 2010 and 2011, respectively)                                   | 101     | 64     |
| h) | Equipment loan bearing interest at the Euribor 3 months rate plus 0.80% due December 2012 (1.80% and 2.16% at December 31, 2010 and 2011, respectively)                                | 98      | 63     |
| i) | Research loan from the Italian Ministry for University and Research, interest at 1% per annum, due January 2012  | 65      | -      |
|    |  | 2,857   | 2,049  |
|    | Less current maturities  | (1,098) | (504 ) |
|    | Total  | €1,759  | €1,545 |

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The equipment loan of €188 requires the Company to maintain €5,000 of net shareholders' equity determined in accordance with Italian generally accepted accounting principles. The Company was in compliance with this covenant at December 31, 2010 and 2011. There are no other covenants associated with the Company's loans.

In June 2011, in connection with a national agreement among the Italian Bank Association and the Italian Ministry of Economics and Enterprise Organizations, companies that met certain criteria, such as good standing, and qualified as a small or medium enterprise, were eligible to apply for a deferment on payment of 50% of the current portion of any long term debt payments due in the next twenty-four months. Except with respect to our research loan incurred with the Italian Ministry for University and Research, which was not eligible for deferment, we obtained such deferment on payment of our principal loan, which will permit the postponement of cash outflows in the amounts of €200 and €400 as of December 31, 2011 and 2012, respectively.

The maturities of long-term debt are as follows:

|            | December<br>31, |
|------------|-----------------|
| 2013       | 410             |
| 2014       | 295             |
| 2015       | 240             |
| 2016       | 240             |
| Thereafter | 360             |
| Total      | €1,545          |

## 11. INCOME TAXES

The Company's components of income before provision for income taxes are as follows:

|          | Years Ended December<br>31, |       |         |
|----------|-----------------------------|-------|---------|
|          | 2009                        | 2010  | 2011    |
| Domestic | (4,525)                     | 4,474 | 4,655   |
| Foreign  | -                           | -     | (1,134) |
|          | (4,525)                     | 4,474 | 3,521   |

The components of the provision for income taxes are as follows:

|                          | As of December<br>31, |       |       |
|--------------------------|-----------------------|-------|-------|
| (in thousand)            | 2009                  | 2010  | 2011  |
| Current                  |                       |       |       |
| Domestic                 | €                     | €317  | €677  |
| Foreign                  | -                     | 80    | 134   |
| Total Current Provision  | €                     | €397  | €811  |
| Deferred                 |                       |       |       |
| Domestic                 | €                     | €     | €     |
| Foreign                  | -                     | -     | -     |
| Total Deferred Provision | €0,00                 | €0,00 | €0,00 |

Total Tax Provision € 697 811

Reconciliation of income tax computed at the Italian statutory tax rate to the Company's tax expense/(benefit) for the years ended December 31, 2009, 2010 and 2011 is as follows:

|  | For the Year Ended December 31, |        |         |         |         |         |
|--|---------------------------------|--------|---------|---------|---------|---------|
|  | 2009                            |        | 2010    |         | 2011    |         |
|  | Tax                             | Rate % | Tax     | Rate %  | Tax     | Rate %  |
| (Loss)/Profit Before Tax at statutory rate | (1,244)                         | 27.5   | 1,230   | 27.5    | 968     | 27.5    |
| Movement in valuation allowance            | (133 )                          | 2.9    | (2,782) | (62.2 ) | (1,252) | (35.6 ) |

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|  |       |         |     |      |     |      |
|--|-------|---------|-----|------|-----|------|
| Expired NOLs                               | 860   | (19.0 ) | 673 | 15.1 | -   | -    |
| Other                                      | 190   | (4.2 )  | 367 | 8.2  | -   | -    |
| Italian Regional tax - IRAP                | -     | -       | 317 | 7.1  | 380 | 10.8 |
| Swiss minimum tax                          | -     | -       | 81  | 1.8  | 134 | 3.8  |
| Stock options                              | 381   | (8.4 )  | 420 | 9.4  | 458 | 13.0 |
| Permanent differences from Tax Calculation | (55 ) | 1.2     | 91  | 2.0  | 123 | 3.5  |
| Total                                      | -     | -       | 397 | 8.9  | 811 | 23.0 |

