Gentium S.p.A.
Form 424B3
July 13, 2006

**PROSPECTUS**

**Gentium S.p.A.**

**2,409,971 American Depositary Shares**
**Representing 2,409,971 Ordinary Shares**

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The selling security holders identified in this prospectus are offering up to 2,409,971 American Depositary Shares ("ADSs"), each representing one ordinary share of our company, Gentium S.p.A. Of the ADSs offered hereby, 1,943,525 are outstanding and 466,446 may be issued upon exercise of warrants that were issued to the selling security holders listed herein. Our ADSs are listed on the Nasdaq National Market under the symbol "GENT." The lasted reported sale price for our ADSs on the Nasdaq National Market on July 10, 2006 was $14.20 per ADS.

We will not receive any proceeds from the sale of ADSs by the selling security holders. We are not offering any ADSs for sale under this prospectus. If the warrants are exercised in full, we would receive proceeds of $6,988,915.90. See "Selling Security Holders" beginning on page 23 for a list of the selling security holders. See "Plan of Distribution" beginning on page 29 for a description of how the ADSs can be sold.

**Our business and an investment in our ADSs involve significant risks. These risks are described under the caption "Risk Factors" beginning on page 5 of this prospectus.**

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

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July 13, 2006

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form F-3 that we filed with the Securities and Exchange Commission (or the SEC) using a "shelf registration" process. Under this process, the selling security holders listed in the table commencing on page 23 may, from time to time, sell the offered securities described in this prospectus in one or more offerings, up to a total of 2,409,971 ADSs.

This prospectus does not contain all of the information included in the registration statement and the exhibits thereto. This prospectus includes statements that summarize the contents of contracts and other documents that are filed as exhibits to the registration statement. These statements do not necessarily describe the full contents of such documents, and each such statement made in this prospectus or any prospectus supplement concerning any such documents filed as exhibits to the registration statement is qualified in its entirety by reference to that exhibit. You should refer to those documents for a complete description of these matters. It is important for you to read and consider all of the information contained in this prospectus and any applicable prospectus supplement before making a decision whether to invest in our ADSs. You should also read and consider the information contained in the documents that we have incorporated by reference as described below under the headings "Incorporation By Reference" and "Where You Can Find More Information" in this prospectus.

You should rely only on the information provided in this prospectus and any applicable prospectus supplement, including the information incorporated by reference. We have not authorized anyone to provide you with additional or different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. We are not offering to sell or soliciting offers to buy, and will not sell, any securities in any jurisdiction where it is unlawful. You should assume that the information contained in this prospectus or in any prospectus supplement, as well as information contained in a document that we have previously filed or in the future will file with the SEC and incorporate by reference in this prospectus or any prospectus supplement, is accurate only as of the date of this prospectus, the applicable prospectus supplement or the document containing that information, as the case may be. Our financial condition, results of operations, cash flows or business may have changed since that date.

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

## PROSPECTUS SUMMARY

This prospectus summary highlights selected information contained elsewhere in this prospectus and the documents incorporated by reference. You should read the following information together with the more detailed information regarding our company and the ADSs being sold in this offering, with information appears elsewhere in this prospectus and in selected portions of our Annual Report on Form 20-F for the year ended December 31, 2005 and other documents filed with the SEC that we have incorporated by reference into this prospectus.

### Our Business Focus

We are a biopharmaceutical company focused on the research, discovery and development of drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. In 1986, our founding company received approval to sell in Italy a drug called "defibrotide" to treat deep vein thrombosis, and, in 1993, it received approval to manufacture and sell defibrotide to both treat and prevent all vascular disease with risk of thrombosis. In 2005, we derived approximately €2.476 million of revenues, or approximately 73.7% of our product sales of €3.361 million, from sales of defibrotide for these uses in Italy to Sirton Pharmaceuticals S.p.A., a subsidiary of our largest shareholder, FinSirton S.p.A., which at June 30, 2006 owned approximately 32% of our ordinary shares. Our primary focus is on the development of defibrotide for other uses in the United States and Europe. We have not received approval by the U.S. Food and Drug Administration, or FDA, or any European regulators to sell defibrotide for these other uses. We do not expect revenues from any of our product candidates until at least 2007 and, as a result, we will require additional funding in order to obtain FDA and European regulatory approvals for our product candidates and for working capital. See "Risk Factors."

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

### Our Advanced Product Candidates

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

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

| | | |
|---|---|---|
| Defibrotide | Treat multiple myeloma | Phase I/II in Italy |

**Our Development and Commercialization Strategy**

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

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

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

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

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

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

• **Increase our marketing capacity, including the use of strategic partnerships**. We have already entered into a strategic license agreement with Sigma-Tau Pharmaceuticals, Inc. to market defibrotide to treat VOD in North America, Central America and South America upon regulatory approval and have granted Sigma-Tau Pharmaceuticals, Inc. a right of first refusal to market defibrotide to prevent VOD, to mobilize and increase the number of stem cells available for transplant and in non-intravenous forms. We intend to pursue similar agreements with Sigma-Tau Pharmaceuticals, Inc. and other strategic partners to market defibrotide in other jurisdictions and to market our other product candidates and/or develop such capacity internally.

**Manufacturing and Product Sales**

We manufacture defibrotide, calcium heparin, sulglicotide and other miscellaneous pharmaceutical products at our manufacturing facility near Como, Italy, and we lease our affiliate Sirton's facility to manufacture urokinase. Urokinase and calcium heparin are active pharmaceutical ingredients used to make other drugs. Sulglicotide is intended to be used to treat peptic ulcers. During 2002, 2003, 2004 and 2005, 100%, 100%, 92% and 97%,

respectively, of our total product sales came from sales of these products to Sirton. Our revenues from the sales of these products to date have been generated only in Italy and, in 2004, also in Korea and amounted to €5.9 million, €6.5 million, €3.1 million and €3.3 million in 2002, 2003, 2004 and 2005, respectively. In 2004 we completed an upgrade to our facilities that cost approximately €7.2 million which we believe will facilitate the FDA and European regulatory approval process for our product candidates and enable our future production. In anticipation of the renovations, we temporarily increased our production shifts and deliveries in 2003 and suspended our production for approximately seven months in 2004. Period to period comparisons of our results will therefore be difficult.

**Risk Factors**

We have generated limited revenues to date, most of which have been derived from sales to Sirton. Our general and administrative expenses have increased as we internalized certain of our administrative services which were previously provided by Sirton and FinSirton and adapted to being a public reporting company. We do not have regulatory approvals for the sale of defibrotide to treat or prevent VOD and will be required to perform further clinical trials for these and other uses. The approval process for new drugs is lengthy and expensive and if we fail to raise additional funds in the future or enter into collaborative agreements, we may be unable to continue the development of our product candidates. See "Risk Factors."

**Corporate Information and Executive Offices**

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

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

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

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

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

**Recent Developments**

Private Placement

On June 6, 2006, we issued 1,943,525 ADSs at a price per ADS of $11.39 and warrants to purchase an aggregate of 388,705 ADSs, exercisable at $14.50 per ADS in a private placement. We also issued warrants to purchase 77,741 ADSs, exercisable at $17.40 per ADS, to one of the placement agents. We entered into a registration rights agreement with the investors and placement agent under which we agreed to register the resale of the ADSs issued and the ADSs issuable upon exercise of the warrants. We agreed to file the registration statement by July 6, 2006 and to cause it to be declared effective by the earlier of September 6, 2006 (extendable to October 6, 2006 if we receive comments from the Securities and Exchange Commission) and ten trading days after we receive notice from the Securities and

Exchange Commission that it will not review the registration statement. If we fail to meet these filing and effectiveness deadlines, fail to file a pre-effective amendment and respond to comments from the Securities and Exchange Commission within twenty trading days from receipt of such comments or the registration statement ceases to be effective or the prospectus not usable for twenty consecutive trading days or an aggregate of thirty trading days in any twelve month period, then we must pay the investors liquidated damages equal to 1% of their purchase price per month, prorated for any period of less than one month and subject to a cap of 10% of the purchase price paid by each investor.

Debt Restructuring

On June 28, 2006, we entered into a Loan Contract with Banca Nazionale Del Lavoro S.p.A. pursuant to which we restructured our two outstanding loans with Banca Nazionale. The first of these outstanding loans was originally granted in November 1996 for €1.291 million and was secured by mortgage on some of our real estate. As of June 28, 2006 the outstanding principal was €67,954.95 and accrued but unpaid interest was €535.97. The second of these outstanding loans was originally granted in July 2004 for €2.0 million and was secured by a mortgage on some of our real estate, a mortgage on some of Sirton's real estate and a guarantee by FinSirton. As of June 28, 2006, the outstanding principal was €1.8 million and accrued but unpaid interest was €29,152.60.