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Significant components of deferred tax assets are as follows:

| (in thousand)                   | 2010     | 2011     |
|---------------------------------|----------|----------|
| Deferred tax assets:            |          |          |
| Net operating losses            | €14,991  | €3,973   |
| Capitalization of R&D costs     | 6,412    | 6,363    |
| Property, plant and equipment   | 360      | 380      |
| Write down of intangible assets | 1,278    | 1,181    |
| Allowance on doubtful account   | 7        | 162      |
| Inventory write-off             | 347      | 277      |
| Other                           | 224      | 31       |
| Total deferred tax assets       | €23,619  | €2,367   |
| Deferred tax liabilities:       |          |          |
| Total deferred tax liabilities  | -        | -        |
| Net deferred tax assets         | 23,619   | 22,367   |
| Valuation Allowance             | (23,619) | (22,367) |
| Net deferred taxes              | -        | €        |

As of December 31, 2011, the gross net operating losses (NOLs) amount to approximately €51,320. Under the Italian tax law, NOLs cannot be carried back. Under a newly enacted tax rule issued in 2011, tax losses can be carried forward indefinitely, however such tax losses can only be used to offset 80% of taxable income. The deferred tax asset related to NOLs also includes NOLs generated by Gentium GmbH (€1,100). According to the Swiss tax law, these NOLs can be carried forward for seven years and will begin to expire in 2019.

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, and has determined that it is not more likely than not the Company will realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been recognized on the Company's deferred tax assets. The Company's valuation allowance decreased by €1,252 for the year ended December 31, 2011 and decreased by €2,782 for the year ended December 31, 2010.

The Company's only foreign subsidiary, Gentium GmbH, was incorporated during 2011. At the end of the year this entity has generated a loss and accordingly, there are no unremitted earnings for the periods presented. Therefore, the Company has not recognized any deferred tax liabilities for unremitted earnings.

As of December 31, 2011, according to ASC740-10-50 (formerly FIN 48), the Company has no uncertain tax positions and has no accrued interest or penalties related to such uncertain tax positions. Also in the previous year the



Company had no uncertain tax positions. No changes in the Company's uncertain tax positions are expected in the next 12 months.

Fiscal years from 2007 to 2011 are still subject to income tax assessment.

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## 12. SHAREHOLDERS' EQUITY

The Company had 14,956,317 and 14,969,150 ordinary shares, each of no par value issued and outstanding on December 31, 2010 and December 31, 2011, respectively. On December 31, 2011, the total number of authorized shares was 19,656,317. Authorized capital is as follows:

|                                   | December 31 |            |
|-----------------------------------|-------------|------------|
|                                   | 2010        | 2011       |
| Issued and outstanding            | 14,956,317  | 14,969,150 |
| Reserved for stock option plans   | 2,500,000   | 4,687,167  |
| Reserved for exercise of warrants | 846,300     | -          |
|                                   | 18,302,617  | 19,656,317 |

On April 28, 2006, our shareholders approved an amendment to our bylaws, which granted certain powers to our board of directors, pursuant to the provisions of Articles 2443 and 2420, part 3 of the Italian Civil Codes, including the power to increase the capital of the company in cash, up to €90 million of par value, in one or more transactions, and to issue convertible bonds (even subordinated) and increase the capital of the Company, in one or more transactions, up to Euro 10 million of par value, through the issuance of ordinary shares reserved for the conversion of such convertible bonds, and in both cases also with the faculty to issue warrants by means of the same resolution of the board of directors providing for the relevant capital increase and in each case, exclude or limit the option right of the shareholders if the Board of Directors determines that exclusion or limitation to be in the interest of the Company. Such delegation of powers expired after five years. On May 9, 2011, our shareholders renewed this resolution for additional five years starting from the date of the resolution of the 2011 Extraordinary Shareholders' meeting approving the amendment. As of December 31, 2011, our board of directors authorized the issuance of 4,549,435 ordinary shares in connection with this resolution by our shareholders.

On June 30, 2009, our shareholders approved an amendment to our bylaws, which granted certain powers to our board of directors, pursuant to article 2443 of the Italian Civil Code, including the power to increase the capital of our company in cash, up to an amount equal to €100 million, on a separable basis, in one or more transactions, for the purpose of a rights offering with the faculty 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 and with the faculty to reserve 1/4 of any such capital increase to employees under the Company's equity incentive plans in effect from time to time, and the power to cancel the par value of the ordinary shares of the Company, which was completed on June 30, 2009. As of December 31, 2011, our board of directors has not authorized the issuance of any shares pursuant to this resolution by our shareholders.