In April 2006, as the first part of the restructuring of these loans, Banca Nazionale released Sirton from its mortgage and FinSirton from its guarantee with respect to the July 2004 loan. We deposited €550,000 into escrow with Banca Nazionale to secure repayment of the loan. FinSirton agreed to transfer certain real estate to us as well.

On June 28, 2006, the new Loan Contract we entered into with Banca Nazionale effected the following restructuring of our loans with Banca Nazionale.

- The two existing loans were extinguished;
- Banca Nazionale released our €550,000 cash escrow deposit;
- Banca Nazionale released our existing mortgages on our real estate property;
- Banca Nazionale granted us a new, increased loan for €2.8 million that bears interest at the six month Euribor rate plus 1.00%, the principal of which will be repaid in 14 instalments, every six months, starting from December 27, 2007 until final maturity in 2014 and the interest on which will be paid every six months starting from June 27, 2006; and
- We granted Banca Nazionale an expanded mortgage on certain of our land and buildings valued at €4.7 million.

## RISK FACTORS

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

### Risks Relating to Our Business

**We have generated limited revenues from commercial sales of our products to date, our revenues have declined significantly since 2003, and we do not know whether we will ever generate significant revenues or achieve profitability.**

We are focused on product development and have generated limited revenue from commercial sales of our products to date since 2003, because Sirton Pharmaceuticals S.p.A., our primary customer, has had a decrease in demand for some of the products we sell to it, as discussed below. In 2004, we had total product sales of €3.113 million and in 2005 we had total product sales of €3.361 million**.**

We do not expect our total product sales to materially increase unless we are able to sell our product candidates, and we will continue to incur significant expenses as we research, develop, test and seek regulatory approval for these product candidates. While we were profitable in 2002 and 2003, we incurred a net loss of €581 thousand in 2001, a net loss of €7.0 million in 2004 and a net loss of €12.3 million in 2005. Our general and administrative expenses have increased as we added personnel to support our operations in connection with our development of our product candidates, internalized certain administrative services that were performed for us by our largest shareholder, FinSirton, and our affiliate, Sirton, and supported our operations in connection with being a public company. As a result, we anticipate incurring substantial and increasing losses for the foreseeable future. We cannot assure you that we will ever become profitable. If we fail to achieve profitability within the time frame expected by investors or securities analysts, the market price of our ADSs may decline.

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

Substantially all of our product sales in 2001, 2002 and 2003, approximately 92% of our product sales in 2004 and approximately 97% of our product sales in 2005 have been from the sale of our active pharmaceutical ingredients and products to Sirton, which has recently experienced financial difficulties. Sirton sells its finished products to one customer, Crinos, which sells them to the retail market. Our products have seen decreased demand over the past several years due to various market factors. As a result, Sirton's demand for these products has decreased over the past several years, and may continue to decrease over the next several years until and unless both we and Sirton develop new customers. If we and Sirton are unsuccessful at developing new customers and the demand for our products continues to decrease, it could increase our need for additional capital, and our business could be adversely affected.

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

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

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

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

**At present, we do not have sole control of the distribution of defibrotide in Italy, and we may not be able to gain such control, which may adversely affect our clinical trials and our pricing of defibrotide.**

Because defibrotide is on the market in Italy, we believe it has been purchased and sold in other countries where its use is not licensed or permitted. This could impact our ability to enroll patients in our trials and the timing of such enrollments. Also, in the future, it could have a negative impact on our ability to appropriately price defibrotide for new indications, unless we can control the distribution of defibrotide in Italy. There can be no assurance of our ability to do so.

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

We intend to apply for FDA and other regulatory agency approval for our additional product candidates, including other uses of defibrotide, in the future, and these additional product candidates will require that we conduct clinical trials and undergo the regulatory approval process. The commencement and completion of these clinical trials could be delayed or prevented by a variety of factors, including:

- delays in identifying and reaching agreement on acceptable terms with institutional review boards of clinical trial providers and prospective clinical trial sites;
- delays in obtaining FDA or other regulatory agency clearance to commence a clinical trial;
- delays in the enrollment of patients;
- lack of effectiveness of the product candidate during clinical trials; or
- adverse events or safety issues.

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

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

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

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

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

Furthermore, the committee of clinical investigators who sponsored a Phase II/III clinical trial of defibrotide to treat VOD in Europe that was conducted by Consorzio Mario Negri Sud cancelled the trial in October 2005 due to a lack of enrollees. In addition, the National Institute of Tumors in Milan cancelled a Phase I clinical trial of defibrotide to increase the number of stem cells available for transplant in December 2005 due to a lack of eligible enrollees. We are co-sponsoring with the European Group for Blood and Marrow Transplantation a Phase II/III clinical trial in Europe of defibrotide to prevent VOD in children, and a Phase II/III clinical trial in Europe of defibrotide to prevent VOD and transplant associated microangiopathy in adults. The participants in both of these trials randomly receive either defibrotide or no treatment. We may have difficulty enrolling participants in these trials as patients may be reluctant to take the risk of not receiving treatment with defibrotide. Further, because defibrotide is available on the market in Italy, we believe it has been purchased and sold in other countries where its use is not licensed. This could impact our ability to enroll patients in our trials and the timing of such enrollments. Our other clinical trials may also be discontinued if we or the sponsors are not successful in enrolling participants.

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

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

- restrictions on such products or manufacturing processes;
- withdrawal of the products from the market;
- voluntary or mandatory recalls;
- fines;
- suspension of regulatory approvals;

- product seizures; or
- injunctions or the imposition of civil or criminal penalties.

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

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

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

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

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

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

We do not have the personnel capacity to conduct or manage all of the clinical trials that we intend for our product candidates. We rely on third parties to assist us in managing, monitoring and conducting most of our clinical trials. We expect to enter into clinical trial agreements with numerous centers in the United States and Canada regarding our Phase III clinical trial of defibrotide to treat VOD with multiple-organ failure. We have entered into co-sponsoring agreements with the European Group for Blood and Marrow Transplantation, regarding a Phase II/III clinical trial of defibrotide to prevent VOD in children in Europe and a Phase II/III clinical trial of defibrotide to prevent VOD and transplant associated microangiopathy in adults in Europe. We have entered into an agreement with Bradstreet Clinical Research & Associates, Inc. to perform clinical research project management services in connection with clinical trials conducted in the United States and agreements with KKS-UKT, GmbH and MDS Pharma Services Italy SpA to provide such services for our clinical trials in Europe. If these third parties fail to comply with applicable

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

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

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

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

- the successful and continued development of our existing product candidates in preclinical and clinical testing;
- the costs associated with protecting and expanding our patent and other intellectual property rights;
- future payments, if any, received or made under existing or possible future collaborative arrangements;
- the timing of regulatory approvals needed to market our product candidates; and
- market acceptance of our products.

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

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

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

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

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

ability to successfully commercialize our product candidates or otherwise manage our business effectively could be seriously harmed. Dr. Ferro's employment agreement with us is for a period of three years with a two year renewal option and prohibits her from competing with us during the term of her employment and for a period of one year after the termination of her employment. Dr. Ferro's employment agreement provides that she is not obligated to spend more than 75% of her time working for our company

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

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

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

Prior to our initial public offering in June 2005, we were a relatively small, family run Italian business. We had not been required to close our accounting records on a monthly or even quarterly basis. A very small accounting team handled the accounts for not only us, but also our then-parent, FinSirton S.p.A., and sister companies, Sirton and Foltene Pharmaceuticals S.p.A., all of which are also private companies. Therefore, the internal control structure was not adequate for a company publicly listed and reporting in the United States. Also, the financial reporting environment in Italy for private companies is significantly different than for public companies in the United States.

As an Italian company publicly listed in the United States, we are required by Italian law to keep our books according to the local statutory accounting methods, but we also prepare U.S. GAAP based financial statements for our Securities Act registration statements and Exchange Act reports. The preparation of our U.S. GAAP based financial statements is a manual process which involves the transformation of our Italian statutory financial statements into U.S. GAAP through a significant number of complex accounting adjustments and processes. This process also requires an ongoing review and update of the applicable U.S. GAAP that should be applied to the underlying Italian financial statements. This process is complicated and time-consuming and requires significant attention and time of our senior accounting personnel. Moreover, U.S. GAAP accounting adjustments tend to result in large differences between our Italian statutory and U.S. GAAP based financial statements.

When we started the process of preparing for our initial public offering, one of the first needs we identified to solve these issues was that of a full time, dedicated finance professional with knowledge of both U.S. and Italian accounting principles. We believe we satisfied that need by hiring Mr. Salvatore Calabrese, our Vice-President, Finance, in February of 2005. However, our independent registered public accounting firm informed us during the course of auditing our 2005 financial statements that our financial statement close process and the transformation of our Italian statutory financial statements into U.S. GAAP still did not reduce to an acceptably low level the risk that errors in amounts that would be material in relation to those financial statements may occur and may not be detected within a timely period by management in the normal course of business at December 31, 2005. Our independent registered public accounting firm considered these deficiencies in determining the nature, timing and extent of their procedures in their audit of our 2005 financial statements, and those deficiencies did not affect their report on our 2005 financial statements. The following highlights the issues identified and the steps that we are taking to remedy these items. We believe that all material weakness issues will be resolved during 2006.

· *Issue:* For the first six months of 2005, we still relied on FinSirton for most of the data processing related to our significant processes, such as inventory costing, payroll and general ledger. We also had limited control over FinSirton's information technology system related to the input or output of data. Additionally, we had no direct control over the security of data and access controls related to the control environment.

*Remedy:* During the second six months of 2005, we established our own six (6) person accounting, controlling and reporting department, separate from FinSirton, which includes not only Mr. Calabrese but also Roberta Grandini as our controller. Ms. Grandini is experienced in U.S. GAAP and was previously the controller for the Italian subsidiary of a U.S. public biotechnology company. In addition, we purchased and have installed our own information

technology system which will allow us to have full control, including information security control, over our data processing, including our underlying books and records. At June 30, 2006, this transition from FinSirton's accounting department and information technology system to our accounting department and information technology system had been completed.

· *Issue:* Our process for budgeting, awarding, tracking and verifying research and development contracts and costs has historically been handled outside of the general accounting system. We have not had controls surrounding this process to closely monitor such areas as actual costs versus budgeted costs, actual costs billed versus the contractual amounts and the timing of when those costs have been incurred.

*Remedy:* As mentioned above, during the second half of 2005, we established and expanded our own independent accounting department. In addition to Mr. Calabrese and Ms. Grandini, this department includes a contract administrator who now has primary responsibility for controlling the research and development contracts and costs. We also established internal procedures for purchases, cash disbursements, limits of authorization and segregation of duties. These procedures include requirements that all research and development expenditures be accompanied by a budget estimate, and any deviations be adequately explained. Additionally, the procedures require that expenses over €2,500 not previously budgeted must be approved by the internal control department, Mr. Calabrese and by our medical director before any purchase requests or contracts may be signed. Furthermore, on a quarterly basis, we perform an analysis of actual expenses versus budgeted expenses, and such analysis is presented and discussed with our management, our Audit Committee and the Board of Directors as a whole.

· *Issue*: Our overall control environment continued to have difficulties in 2005 in closing our accounting records on a timely basis, given (i) the lack of personnel dedicated to performing such services for us, separate from our affiliated companies, (ii) our reliance upon FinSirton's information technology system and (iii) the need for us to prepare Italian statutory financial statements and then manually convert those statements into U.S. GAAP financial statements.

*Remedy:* We believe that our establishment of and expansion of our own, independent accounting department, including Mr. Calabrese and Ms. Grandini, and the acquisition of our own independent information technology system, will solve points (i) and (ii) above. In addition, although we will continue to need to prepare both Italian statutory financial statements and U.S. GAAP based financial statements, we believe that the expansion of our accounting department will help us close our records more quickly and that the establishment of our new information technology system will reduce the overall complexity of the process and the risk of errors.

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

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

Since 2003, our revenues have fluctuated significantly due to the need to temporarily cease operations at our manufacturing facility for an upgrade to the facility for seven months in 2004 and increase production at the facility in 2003 to stockpile inventory in anticipation of this cessation. Our revenues have also fluctuated due to changes in the amounts of each of our products that we sell in different periods. Due to the fact that we do not sell directly to the end-user, the timing of manufacturer orders can cause variability in sales. In 2005, we experienced higher sales volume in the second and in the fourth quarters; however we cannot predict if such fluctuation will happened in future years. Until we have successfully developed and commercialized a product candidate, we expect that substantially all of our revenues will result from the sale of our existing products. We expect that our operating results will vary significantly from quarter to quarter and year to year as a result of the timing and extent of:

· our research and development efforts;

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

- the execution or termination of collaborative arrangements;
- the receipt of grants;
- the initiation, success or failure of clinical trials; and
- the manufacture of our product candidates, or other development related factors.

Some of Series A senior convertible promissory notes we issued in the fourth quarter of 2004 and the first quarter of 2005 were converted into our ordinary shares upon the closing of our initial public offering in June 2005 and the remainder were repaid in June and July 2005. Our results of operations in 2004 and 2005 reflect the interest expense we incurred on those notes. That interest expense included the amortization of the debt issue costs and of the original issue discount resulting from the inclusion of the warrants with the notes and the amortization of the value of the beneficial conversion feature resulting from the effective conversion price since the conversion ratio, which is equal to the principal amount of the notes divided by $8.10 (ninety percent (90%) of the initial offering price per ADS in our initial public offering), was less than the fair value of our ordinary shares at the time of issuance of the notes, which was $10.00. During 2004 and 2005, we incurred €1.828 million and €4.095 million, respectively, of interest expense on these notes (including amortization of original issue discount and debt issue costs). As a result, our interest expense, pre-tax income (loss) and net income (loss) for those periods was less than it would have been otherwise.

Accordingly, our revenues and results of operations for any period may not be comparable to the revenues or results of operations for any other period.

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

We conduct most of our manufacturing operations in one facility located in Villa Guardia, near Como, Italy. This facility could be damaged by fire, floods, earthquake, power loss, telecommunication and information system failures, terrorism or similar events. Our insurance covers losses to our facility, including the buildings, machinery, electronic equipment and goods, for approximately €15 million, but does not insure against all of the losses listed above, including terrorism and some types of flooding. Although we believe that our insurance coverage is adequate for our current and proposed operations, there can be no guarantee that it will adequately compensate us for any losses that may occur. We are not insured for business interruption and we have no replacement manufacturing facility readily available.

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

Our largest shareholder is FinSirton, which owned approximately 32% of our ordinary shares at June 30, 2006. Dr. Ferro, who is our Chief Executive Officer and President and one of our directors, together with members of her family, controls FinSirton. FinSirton provides some of our office space, and corporate, payroll and information technology services. Sirton, which is a wholly owned subsidiary of FinSirton, has been and currently is our principal customer. Sirton also provides us with a number of business services such as, quality control and infrastructure services, and leases us office and manufacturing space.

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

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

Our industry is highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. While we are unaware of any other products or product candidates that treat or prevent VOD or the apoptosis that our product candidate oligotide is designed to treat, we

believe that other companies have products or are currently developing products to treat some of the same disorders and diseases that our other product candidates are designed to treat. These companies include AnorMED Inc., AstraZeneca International, British Biotech plc, Abbott Laboratories, The Bayer Group, GlaxoSmithKline plc, Bristol-Myers Squibb Company, Eli Lilly Company, Boehringer Ingelheim, Axcan Pharma Inc., The Proctor & Gamble Company, Solvay Pharmaceuticals, Inc., Millenium Pharmaceuticals, Inc., ARIAD Pharmaceuticals, Inc., Celgene Corp., Titan Pharmaceuticals, Inc., Cell Genesys, Inc., Human Genome Sciences, Inc., Chugai Pharmaceutical Co., Ltd., The National Cancer Institute, Seattle Genetics, Inc., EntreMed, Inc., NeoRxx Corporation, Xcyte Therapies, Inc., Amgen, Inc., CuraGen Corporation, Aesgen, Inc. and Endo Pharmaceutical Holdings Inc.

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

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

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

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

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

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

Because of the extensive time required for the development, testing and regulatory review of a product candidate, it is possible that before any of our product candidates can be approved for sale and commercialized, our relevant patent rights may expire or remain in force for only a short period following commercialization. Our issued United States patents expire between 2008 and 2019, and our United States patents for which we have submitted applications will expire between 2008 and 2026. Our United States patent covering defibrotide expires in 2010, and our U.S. patent covering the chemical process for extracting defibrotide expires in 2008. Our European patent covering both defibrotide and the chemical process for extracting defibrotide expires in 2007. There may be no opportunities to extend these patents and thereby extend FDA approval exclusivity, in which case we could face increased competition for our products that are derived from defibrotide. Patent expiration could adversely affect our ability to protect future

product development and, consequently, our operating results and financial position.