On May 9 2011, our shareholders approved an amendment to our bylaws, which granted certain powers to our board of directors, pursuant to article 2441, fifth paragraph of the Italian Civil Code, 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. We have used this approval to increase the number of ordinary shares of the Company authorized under our 2007 Stock Option Plan to 3,200,000.

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**Warrants**

A summary of the warrant activity for the three years ended December 31, 2011 is presented below.

|                            | Warrants | Weighted<br>Average<br>Exercise Price |          |
|----------------------------|----------|---------------------------------------|----------|
| Balance, December 31, 2008 | 846,300  | €6.29                                 | \$ 11.75 |
| Granted                    | -        | -                                     | -        |
| Exercised                  | -        | -                                     | -        |
| Cancelled                  | -        | -                                     | -        |
| Balance, December 31, 2009 | 846,300  | €6.29                                 | \$ 11.75 |
| Granted                    | -        | -                                     | -        |
| Exercised                  | -        | -                                     | -        |
| Cancelled                  | 523,774  | €6.90                                 | \$ 9.66  |
| Balance, December 31, 2010 | 322,526  | €11.35                                | \$ 15.20 |
| Granted                    | -        | -                                     | -        |
| Exercised                  | -        | -                                     | -        |
| Cancelled                  | 322,526  | €11.35                                | \$ 15.20 |
| Balance, December 31, 2011 | -        | -                                     | -        |

There are no outstanding warrants as of December 31, 2011:

|   | Number of<br>warrants<br>issued | Number of<br>warrants<br>exercised | Number of<br>warrants<br>cancelled | Number of<br>warrants<br>outstanding |
|---|---------------------------------|------------------------------------|------------------------------------|--------------------------------------|
| Warrant issued in conjunction with promissory notes | 503,298                         | 22,734                             | 480,564                            | -                                    |
| Initial Public Offering                             | 151,200                         | 107,990                            | 43,210                             | -                                    |
| 2005 private placement                              | 713,518                         | 713,518                            | -                                  | -                                    |
| 2006 private placement                              | 466,446                         | 143,920                            | 322,526                            | -                                    |
| Total   | 1,834,462                       | 988,162                            | 846,300                            | -                                    |

In connection with a private placement in 2006, the Company issued warrants for the purchase of an aggregate of 388,705 ordinary shares at an exercise price of \$14.50 per ordinary share. In addition, the Company issued a five year warrant for the purchase of 77,741 ordinary shares at an exercise price of \$17.40 per ordinary share to one of placement agent. The warrants were fully vested, exercisable at the option of the holder, in whole or in part, and expire five years from the date of grant. Through December 31, 2011, we had issued 143,920 ordinary shares upon exercise of these warrants for proceeds of \$2,087 (€1,490). On April 28, 2011, 322,526 warrants expired without having been exercised. As of December 31, 2011, there were no warrants outstanding.

### 13. EQUITY INCENTIVE PLANS.

The Company currently has two option plans in place: an Amended and Restated 2004 Equity Incentive Plan, which includes an Amended and Restated 2004 Italy Stock Award Sub-Plan, and a 2007 Stock Option Plan (collectively, the “Plans”).

#### *Amended and Restated 2004 Equity Incentive Plan*

Certain of the Company’s employees and directors participate in the Amended and Restated 2004 Equity Incentive Plan and Italy Stock Award Plan. These plans were initially adopted on September 30, 2004 and amended on April 27, 2007. The plans provide for the issue of incentives awards for up to 1,500,000 ordinary shares to employees, consultants, directors, and non-employee directors. Awards may be in the form of either incentive or non-qualified options. Our compensation committee determines the price of share options granted under the incentive plan, with the provision 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. The term of share options granted under the incentive plan generally may not exceed ten years, although the shareholders’ authorization for a capital increase relating to the ordinary shares issuable upon exercise of such options expires on September 30, 2019. As of December 31, 2011, there were 1,135,067 shares underlying outstanding options and 352,100 shares available for future grants under this plan.

Options granted under the incentive plan vest at the rate determined by our compensation committee. Typically, options granted under the incentive plan to officers and employees 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.

#### *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 lower than the average of the closing price of our ordinary shares as listed on the American Stock Exchange or the Nasdaq Global Market System, as applicable, over the 30 days preceding the date of grant.