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

**Risks Related to Ownership of the ADSs**

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

Our largest shareholder, FinSirton, owned approximately 32% of our outstanding ordinary shares at June 30, 2006. Dr. Laura Ferro, who is our Chief Executive Officer and President and one of our directors, together with members of her family, controls FinSirton. As a result, Dr. Ferro and her family, through FinSirton, will substantially control the outcome of all matters requiring approval by our security holders, including the election of directors and the approval of mergers or other important corporate events. They may exercise this ability in a manner that advances their best interests and not necessarily yours. In particular, Dr. Ferro may use her control over FinSirton's shareholdings in our company to resist any attempts to replace her or other members of our board of directors or management or approve or reject mergers and other important corporate events. Also, the concentration of our beneficial ownership may have the effect of delaying, deterring or preventing a change in our control, or may discourage bids for the ADSs or our ordinary shares at a premium over the market price of the ADSs. The significant concentration of share ownership may adversely affect the trading price of the ADSs due to investors' perception that conflicts of interest may exist or arise.

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

Some of our executive officers and directors and our current largest shareholder, FinSirton, agreed with the underwriters of our initial public offering to a lock-up of an aggregate of 3,750,000 outstanding ordinary shares and 822,000 ordinary shares issuable upon exercise of certain options for a period of 18 months after the effective date of the registration statement relating to our initial public offering of securities, provided, however, that if the average price per ADS equals or exceeds 200% of the initial public offering price of the ADSs in our initial public offering for a minimum of twenty continuous trading days, the ordinary shares may be released from the lock-up at the request of the holder, which could result in the release from the lock-up restrictions of the 3,750,000 outstanding shares held by FinSirton and the 822,000 ordinary shares issuable upon exercise of the options. Sales of a substantial number of ADSs representing these ordinary shares in the public market could depress the market price of the ADSs and impair our ability to raise capital through the sale of additional equity securities. The underwriters, in their sole discretion and at any time without notice, may release all or any portion of the ordinary shares held by our officers, directors, and FinSirton subject to these lockup agreements. Our other 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. The registration of which this prospectus forms a part registers the resale of 1,943,525 outstanding ordinary shares and 466,446 ordinary shares and ADSs issuable upon the exercise of warrants by certain selling security holders. We have filed a registration statement registering the resale of some of our other outstanding restricted ADSs and most ADSs issuable upon exercise of outstanding warrants. Such registration and ultimate sale of the securities in the markets may adversely affect the market for the ADSs.

**Risks Relating to Being an Italian Corporation**

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

We were incorporated under the laws of the Republic of Italy. The principal laws and regulations that apply to our operations, those of Italy and the European Union, are different from those of the United States. In order to issue new equity or debt securities convertible into equity, with some exceptions, we must increase our authorized capital.

There are two ways for us to increase our authorized capital. The first way is to obtain shareholder approval. In order to do so, our board must meet and resolve to recommend to our shareholders that they approve an amendment to our bylaws to increase our capital. Our security holders must then approve that amendment to our bylaws in a formal meeting duly called, with the favorable vote of the required majority, which may change depending on whether the meeting is held on a first or subsequent call.

The second way is that our shareholders can authorize the board of directors to increase our capital, but the board may exercise such power for only five years. At the end of those five years, the authorized capital expires, and our board and shareholders would need to meet again to authorize a new capital increase. Our security holders authorized our board of directors to increase our capital by up to €90 million of par value for ordinary shares and €10 million for ordinary shares issuable upon conversion of convertible bonds on April 28, 2006, which our board can exercise until April 28, 2011.

In either case, these meetings take time to call. In addition, a notary public must verify the compliance of the capital increase with our bylaws and applicable Italian law. Further, under Italian law, our existing shareholders and any holders of convertible securities have preemptive rights to acquire any such shares on the same terms as are approved concurrent with the new increase of the authorized capital pro rata based on their percentage interests in our company. The shareholders or board of directors can "exclude" or limit the pre-emptive right, but only for certain specific reasons.

Italian law also provides that if the shareholders vote to increase our capital or authorize our board of directors to increase our capital, dissenting, abstaining or absent security holders representing more than 5% of the outstanding shares of our company may, for a period of 90 days following the filing of the shareholders' resolutions with the Registry of Companies, challenge such capital increase if the increase was not in compliance with Italian law. If our board of directors resolves to increase our capital, our board of statutory auditors, any member of our board of directors and any shareholder who was prejudiced may challenge that resolution for a period of 90 days following the adoption of the resolution. Finally, if a shareholders' or board of directors' meeting authorizing a capital increase was not properly called and held, any interested person may challenge the capital increase for a period of three years following the filing of the security holders' approval with the Registry of Companies or 180 days following the filing of the board resolution with the Registry of Companies.

Once our security holders authorize a capital increase, we must issue all of those authorized shares before the security holders may authorize a new capital increase, unless the security holders vote to cancel the previously authorized shares. These restrictions could limit our ability to issue new equity or convertible debt securities on a timely basis.

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

Italian law provides that we may not issue debt securities for an amount exceeding twice the amount of the sum of the aggregate par value of our ordinary shares (which we call our capital), our legal reserve and any other disposable reserves appearing on our latest Italian GAAP balance sheet approved by our security holders. 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 Italian GAAP capital. One of the other reserves that we maintain on our balance sheet is a "share premium reserve", meaning amounts paid for our ordinary shares in excess of the capital. At December 31, 2005, the sum of our capital, legal reserves and other reserves on our Italian GAAP balance sheet was €29.6 million. If we issue debt securities in the future, until such debt securities are repaid in full, we may not voluntarily reduce our capital or our reserves (such as by declaring dividends) if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt. If our equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of our equity, some legal scholars are of the opinion that the ratio must be restored by a recapitalization of our company. If our equity is reduced, we could recapitalize by issuing new shares or having our security holders 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 security holders would be willing to contribute additional capital.

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

Italian law requires us to reduce our security holders' equity and, in particular, our capital (aggregate par value of our ordinary shares) to reflect on-going losses. We are also required to maintain a minimum capital of €120 thousand. At December 31, 2005, our Italian GAAP capital was approximately €9.611 million. If we suffer losses from operations that would reduce our capital to less than €120 thousand, then either we must increase our capital (which we could do by issuing new shares or having our security holders contribute additional capital to our company) or convert the form of our company into an S.r.l., which has a lower capital requirement of €10 thousand. If we did not take these steps, a court could liquidate our company.

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

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

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

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

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

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

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

We are incorporated under the laws of the Republic of Italy. As a result, the rights and obligations of our security holders are governed by Italian law and our bylaws, and are in some ways different from those that apply to U.S. corporations. Some of these differences may result in the depositary (on your behalf) having fewer rights as a shareholder than you would if you were a shareholder of a U.S. corporation. We have presented a detailed comparison of the Italian laws applicable to our company against Delaware law in "*Item 10, Additional Information, Comparison of Italian and Delaware Corporate Laws"* of our annual report on Form 20-F for the year ended December 31, 2005, which is incorporated herein by reference. We compared the Italian laws applicable to our company against Delaware law because Delaware is the most common state of incorporation for U.S. public companies.

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

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

## FORWARD-LOOKING STATEMENTS

This prospectus may contain forward-looking statements that involve substantial risks and uncertainties regarding future events or our future performance. When used in this prospectus, the words “anticipate,” “believe,” “estimate,” “may,” “intent,” “continue,” “will,” “plan,” “intend,” and “expect” and similar expressions 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 prospectus or incorporated by reference, provide examples of risks, uncertainties and events that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. Before you invest in our ordinary shares or ADSs, you should be aware that the occurrence of the events described in the “Risk Factors” section and elsewhere in this prospectus could have a material adverse effect on our business, performance, operating results and financial condition. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements set forth in this prospectus. Except as required by federal securities laws, we are under no obligation to update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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

## PRESENTATION OF FINANCIAL INFORMATION

Our financial statements are all expressed in euros. Assets and liabilities denominated in United States dollars or other foreign currencies have been converted into euros at the Noon Buying Rate in New York City as certified by the Federal Reserve Bank of New York on the date of the applicable financial statement. Transactions that were conducted in United States dollars or other foreign currencies have been converted into euros at the Noon Buying Rate in New York City as certified by the Federal Reserve Bank of New York on the date of such transactions. On June 30, 2006, the Noon Buying Rate was euro 1.00 to U.S.$1.2779.

Our fiscal year ends on December 31 of each year. Where this prospectus refers to a particular year, this means the fiscal year unless otherwise indicated.

## INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference documents we file with the SEC, which means that we can disclose information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and certain later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents:

(i) our Annual Report on Form 20-F for the fiscal year ended December 31, 2005, filed with the SEC on May 30, 2006; and

(ii) all of our Reports on Form 6-K furnished to the SEC between the date of filing of our Annual Report on Form 20-F with the SEC and the date of this prospectus.