#### *Amended 2007 Stock Option Plan*

On April 27, 2007, the Company's shareholders approved the 2007 Stock Option Plan providing for options that may be granted to the Company's directors, employees and consultants to purchase up to 3,200,000 ordinary shares. As of December 31, 2011, there were 1,063,008 shares underlying outstanding options and 2,136,992 shares available for future grants under this plan. Shares subject to options that have expired or otherwise terminated without being exercised in full become available again for issuance under the plan.

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 the options. The board of directors has delegated responsibility for administration of the 2007 Stock Option Plan to the compensation committee.

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

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

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 under applicable laws, rules and regulations. The 2007 Stock Option Plan will terminate on March 26, 2022 unless earlier terminated by the board of directors or a committee appointed by the board of directors.

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The following table lists the balances available under the Plans at December 31, 2011.

|   | Amended and<br>Restated 2004<br>Equity Incentive<br>Plan | Amended<br>2007<br>Stock<br>Option Plan |
|---|--|---|
| Number of shares authorized   | 1,560,000  | 3,200,000                               |
| Number of option granted since inception                            | 2,628,400  | 1,386,078                               |
| Number of options exercised   | 72,833   | -                                       |
| Number of options cancelled/expired                                 | 1,360,000  | 323,070                                 |
| Number of shares available for grant and available for future grant | 352,100  | 2,136,992                               |

Stock-based compensation cost is measured at the grant date on the basis of fair value of the award ultimately expected to vest and is recognized as expenses over the service period, which is generally the vesting period. The Company recorded non-cash compensation expenses of €1,386, €1,523 and €1,666 for the years ended December 31, 2009, 2010 and 2011, respectively.

|                                | Year<br>ended<br>December<br>31,<br>2009 | Year<br>ended<br>December<br>31,<br>2010 | Year<br>ended<br>December<br>31,<br>2011 |
|--------------------------------|--|--|--|
| Cost of goods sold             | 59                                       | 66                                       | 39                                       |
| Research and development       | 267                                      | 237                                      | 157                                      |
| General and administrative     | 1,060                                    | 1,220                                    | 1,354                                    |
| Sales and Marketing            | -  | -  | 116                                      |
| Total stock based compensation | 1,386                                    | 1,523                                    | 1,666                                    |



There were no options granted to officers, employees, directors and consultants in the year ended December 31, 2009. The weighted average grant-date fair market value of options granted to officers, employees and directors in the year ended December 31, 2010, as of the date of the grants, was \$3.18. The weighted average grant-date fair market value of options granted to officers, employees and directors in the year ended December 31, 2011, as of the date of the grants, was \$5.81. The valuation of options granted was based on the following weighted average assumptions:

|                                 | Year ended<br>December 31,<br>2009 | Year ended<br>December 31,<br>2010 | Year ended<br>December 31,<br>2011 |            |   |
|---------------------------------|------------------------------------|------------------------------------|------------------------------------|------------|---|
| Risk free interest rate         | -                                  | 2.49                               | %                                  | 3.19       | % |
| Expected dividend yield         | -                                  | 0                                  | %                                  | 0          | % |
| Expected stock price volatility | -                                  | 92.59                              | %                                  | 92.82      | % |
| Expected term                   | -                                  | 5.77 years                         |                                    | 5.44 years |   |

For all stock options granted after December 31, 2009, the fair value of the award is estimated on the date of grant 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 options will be exercised prior to the end of its contractual life, the probability of termination or retirements 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 that value calculated using the Black-Scholes model.

The binomial model accounts for volatility in the price of the Company's stock, the risk-free interest rate, the estimated life of the option, the closing market price of the Company's stock and the exercise price of the stock. Some of these inputs are highly subjective assumptions which can vary over time. In order to determine the expected volatility, the Company analyzed available information, including past experience of a group of stocks in the industry having similar traits. The risk-free rate for the expected term of the option is based on the U.S. Treasury yield curve in effect at the time of grant. The Company assumed that no dividends would be paid during the expected term of the options.

All of the Company's stock options vest ratably through continued employment over the vesting period. Once vested, options become exercisable immediately. Share-based compensation expenses recognized in the statement of operations are based on awards ultimately expected to vest, reduced for estimated forfeitures. Based on historical data, the pre-vesting forfeiture percentage was estimated to be approximately zero. If pre-vesting forfeitures occur in the future, the Company will record the effect of such forfeitures as they occur.

The Company expects to incur significant non-cash compensation expenses for option grants in the future. As of December 31, 2011, compensation costs not yet recognized totaled €2,682, which are expected to be expensed over a maximum vesting period of 36 months.