All annual reports we file with the SEC pursuant to the Exchange Act on Form 20-F after the date of this prospectus and prior to the termination of the offering shall be deemed to be incorporated by reference into this prospectus and to be part hereof from the date of filing of such documents. We may incorporate by reference any Form 6-K subsequently submitted to the SEC by identifying in such Form that it is being incorporated by reference into this prospectus. Any statement made in this prospectus, a prospectus supplement or a document incorporated by reference in this prospectus or a prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus and any applicable prospectus supplement to the extent that a statement contained in an amendment to the registration statement, any subsequent prospectus supplement or in any other subsequently filed document incorporated by reference herein or therein adds, updates or changes that statement. Any statement so affected will not be deemed, except as so affected, to constitute a part of this prospectus or any applicable prospectus supplement.

We shall undertake to provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus has been delivered, upon the written or oral request of any such person to us, a copy of any or all of the information referred to above that have been or may be incorporated into this prospectus by reference, including exhibits that are specifically incorporated by reference to such information. Requests for such copies should be directed to Gentium S.p.A., Piazza XX Settembre 2, Villa Guardia (Como), Italy, Attention: Salvatore Calabrese, Vice-President Finance, telephone +39-031-385-287.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. This prospectus is an offer to sell or to buy only the securities referred to in this prospectus, and only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or any prospectus supplement is current only as of the date on the front page of those documents. Also, you should not assume that there has been no change in our affairs since the date of this prospectus or any applicable prospectus supplement,

## WHERE YOU CAN FIND MORE INFORMATION

We file and submit reports, including annual reports on Form 20-F, and other information with the Securities and Exchange Commission pursuant to the rules and regulations of the SEC that apply to foreign private issuers. You may read and copy any materials filed with the SEC at its Public Reference Room at 100 F Street N.E., Washington, D.C. 20459. You may obtain information on the operation of the Public Reference Room by calling the SEC at l-800-SEC-0330. The registration statement of which this prospectus is a part, and other public filings with the SEC, are also available on the website maintained by the SEC at http://www.sec.gov. Our website is located at www.gentium.it. The information contained on our website is not part of this prospectus.

## SERVICE OF PROCESS AND ENFORCEMENT OF JUDGMENTS

We are a *società per azioni* (stock company) organized under the laws of the Republic of Italy. Substantially all of our directors, executive officers, and certain experts named herein, reside in the Republic of Italy. All or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or such persons or to enforce judgments obtained in the United States courts predicated upon the civil liability provisions of the Federal securities laws of the United States against us or such persons in United States courts. We have been advised that (a) enforceability in Italy, in actions for enforcement of final judgments of United States courts, of civil liabilities predicated upon the Federal securities laws of the United States is subject, among other things, to the Italian courts' determination that certain jurisdictional and procedural standards were satisfied in the U.S. proceeding, that the U.S. decision is not contrary to an existing Italian decision, that the matter is not the subject of a concurrent proceeding in Italy, and that enforcement would not violate Italian public policy; and (b) in original actions in Italy to enforce such liabilities, an Italian court would examine the merits of the claim in accordance with Italian substantive law and procedure and not necessarily apply United States substantive law. We have expressly submitted to the nonexclusive jurisdiction of New York State and United States federal courts sitting in The City of New York for the purpose of any suit, action or proceeding arising out of the this public offering. We have appointed CT Corporation System, 111 Eighth Avenue, 13th Floor, New York, New York 10011, as our agent upon whom process may be served in any action.

## DETERMINATION OF OFFERING PRICE

The selling security holders may offer and sell their ADSs on the Nasdaq National Market System at prevailing market prices. The selling security holders may also offer and sell their ADSs in privately negotiated transactions at prices other than the market price.

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## CAPITALIZATION AND INDEBTEDNESS

The following table summarizes our capitalization and indebtedness as of March 31, 2006 on an actual basis and on a pro forma basis to reflect our issuance, receipt and use of the net proceeds of the following securities issued after March 31, 2006:

- 18,334 ordinary shares issued in April 2006 upon exercise of a warrant issued in connection with our Series A senior convertible promissory notes at a price per share of $9.52, for proceeds of $174,540;
- 93,524 ordinary shares issued in April 2006 upon the exercise of warrants issued in connection with our October 2005 private placement at a price per share of $9.69, for aggregate proceeds of $906,248; and
- 1,943,525 ADSs issued in June 2006 in a private placement at a price per share of $11.39 for net proceeds of $20,438,892 after deducting placement fees of $1,322,598 and estimated offering expenses of $375,260.

You should read the following table in conjunction with our financial statements and related notes from our annual report on Form 20-F and other reports on Form 6-K incorporated by reference into this prospectus.

| | | **As of March 31, 2006 Actual** *(unaudited)* | | **Pro Forma For Issuances after March 31, 2006** *(unaudited)* |
|---|---|---|---|---|
| **Indebtedness:** | | | | |
| Mortgage loans secured by real property | € | 1,936 | € | 1,936 |
| Loans secured by equipment | | 646 | | 646 |
| Other | | 418 | | 418 |
| | | 3,000 | | 3,000 |
| Less current maturities | | 797 | | 797 |
| | | 2,203 | | 2,203 |
| **Security holders' equity:** | | | | |
| Ordinary shares, par value €1.00 per share, 12,690,321 shares authorized, actual; 15,100,299 shares authorized, pro forma; 9,610,630 shares issued and outstanding, actual; 11,666,013 shares issued and outstanding, pro forma | | 9,611 | | 11,666 |
| Additional paid-in capital | | 33,306 | | 49,070 |
| Accumulated deficit | | (28,332) | | (28,332) |
| Total Security holders' Equity | | 14,585 | | 32,404 |
| Total Capitalization | € | 16,788 | € | 34,607 |

## PRICE HISTORY

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

Trading in our ADSs on the Nasdaq National 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, for each of the periods indicated, the high and low closing prices per ADS as reported by the American Stock Exchange and Nasdaq, as applicable.

| | Price Range of ADSs | |
|---|---|---|
| | **High** | **Low** |
| **2005** | | |
| Second Quarter (beginning June 16, 2005) | $ 9.10 | $ 8.77 |
| Third Quarter | $ 8.99 | $ 6.92 |
| Fourth Quarter | $ 8.68 | $ 7.05 |
| **2006** | | |
| First Quarter | $ 13.25 | $ 7.85 |
| Second Quarter | $ 19.76 | $ 12.17 |
| **Month Ended** | | |
| January 31, 2006 | $ 9.55 | $ 7.85 |
| February 28, 2006 | $ 10.05 | $ 9.20 |
| March 31, 2006 | $ 13.25 | $ 9.78 |
| April 30, 2006 | $ 19.76 | $ 13.01 |
| May 31, 2006 | $ 17.45 | $ 11.48 |
| June 30, 2006 | $ 15.00 | $ 12.60 |
| July 31, 2006 (through July 12, 2006) | $ 14.33 | $ 13.85 |

The closing price of the ADSs on Nasdaq on July 12, 2006 was $14.24.

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Sources: American Stock Exchange and the Nasdaq Stock Market.

## SHARE CAPITAL

### Authorized Shares

At March 31, 2006, our authorized ordinary shares consisted of 12,690,321 ordinary shares, par value of one euro per share, and 9,610,630 ordinary shares were outstanding. At June 30, 2006, our authorized ordinary shares consisted of 15,100,292 ordinary shares, par value one euro per share, and 11,666,013 ordinary shares were outstanding.

Of our 15,100,292 authorized ordinary shares at June 30, 2006:

- 11,666,013 are outstanding;
- 1,560,000 are reserved for issuance upon exercise of options granted and available for grant under our share option plans;
- 484,964 are reserved for issuance upon exercise of warrants issued in connection with our Series A senior convertible promissory notes;
- 151,200 are reserved for issuance upon exercise of purchase options granted to the underwriters' of our initial public offering;
- 619,994 are reserved for issuance upon the exercise of warrants issued in connection with our October 2005 private placement;
- 466,446 are reserved for issuance upon the exercise of warrants issued in connection with our June 2006 private placement, including warrants issued to one of our placement agents; and
- 151,675 shares are available for future issuance in certain situations.

### Warrants

As of June 30, 2006, we had outstanding the following warrants:

- warrants to purchase 484,964 ordinary shares at a price of $9.52 per share, issued in connection with the issuance of our Series A notes, which became exercisable upon the closing of our initial public offering on June 21, 2005 and expire five years and three months after the date of issuance of the warrants;
- "purchase options" to purchase 151,200 ordinary shares at a price of $11.25 per share issued to our underwriters in connection with our initial public offering, which became exercisable on June 16, 2006 and expire on June 16, 2010;
- warrants to purchase 619,994 ordinary shares at a price of $9.69 per share, issued in connection with our October 2005 private placement, which became exercisable on April 3, 2006 and expire on April 3, 2011;
- warrants to purchase 388,705 ordinary shares at a price of $14.50 per share, issued in connection with our June 2006 private placement, which will become exercisable on December 6, 2006 and expire on April 28, 2011; and
- warrants to purchase 77,741 ordinary shares at a price of $17.40 per share, issued to one of our placement agents for the June 2006 private placement, which will become exercisable on December 6, 2006 and expire on April 28, 2011.

### Options

As of June 30, 2006 we had outstanding options to purchase a total of 1,137,000 ordinary shares. Our share option plans authorize the issuance of up to 1,560,000 ordinary shares. At June 30, 2006, 423,000 ordinary shares are available for future issuance under our share option plans.

**Share History**

The following history of our share capital for the years ended December 31, 2003, 2004 and 2005, as well as January 1, 2006 through June 30, 2006 supplements the disclosure in our annual report on Form 20-F for the year ended December 31, 2005, which we incorporate by reference herein.

*Increase in Authorized Capital*

On May 31, 2006, pursuant to the April 28, 2006 amendment to our bylaws, our board of directors approved a capital increase to allow for the issuance of 1,943,525 ordinary shares and 466,446 ordinary shares upon the exercise of warrants in connection with our June 2006 private placement.

*Exercises of Warrants*

In April 2006, we issued 18,334 ordinary shares upon exercise of a warrant issued in connection with our Series A senior convertible promissory notes at a price per share of $9.52, for proceeds of $174,539.68.

In April 2006, we issued 93,524 ordinary shares upon the exercise of warrants issued in connection with our October 2005 private placement at a price per share of $9.69, for aggregate proceeds of $906,247.56.

*June 2006 Private Placement*

In June 2006, we issued 1,943,525 ordinary shares at $11.39 per share for gross proceeds of $22,136,749.75 together with warrants to purchase an aggregate of 388,705 ordinary shares at an exercise price of $14.50 per share in a private placement. We also issued warrants to purchase 77,741 ordinary shares at an exercise price of $17.40 to one of our placement agents for the private placement.

*Options and restricted stock*

In March 2006, we issued options to purchase 15,000 ordinary shares at a price of $12.00 per share to a consultant under our 2004 Equity Incentive Plan.

In April 2006, we issued options to purchase an aggregate of 40,000 ordinary shares at a price of $17.35 per share to our non-employee directors as automatic grants under our 2004 Equity Incentive Plan.

In June 2006, we issued options to purchase 90,000 ordinary shares at a price of $12.60 to an executive officer under our 2004 Equity Incentive Plan.

## USE OF PROCEEDS

We will not receive any proceeds from the sale by the selling security holders of the securities offered in this prospectus. Although we will receive proceeds from any exercise of outstanding warrants, we will not receive any proceeds from sales of the underlying ADSs by the selling security holders. We will pay all of the expenses of the offering, including the expenses of the selling security holders, other than any underwriters' discounts and commissions and any fees and disbursements of counsel to the selling security holders. We expect that the selling security holders will sell their ADSs as described under "Plan of Distribution".

## SELLING SECURITY HOLDERS

Our ADSs to which this prospectus relates are being registered for resale by the selling security holders.

The selling security holders may resell all, a portion or none of such ADSs from time to time. The table below sets forth with respect to each selling security holder, based upon information available to us as of June 30, 2006, the number and percentage of ADSs (or, in the case of security holders who currently hold ordinary shares or securities exercisable into ordinary shares, the number and percentage of ordinary shares) beneficially owned before this offering, the number of ADSs registered for resale by this prospectus and the number and percent of ADSs that will be beneficially owned immediately after this offering assuming the sale of all of the registered ADSs.

Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC. ADSs or ordinary shares underlying our convertible securities that are exercisable within 60 days from June 30, 2006 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.

| | **ADSs Beneficially Owned Before The Offering** | | **ADSs Offered** | **ADSs Beneficially Owned After The Offering** | |
|---|---|---|---|---|---|
| **Holder** | ADSs | Percent | | ADSs | Percent |
| Alexandra Global Master Fund Ltd. (1) | 484,978 | 4.1 | 120,000 | 384,978 | 3.2 |
| ANIMA S.G.R.p.A. - Rubrica Anima America (2) | 10,000 | * | 12,000 | 0 | 0 |
| ANIMA S.G.R.p.A. - Rubrica Anima Fondattivo (3) | 5,000 | * | 6,000 | 0 | 0 |
| ANIMA S.G.R.p.A. - Rubrica Anima Fondo Trading (4) | 15,000 | * | 18,000 | 0 | 0 |
| Atlas Master Fund, Ltd. (5) | 20,169 | * | 24,203 | 0 | 0 |
| BBT Fund, L.P. (6) | 94,400 | * | 42,480 | 59,000 | * |
| BIM Intermobiliare SGR - Fondo Azionario Globale (7) | 28,400 | * | 12,000 | 18,400 | * |
| BIM Intermobiliare SGR - Fondo Azionario Italia (8) | 258,400 | 2.2 | 120,000 | 158,400 | 1.4 |
| BIM Intermobiliare SGR - Fondo Azionario Small Cap Italia (9) | 266,413 | 2.3 | 72,000 | 206,413 | 1.8 |
| BIM Intermobiliare SGR - Fondo Bilanciato (10) | 28,400 | * | 12,000 | 18,400 | * |
| Boxer Capital LLC (11) | 159,500 | 1.4 | 191,400 | 0 | 0 |
| Cap Fund, L.P. (12) | 46,400 | * | 20,880 | 29,000 | * |
| Caxton Advantage Life Sciences Fund, L.P. (13) | 79,700 | * | 95,640 | 0 | 0 |
| Clipperbay & Co. (14) | 450,000 | 3.9 | 540,000 | 60,253 | * |
| Generation Capital Associates (15) | 60,253 | * | 24,000 | 0 | 0 |
| Iroquois Master Fund LTD (16) | 24,000 | * | 28,800 | 0 | 0 |
| Mallette Capital Biotech Fund LP (17) | 71,284 | * | 85,541 | 0 | 0 |
| Mallette Capital Master Fund LTD (18) | 162,741 | 1.4 | 195,289 | 0 | 0 |
| Meliorbanca Spa (19) | 40,000 | * | 24,000 | 20,000 | * |
| Merlin BioMed Long Term Appreciation, LP (20) | 15,000 | * | 18,000 | 0 | 0 |
| Merlin Biomed Offshore Fund (21) | 25,000 | * | 30,000 | 0 | 0 |

| | | | | | |
|---|---|---|---|---|---|
| Merlin Nexus II, LP (22) | 119,600 | 1.0 | 143,520 | 0 | 0 |
| Perceptive Life Sciences Master Fund Ltd. (23) | 50,000 | * | 60,000 | 0 | 0 |
| RAQ, LLC (24) | 19,160 | * | 22,992 | 0 | 0 |
| SRI Fund, L.P. (25) | 19,200 | * | 8,640 | 12,000 | * |
| Straus-GEPT Partners, LP (26) | 93,250 | * | 47,820 | 53,400 | * |
| Straus Partners LP (27) | 93,250 | * | 47,820 | 53,400 | * |
| Symphonia Sicav Azionario Euro (28) | 10,000 | * | 12,000 | 0 | 0 |
| ThinkEquity Partners LLC (29) | 0 | 0 | 77,741 | 0 | 0 |
| Valesco Healthcare Master Fund, L.P. (30) | 28,740 | * | 34,488 | 0 | 0 |
| Visium Balanced Fund, LP (31) | 56,422 | * | 67,706 | 0 | 0 |
| Visium Balanced Offshore Fund, Ltd. (32) | 87,926 | * | 105,511 | 0 | 0 |
| Visium Long Bias Fund, LP (33) | 17,393 | * | 20,872 | 0 | 0 |
| Visium Long Bias Offshore Fund, Ltd. (34) | 57,190 | * | 68,628 | 0 | 0 |
| Total ADSs Offered: | | | 2,409,971 | | |

* Less than 1%

(1) Address is c/o Alexandra Investment Management, LLC, 767 Third Avenue, 39th Floor, New York, New York 10017. ADSs beneficially owned before the offering include 84,978 ADSs issuable upon exercise of warrants that are currently exercisable. ADSs offering include 20,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Alexandra Investment Management, LLC serves as investment advisor to Alexandra Global Master Fund Ltd. Mikhail A. Filimonov and Dimitri Sogoloff are managing members of Alexandra Investment Management, LLC. By reason of such relationship, Alexandra Investment Management, LLC, Mr. Filimonov and Mr. Sogoloff may be deemed to share dispositive and/or voting control over the ADSs beneficially owned and offered by Alexandra Global Master Fund Ltd. and therefore may be deemed to be beneficial owners of such securities. Alexandra Investment Management, LLC, Mr. Filimonov and Mr. Sogoloff each disclaims such beneficial ownership.