A summary of the Company's stock option activity based on the exchange rate in effect at the grant date is as follows:

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|   | Shares Available for Grant | Shares     | Weighted Average Exercise Price |          |
|---|----------------------------|------------|---------------------------------|----------|
| Options outstanding at December 31, 2008  | 672,822                    | 1,797,178  | €8.96                           | \$ 12.08 |
| Granted                                   | -                          | -          | -                               | -        |
| Exercised                                 | -                          | -          | -                               | -        |
| Cancellations                             | -                          | (200,148 ) | €8.88                           | \$ 11.82 |
| Options outstanding at December 31, 2009  | 672,822                    | 1,597,030  | €8.96                           | \$ 12.12 |
| Granted                                   | (1,410,000 )               | 1,410,000  | €3.68                           | \$ 4.82  |
| Exercised                                 | -                          | -          | -                               | -        |
| Cancellations                             | 1,213,537                  | (983,389 ) | €9.89                           | \$ 12.80 |
| Options outstanding at December 31, 2010  | 476,359                    | 2,023,641  | €4.83                           | \$ 6.70  |
| Available under revised stock option plan | 2,200,000                  | -          |                                 |          |
| Granted                                   | (657,300 )                 | 657,300    | €5.81                           | \$ 8.54  |
| Exercised                                 | (12,833 )                  | (12,833 )  | €6.65                           | \$ 7.97  |
| Cancellations                             | 482,865                    | (470,033 ) | €7.57                           | \$ 9.66  |
| Options outstanding at December 31, 2011  | 2,489,092                  | 2,198,075  | €4.53                           | \$ 6.61  |

Cash received for exercised stock options amounted to nil, nil and €77 in the years ended December 31, 2009, 2010 and 2011, respectively. The intrinsic values of options exercised in 2009, 2010 and 2011 were nil, nil, and 14, respectively. The total fair values of options vested during 2009, 2010 and 2011 were \$7,607, \$3,031, and \$3,503, respectively.

The following table summarizes outstanding and exercisable options as of December 31, 2011, based on the exchange rate in effect on December 31, 2011:

| Exercise Price   | Options Outstanding |  |                                 | Options Exercisable |                                 |
|------------------|---------------------|--|---------------------------------|---------------------|---------------------------------|
|                  | Number Outstanding  | Weighted-Average Years Remaining on Contractual Life | Weighted Average Exercise Price | Number Exercisable  | Weighted Average Exercise Price |
| €3.53 (\$4.57)   | 495,767             | 7.35   | €3.53 (\$4.57)                  | 206,036             | €3.53 (\$4.57)                  |
| €3.86 (\$5.00)   | 705,900             | 8.33   | €3.86 (\$5.00)                  | 402,631             | €3.86 (\$5.00)                  |
| €4.24 (\$5.49)   | 75,000              | 8.92   | €4.24 (\$5.49)                  | 8,333               | €4.24 (\$5.49)                  |
| €4.64 (\$6.00)   | 30,000              | 9.87   | €4.64 (\$6.00)                  | -                   | €4.64 (\$6.00)                  |
| €4.68 (\$6.06)   | 123,000             | 9.86   | €4.68 (\$6.06)                  | -                   | €4.68 (\$6.06)                  |
| €5.47 (\$7.08)   | 15,000              | 3.82   | €5.47 (\$7.08)                  | 15,000              | €5.47 (\$7.08)                  |
| €6.84 (\$8.85)   | 68,000              | 9.57   | €6.84 (\$8.85)                  | -                   | €6.84 (\$8.85)                  |
| €6.96 (\$9.00)   | 212,000             | 3.51   | €6.96 (\$9.00)                  | 212,000             | €6.96 (\$9.00)                  |
| €7.16 (\$9.26)   | 315,300             | 9.17   | €7.16 (\$9.26)                  | 8,758               | €7.16 (\$9.26)                  |
| €7.66 (\$9.91)   | 60,000              | 9.35   | €7.66 (\$9.91)                  | -                   | €7.66 (\$9.91)                  |
| €10.80 (\$13.98) | 14,108              | 6.00   | €10.80 (\$13.98)                | 14,108              | €10.80 (\$13.98)                |
| €11.44 (\$14.80) | 7,500               | 5.96   | €11.44 (\$14.80)                | 7,500               | €11.44 (\$14.80)                |

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|                  |           |      |                  |         |                  |
|------------------|-----------|------|------------------|---------|------------------|
| €12.77 (\$16.52) | 52,500    | 5.85 | €12.77 (\$16.52) | 52,500  | €12.77 (\$16.52) |
| €14.65 (\$18.95) | 24,000    | 5.23 | €14.65 (\$18.95) | 24,000  | €14.65 (\$18.95) |
|                  | 2,198,075 |      |                  | 950,866 |                  |

At December 31, 2011 the aggregate intrinsic value of the outstanding options and the aggregate intrinsic value of the exercisable options was nil.