(2) Address is c/o ANIMA S.G.R.p.A., Via Brera 18, 20121 Milan, Italy. ADSs offered include 2,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(3) Address is c/o ANIMA S.G.R.p.A., Via Brera 18, 20121 Milan, Italy. ADSs offered include 1,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(4) Address is c/o ANIMA S.G.R.p.A., Via Brera 18, 20121 Milan, Italy. ADSs offered include 3,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(5) Address is c/o Balyasny Asset Management LP, 650 Madison Avenue, 19th Floor, New York, New York 10022. ADSs offered include 4,034 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Balyasny Asset Management LP is the investment advisor to Atlas Master Fund, Ltd. and Dmitry Balyasny is the sole managing member of the general partner of Balyasny Asset Management LP. By reason of such relationships, Balayasny Asset Management LP and Mr. Balyasny share dispositive and voting control over the ADSs beneficially owned and offered by Atlas Master Fund Ltd. and therefore beneficially own such securities.

(6) Address is c/o BBT Genpar, L.P., 201 Main Street, Suite 3200, Fort Worth, Texas 76102. ADSs offered include 7,080 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. BBT Genpar, L.P. is the managing general partner of BBT Fund, L.P. BBT-FW, Inc. is the sole general partner of BBT Genpar, L.P. Sid. R. Bass is the sole director and security holder of BBT-FW, Inc. By reason of such relationships, BBT Genpar, L.P., BBT-FW, Inc. and Mr. Bass may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by BBT Fund, L.P. and therefore may be deemed to be beneficial owners of such securities.

(7) Address is c/o BIM Intermobiliare SGR, Via Gramsci 7, 10121 Torino, Italy. ADSs beneficially owned prior to the offering include 2,400 ADSs issuable upon exercise of warrants that are currently exercisable. ADSs offered include 2,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Paolo D'Alfonso is the chief investment officer of BIM Intermobiliare SGR - Fondo Azionario Globale. By reason of such relationship, Mr. D'Alfonso may be deemed to have voting and/or dispositive control over the ADSs beneficially owned and offered by BIM Intermobiliare SGR - Fondo Azionario Globale and therefore may be deemed to be a beneficial owner of such securities.

(8) Address is c/o BIM Intermobiliare SGR, Via Gramsci 7, 10121 Torino, Italy. ADSs beneficially owned prior to the offering include 40,000 ADSs issuable upon exercise of warrants that are currently exercisable. ADSs offered include 20,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Paolo D'Alfonso is the chief investment officer of BIM Intermobiliare SGR - Fondo Azionario Italia. By reason of

such relationship, Mr. D'Alfonso may be deemed to have voting and/or dispositive control over the ADSs beneficially owned and offered by BIM Intermobiliare SGR - Fondo Azionario Italia and therefore may be deemed to be a beneficial owner of such securities.

(9) Address is c/o BIM Intermobiliare SGR, Via Gramsci 7, 10121 Torino, Italy. ADSs beneficially owned prior to the offering include 10,214 ADSs issuable upon exercise of warrants that are currently exercisable. ADSs offered include 12,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Paolo D'Alfonso is the chief investment officer of BIM Intermobiliare SGR - Fondo Azionario Small Cap Italia. By reason of such relationship, Mr. D'Alfonso may be deemed to have voting and/or dispositive control over the ADSs beneficially owned and offered by BIM Intermobiliare SGR - Fondo Azionario Small Cap Italia and therefore may be deemed to be a beneficial owner of such securities.

(10) Address is c/o BIM Intermobiliare SGR, Via Gramsci 7, 10121 Torino, Italy. ADSs beneficially owned prior to the offering include 2,400 ADSs issuable upon exercise of warrants that are currently exercisable. ADSs offered include 2,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Paolo D'Alfonso is the chief investment officer of BIM Intermobiliare SGR - Fondo Bilanciato. By reason of such relationship, Mr. D'Alfonso may be deemed to have voting and/or dispositive control over the ADSs beneficially owned and offered by BIM Intermobiliare SGR - Fondo Bilianciato and therefore may be deemed to be a beneficial owner of such securities.

(11) Address is c/o Tavistock Life Sciences, 9381 Judicial Drive, 200, San Diego, California 92121. ADSs offered include 31,900 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Shehan Dissonayake is the chief executive officer of Boxer Capital LLC. By reason of such relationship, Ms. Dissonayake may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Boxer Capital LLC and therefore may be deemed to be a beneficial owner of such securities.

(12) Address is c/o CAP Genpar, L.P., 201 Main Street, Suite 3200, Fort Worth, Texas 76102. ADSs offered include 3,480 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. CAP Genpar, L.P. is the managing general partner of CAP Fund, L.P. CAP-FW, Inc. is the sole general partner of CAP Genpar, L.P. Sid. R. Bass is the sole director and security holder of CAP-FW, Inc. By reason of such relationships, CAP Genpar, L.P., CAP-FW, Inc. and Mr. Bass may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by CAP Fund, L.P. and therefore may be deemed to be beneficial owners of such securities.

(13) Address is c/o Caxton Advantage Venture Partners, 500 Park Avenue, New York, New York 10022. ADSs offered include 15,940 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(14) Address is c/o Capital Research Management Co., 333 South Hope Street, Los Angeles, California, 90071. ADSs offered include 90,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Clipperbay & Co. is the nominee name for SMALLCAP World Fund, Inc. Capital Research and Management Company is the investment advisor of SMALLCAP World Fund, Inc. By reason of such relationships, SMALLCAP World Fund, Inc. and Capital Research and Management Company may be deemed to share voting and dispositive control over the securities owned by Clipperbay & Co. and so may be deemed to beneficially own such securities.

(15) Address is 1085 Riverside Trace, Atlanta, Georgia, 30328. ADSs beneficially owned before the offering include 48,644 ADSs issuable upon exercise of warrants currently exercisable. ADSs offered include 4,000 ADSs issuable upon exercise of warrants not exercisable within 60 days of June 30, 2006. Fred A. Brasch, David A. Rapaport and Frank E. Hart are each an executive officer of, and Mr. Hart is the indirect beneficial owner of, Profit Concepts, Ltd., which is the manager of High Capital Funding, LLC, which is the 100% shareholder of Generation Capital Associates. Mr. Brasch, Mr. Rapaport, Mr. Hart, Profit Concepts, Ltd. and High Capital Funding LLC may be deemed to have voting and/or dispositive control over the ADSs beneficially owned and offered by Generation Capital Associates and so may be deemed to beneficially own such securities.

(16) Address is 641 Lexington Avenue, 26th Floor, New York, New York 10022. ADSs offered include 4,800 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Joshua Silverman has voting and investment control over the ADSs held by Iroquois Master Fund Ltd. Mr. Silverman disclaims beneficial ownership over such securities.

(17) Address is 800 Third Avenue, 9th Floor, New York, New York 10022. ADSs offered include 14,257 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Quinterol Mallette,

MD is the chief executive officer of Mallette Capital Biotech Fund, LP. By reason of such relationship, Dr. Mallette may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Mallette Capital Biotech Fund, LP and therefore may be deemed to beneficially own such securities.

(18) Address is 800 Third Avenue, 9th Floor, New York, New York 10022. ADSs offered include 32,548 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Quinterol Mallette, MD is the chief executive officer of Mallette Capital Master Fund LTD. By reason of such relationship, Dr. Mallette may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Mallette Capital Master Fund LTD and therefore may be deemed to beneficially own such securities.

(19) Address is Via Borromei 5, 20123 Milano, Italy. ADSs offered include 4,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(20) Address is 230 Park Avenue, Suite 928, New York, New York, 10169. ADSs offered include 3,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Stuart Weisbrod shares voting and/or dispositive control control over the ADSs beneficially owned and offered by Merlin BioMed Long Term Appreciation LP and therefore may be deemed to beneficially own such securities.

(21) Address is 230 Park Avenue, Suite 928, New York, New York, 10169. ADSs offered include 5,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Stuart Weisbrod shares voting and/or dispositive control control over the ADSs beneficially owned and offered by Merlin BioMed Offshore Fund and therefore may be deemed to beneficially own such securities.

(22) Address is 230 Park Avenue, Suite 928, New York, New York, 10169. ADSs offered include 23,920 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Dominique Semon shares voting and/or dispositive control control over the ADSs beneficially owned and offered by Merlin Nexus II, LP and therefore may be deemed to beneficially own such securities.

(23) Address is 7284 West Palmetto Park Road, Suite 306, Boca Raton, Florida 33433. ADSs offered include 10,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Joseph Edelman is the managing member of and Andrew C. Sankin is the Chief Operating Officer of Perceptive Advisors, LLC, which is the investment manager of Perceptive Life Sciences Master Fund, Ltd. By reason of such relationships, Mr. Edelman, Mr. Sankin and Perceptive Advisors, LLC may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Perceptive Life Sciences Master Fund, Ltd. Mr. Edelman, Mr. Sankin and Perceptive Advisors, LLC disclaim such beneficial ownership.