#### 14. NET LOSS PER SHARE

The computation of basic earnings per share (EPS) is based upon the weighted-average of our ordinary shares outstanding. The computation of diluted EPS is based upon the weighted-average of our ordinary shares and the dilutive potential of ordinary shares outstanding. Dilutive potential of ordinary shares outstanding refers to the impact of ordinary equivalent shares resulting from the assumed exercise of stock options and warrants (collectively “dilutive securities”) under the treasury stock method.

The computation for basic and diluted EPS was as follows (in thousands, except per share data):

|   | For the Year Ended December 31 |            |            |
|---|--------------------------------|------------|------------|
|   | 2009                           | 2010       | 2011       |
| Income (Numerator):                         |                                |            |            |
| Net income (loss) for basic and diluted EPS | €(4,525                        | ) €4,077   | €2,710     |
| Shares (Denominator):                       |                                |            |            |
| Weighted-average shares for basic EPS       | 14,956,317                     | 14,956,317 | 14,964,021 |
| Effect of dilutive securities               | -                              | -          | 376,839    |
| Weighted-average shares for diluted EPS     | 14,956,317                     | 14,956,317 | 15,340,859 |
| Basic EPS                                   | (0.30                          | ) 0.27     | 0.18       |
| Diluted EPS                                 | (0.30                          | ) 0.27     | 0.18       |

For the year ended December 31, 2009, 2010 and 2011, there were employee stock options, calculated on a weighted average basis, to purchase 1,597,030, 1,508,683 and 644,146 shares, respectively, of our common stock, with exercise prices greater than the average market prices of our common stock for these periods, which are not included in the computation of diluted EPS as their impact would have been anti-dilutive.

For the year ended December 31, 2009, 2010 and 2011, warrants were not included in the computation of diluted EPS. In 2009 and 2010 warrants were not included as their impact would have been anti-dilutive. In 2011, warrants were not included as they expired on April 28, 2011.

## 15. COMMITMENTS AND CONTINGENCIES

In April 2007, the Company entered into a five year term capital lease arrangement to finance €218 in lab equipment purchases. The borrowing is payable in equal monthly installments of €4 over a period of 60 months. The arrangement is classified as a capital lease and expires in March 2012.

In April 2007, the Company entered into a five year term capital lease arrangement to finance €110 in laboratory equipment purchases. The borrowing is payable in equal monthly installments of €2 over a period of 60 months. The arrangement is classified as a capital lease and expires in March 2012.

Future non-cancellable minimum lease payments under operating and capital leases as of December 31, 2011 are:

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|  | Operating Leases | Capital Leases |
|--|------------------|----------------|
| 2012   | € 300            | 21             |
| 2013   | 240              | -              |
| 2014   | 185              | -              |
| 2015   | 185              | -              |
| 2016   | 185              | -              |
| Thereafter                                     | 185              | -              |
| Total minimum lease payments                   | € 1,280          | 21             |
| Less: imputed interest                         |                  | -              |
| Present value of net minimum lease payment     |                  | 21             |
| Less: Current portion of capital lease payment |                  | 21             |
| Long term portion of capital lease payment     |                  | -              |

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As of December 31, 2011, we had €1,966 thousand in future payables under outstanding contracts that are not revocable. Most of these contracts are on a cost plus or actual cost basis.

## 16. RESTRUCTURING CHARGES

On October 4, 2011, as a result of a change in management, the Company incurred a one-time charge of approximately €0.43 million, consisting primarily of severance, employee termination benefits and other exit costs which were classified as research and development expenses in our consolidated statements of operations.

On March 1, 2010, the Company announced management and corporate restructuring changes resulting from a strategic decision to close down its New York office and consolidate the Company's resources and operations into its headquarters in Como, Italy. The closure of the New York office and consolidation of corporate operations resulted in a one time charge of €0.95 million. Additionally, we implemented a workforce reduction and recorded €0.15 million, as one-time employee termination benefits, outplacements costs, termination notice and legal contractual compensation due upon early resolution of the employment agreements.

## 17. INFORMATION REGARDING GEOGRAPHICAL AREA AND MAJOR CUSTOMERS

For the years ended December 31, 2011, 2010 and 2009, total product sales by geographic territory and customer were as follows (euro amounts in thousands):

|           | Year ended<br>December 31,<br>2009 |      | Year ended<br>December 31,<br>2010 |      | Year ended<br>December 31,<br>2011 |      |
|-----------|------------------------------------|------|------------------------------------|------|------------------------------------|------|
| UK        | 4,439                              | 46 % | 10,745                             | 55 % | 12,155                             | 56 % |
| Korea     | 2,694                              | 28 % | 4,521                              | 23 % | 3,402                              | 16 % |
| US        | 465                                | 5 %  | 2,417                              | 12 % | 2,622                              | 12 % |
| Spain     | 738                                | 8 %  | 949                                | 5 %  | 1,137                              | 5 %  |
| Turkey    | -                                  | -    | -                                  | -    | 917                                | 4 %  |
| Australia | -                                  | -    | -                                  | -    | 840                                | 4 %  |
| Italy     | 1,366                              | 13 % | 1,083                              | 5 %  | 599                                | 3 %  |
| Israel    | -                                  | -    | -                                  | -    | 62                                 | 0 %  |
| Total     | 9,702                              | 100% | 19,715                             | 100% | 21,734                             | 100% |

Year ended

Year ended

Year ended

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|                 | December 31,<br>2009 |      | December 31,<br>2010 |      | December 31,<br>2011 |      |
|-----------------|----------------------|------|----------------------|------|----------------------|------|
| Customer "a"    | 1,137                | 12 % | 1,083                | 5 %  | 599                  | 3 %  |
| Customer "b"    | 2,693                | 28 % | 4,501                | 23 % | 3,112                | 14 % |
| Customer "c"    | 35                   | -    | -                    | -    | -                    | -    |
| Customer "d"    | 738                  | 8 %  | 949                  | 5 %  | 1,137                | 5 %  |
| Customer "e"    | 4,439                | 45 % | 10,745               | 55 % | 12,099               | 56 % |
| Customer "f"    | 465                  | 5 %  | 2,417                | 12 % | 2,622                | 12 % |
| Customer "g"    | 195                  | 2 %  | -                    | -    | -                    | -    |
| Customer "h"    | -                    | -    | 20                   | 0 %  | 289                  | 2 %  |
| Other Customers | -                    | -    | -                    | -    | 1,876                | 8 %  |
| Total           | 9,702                | 100% | 19,715               | 100% | 21,734               | 100% |

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**SIGNATURES**

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

GENTIUM S.P.A.  
*(Registrant)*

By: /s/ Khalid Islam  
Dr. Khalid Islam  
Chief Executive Officer

Date: March 30, 2012

## INDEX OF EXHIBITS

### 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.

2.8.2 Form of Ordinary Share Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.

## Exhibit Description

### Investor Rights and Registration Rights Agreements

- 2.9.1 Form of Investors' Rights Agreement between Gentium S.p.A. and holders of the Series A senior convertible promissory notes and warrants dated October 15, 2004, incorporated by reference to Exhibit 4.2.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 2.9.2 Amendment No. 1 to Gentium S.p.A. Series A Senior Convertible Promissory Notes, Warrants, Subscription Agreements and Investor Rights Agreements among Gentium S.p.A. and the other parties thereto dated May 27, 2005, incorporated by reference to Exhibit 4.2.6 to Amendment No. 4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 31, 2005.
- 2.10 Investors' Rights Agreement by and among Gentium S.p.A., Alexandra Global Master Fund Ltd. and Generation Capital Associates made as of January 10, 2005, incorporated by reference to Exhibit 4.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 2.11 Investors' Rights Agreement by and among Gentium S.p.A. and Sigma-Tau Finanziaria S.p.A. made as of April 4, 2005, incorporated by reference to Exhibit 4.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on April 7, 2005.
- 2.12 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of October 14, 2005, incorporated by reference to Exhibit 4.8.3 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
- 2.13 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of June 6, 2006, incorporated by reference to Exhibit 4.9.4 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 2.14 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of February 9, 2007, incorporated by reference to Exhibit 4.10.3 to the Registration Statement on Form F-3, Registration No. 333-141198, previously filed with the SEC on March 9, 2007.

### Equity Incentive and Stock Option Plans

- 4.1.1 Amended and Restated 2004 Equity Incentive Plan, incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-8, Registration No. 333-137534, previously filed with the SEC on September 22, 2006.
- 4.1.2 Amendment No. 1 to Amended and Restated 2004 Equity Incentive Plan, made as of March 26, 2007, incorporated by reference to Exhibit 4.1.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.2.1 Amended and Restated Nonstatutory Share Option Plan and Agreement dated March 23, 2006, incorporated by reference to Exhibit 4.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.

- 4.2.2 Amendment No. 1 to Amended and Restated Nonstatutory Share Option Plan and Agreement, made as of March 26, 2007, incorporated by reference to Exhibit 4.2.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.3 Amended 2007 Stock Option Plan dated May 9, 2011.

## Exhibit Description

### Loan Agreements

- 4.4 Ministry for Universities, Scientific and Technological Research Loan granted to Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., by Sanpaolo Imi S.p.A., dated September 27, 2000, incorporated by reference to Exhibit 10.6 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 4.5 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A. dated June 14, 2006 incorporated by reference to Exhibit 10.7.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 4.6 Loan Agreement for €230,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
- 4.7 Loan Agreement for €500,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
- 4.8 Loan Agreement for €225,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
- 4.9 Financing Contract between Banca Intesa Mediocredito S.p.A. and Gentium S.p.A. dated April 20, 2006, incorporated by reference to Exhibit 4.36.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.10 Loan Agreement, dated June 30, 2006, between San Paolo IMI S.p.A. and Gentium S.p.A. , incorporated by reference to Exhibit 4.43 to the Annual Report on Form 20-F for the year ended December 31, 2006, previously filed with the SEC on April 30, 2007.

### Clinical Trial Agreements

- 4.11.1 Master Services Agreement, dated March 14, 2007, between MDS Pharma Services (US), Inc. and Gentium S.p.A., incorporated by reference to Exhibit 1 to the report on Form 6-K, previously filed with the SEC on March 20, 2007.
- 4.11.2 Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (prospective arm), incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.
- 4.11.3 Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (historical arm), incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.

### License and Distribution Agreements

- 4.12.1 License and Supply Agreement by and between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc. (assignee of Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.) dated December 7, 2001, incorporated by

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reference to Exhibit 10.15 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.

4.12.2 Letter Agreement, dated October 12, 2007, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 99.4 to the report on Form 6-K, previously filed with the SEC on December 12, 2007.

4.12.3\* Amendments to License and Supply Agreement and Letter Agreement, dated December 7, 2001 and October 12, 2007, respectively, effective January 7, 2010, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 2 to the Form 6-K, previously filed with the SEC on January 11, 2010.

Exhibit Description

- 4.13.1 Contract to Supply Active Ingredients between Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 4.24.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.13.2 Amendment No. 1 to Contract to Supply Active Ingredients, effective as of December 7, 2007, by and between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.).
- 4.14.1 Master Agreement, dated December 28, 2006, among Gentium S.p.A., Crinos S.p.A., SFI Stada Financial Investments Ltd. and SFS Stada Financial Services International Ltd., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
- 4.14.2 Distribution Agreement, dated December 28, 2006, between Gentium S.p.A. and Crinos S.p.A., incorporated by reference to Exhibit 6 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
- 4.15\* Technical Transfer Services Agreement, dated February 2, 2009, between Gentium S.p.A. and Patheon Italia S.p.A, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.16.1 Technical Agreement, dated February 26, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.22.1 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.16.2\* Supply and Distribution Agreement, dated March 6, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.22.2 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.17\* Master Contract Clinical Research Agreement, dated September 29, 2009, between US Oncology Clinical Development and Gentium S.p.A., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on December 8, 2009.

Management Services Agreements

- 4.18 Service Agreement between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.25.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 4.19 Service Agreement between Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.26.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.

Leases

- 4.20 Commercial Lease Contract between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. (now Vifarma S.p.A.) dated January 1, 2005, incorporated by reference to Exhibit 10.33 to Amendment No. 2 to the



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Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.

4.21 Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2012

Exhibit Description

Miscellaneous

- 4.22 Form of indemnification agreement between Gentium S.p.A. and each officer and director, incorporated by reference to Exhibit 10.34 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.

Certifications and Consents

- 12.1 Chief Executive Officer Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- 12.2 Chief Financial Officer Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
- 13.1 Chief Executive Officer Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
- 13.2 Chief Financial Officer Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
- 15(a) Consent of Reconta Ernst & Young S.p.A. dated March 30, 2012.