(24) Address is 789 Seventh Avenue, 48th Floor, New York, New York 10019. ADSs offered include 3,832 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(25) Address is c/o SRI Genpar, L.P., 201 Main Street, Suite 3200, Fort Worth, Texas 76102. ADSs offered include 1,440 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. SRI Genpar, L.P. is the managing general partner of SRI Fund, L.P. BBT-FW, Inc. is the sole general partner of SRI Genpar, L.P. Sid. R. Bass is the sole director and security holder of BBT-FW, Inc. By reason of such relationships, SRI Genpar, L.P., BBT-FW, Inc. and Mr. Bass may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by SRI Fund, L.P. and therefore may be deemed to be beneficial owners of such securities.

(26) Address is c/o Straus Asset Management, 605 Third Avenue, New York, New York 10158. ADSs offered include 7,970 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Melville Straus is the managing member of Straus-GEPT Partners, LP. By reason of such relationship, Mr. Straus may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Straus-GEPT Partners, LP and therefore may be deemed to beneficially own such securities.

(27)

Address is c/o Straus Asset Management, 605 Third Avenue, New York, New York 10158. ADSs offered include 7,970 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Melville Straus is the managing principal of Straus Partners, LP. By reason of such relationship, Mr. Straus may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Straus Partners, LP and therefore may be deemed to beneficially own such securities.

(28) Address is c/o Symphonia SGR, Corso Matteotti 5, 20121 Milano, Italy. ADSs offered include 2,000 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Paolo D'Alfonso is the chief executive officer of Symphonia Sicav Azionario Euro. By reason of such relationship, Mr. D'Alfonso may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Symphonia Sicav Azionario Euro and therefore may be deemed to beneficially own such securities.

(29) Address is 600 Montgomery Street, 8th Floor, San Francisco, California 94111. ADSs offered include 77,741 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Michael Moe, Deborah Quazzo and Seth Gersch may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by ThinkEquity Partners LLC and therefore may be deemed to beneficially own such securities.

(30) Address is 787 Seventh Avenue, 48th Floor, New York, New York 10019. ADSs offered include 5,748 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006.

(31) Address is c/o Balyansny Asset Management LP, 650 Madison Avenue, 19th Floor, New York, New York 10022. ADSs offered include 11,284 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Balyasny Asset Management LP is the sub-investment advisor to Visium Balanced Fund, LP and Dmitry Balyasny is the sole managing member of the general partner of Balyasny Asset Management LP. By reason of such relationships, Balayasny Asset Management LP and Mr. Balyasny share dispositive and voting control over the ADSs beneficially owned and offered by Visium Balanced Fund, LP and therefore beneficially own such securities. Visium Capital Management, LLC is the investment advisor to Visium Balanced Fund, LP and Jacob Gottlieb is the managing member of Visium Capital Management, LLC. By reason of such relationships, Visium Capital Management, LLC and Mr. Gottlieb share dispositive and voting control over the ADSs beneficially owned and offered by Visium Balance Fund, LP and therefore beneficially own such securities.

(32) Address is c/o Balyansny Asset Management LP, 650 Madison Avenue, 19th Floor, New York, New York 10022. ADSs offered include 17,585 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Balyasny Asset Management LP is the sub-investment advisor to Visium Balanced Offshore Fund, Ltd. and Dmitry Balyasny is the sole managing member of the general partner of Balyasny Asset Management LP. By reason of such relationships, Balayasny Asset Management LP and Mr. Balyasny share dispositive and voting control over the ADSs beneficially owned and offered by Visium Balanced Offshore Fund, Ltd. and therefore beneficially own such securities. Visium Capital Management, LLC is the investment advisor to Visium Balanced Offshore Fund, Ltd. and Jacob Gottlieb is the managing member of Visium Capital Management, LLC. By reason of such relationships, Visium Capital Management, LLC and Mr. Gottlieb share dispositive and voting control over the ADSs beneficially owned and offered by Visium Balance Offshore Fund, Ltd. and therefore beneficially own such securities.

(33) Address is c/o Balyansny Asset Management LP, 650 Madison Avenue, 19th Floor, New York, New York 10022. ADSs offered include 3,479 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Balyasny Asset Management LP is the sub-investment advisor to Visium Long Bias Fund, LP and Dmitry Balyasny is the sole managing member of the general partner of Balyasny Asset Management LP. By reason of such relationships, Balayasny Asset Management LP and Mr. Balyasny share dispositive and voting control over the ADSs beneficially owned and offered by Visium Long Bias Fund, LP and therefore beneficially own such securities. Visium Capital Management, LLC is the investment advisor to Visium Long Bias Fund, LP and Jacob Gottlieb is the managing member of Visium Capital Management, LLC. By reason of such relationships, Visium Capital Management, LLC and Mr. Gottlieb share dispositive and voting control over the ADSs beneficially owned and offered by Visium Long Bias Fund, LP and therefore beneficially own such securities.

(34) Address is c/o Balyansny Asset Management LP, 650 Madison Avenue, 19th Floor, New York, New York 10022. ADSs offered include 11,438 ADSs issuable upon exercise of warrants that are not exercisable within 60 days of June 30, 2006. Balyasny Asset Management LP is the sub-investment advisor to Visium Long Bias Offshore Fund, Ltd. and Dmitry Balyasny is the sole managing member of the general partner of Balyasny Asset Management LP. By reason of such relationships, Balayasny Asset Management LP and Mr. Balyasny share dispositive and voting control over the ADSs beneficially owned and offered by Visium Long Bias Offshore Fund, Ltd. and therefore beneficially own such securities. Visium Capital Management, LLC is the investment advisor to Visium Long Bias Offshore Fund, Ltd. and Jacob Gottlieb is the managing member of Visium Capital Management, LLC. By reason of such relationships, Visium Capital Management, LLC and Mr. Gottlieb share dispositive and voting control over the ADSs beneficially owned and offered by Visium Long Bias Offshore Fund, Ltd. and therefore beneficially own such securities.

The selling security holders have not within the past three years had any position, office or other material relationship with our company.

The information provided above with respect to the selling security holders has been obtained from such selling security holders. Because the selling security holders may sell all or some portion of the ADSs or ordinary shares beneficially owned by them, only an estimate (assuming the selling security holders sell all of the ADSs or ordinary shares offered in this prospectus) can be given as to the number of ADSs or ordinary shares that will be beneficially owned by the selling security holders after this offering, and as to the percentage of all outstanding ADSs or ordinary shares constituted by such ADSs or ordinary shares. In addition, the selling security holders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time or from time to time since the dates on which they provided the information regarding the ADSs or ordinary shares beneficially owned by them, all or a portion of the ADSs or ordinary shares beneficially owned by them in transactions exempt from the registration requirements of the Securities Act.

## PLAN OF DISTRIBUTION

Each selling security holder and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their ADSs on the Nasdaq National Market System or any other stock exchange, market or trading facility on which the ADSs are traded or in private transactions. These sales may be at fixed or negotiated prices. A selling security holder may use any one or more of the following methods when selling ADSs:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- public or privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- on the Nasdaq National Market System (or through facilities of any national securities exchange or US inter-dealer quotation system of a registered national securities association on which the ADSs are then listed, admitted to unlisted trading privileges or included for quotation);
- broker-dealers may agree with the selling security holders to sell a specified number of such ADSs at a stipulated price per ADSs;
- through underwriters, brokers or dealers (who may act as agents or principals) or directly to one or more purchasers;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling security holders may also sell shares under Rule 144 under the Securities Act of 1933, as amended, if available, rather than under this prospectus.

Broker-dealers engaged by the selling security holders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling security holders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with NASDR Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with NASDR IM-2440.

In connection with the sale of the ADSs or interests therein, the selling security holders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the ADSs in

the course of hedging the positions they assume. The selling security holders may also sell the ADSs short and deliver these securities to close out their short positions, or loan or pledge the ADSs to broker-dealers that in turn may sell these securities. The selling security holders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of ADSs offered by this prospectus, which ADSs such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling security holders may also pledge ADSs to a broker-dealer or other financial institution which, upon default, they may in turn resell.

In addition to the foregoing methods, the selling security holders may offer their ADSs from time to time in transactions involving principals or brokers not otherwise contemplated above, in a combination of such methods or described above or any other lawful methods. The selling security holders may also transfer, donate or assign their ADSs to lenders, family members and others and each of such persons will be deemed to be a selling security holder for purposes of this prospectus. The selling security holders or their successors in interest may from time to time pledge or grant a security interest in some or all of the ADSs, and if the selling security holders default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the ADSs from to time under this prospectus; provided however in the event of a pledge or then default on a secured obligation by the selling security holder, in order for the ADSs to be sold under this prospectus, unless permitted by law, we must distribute a prospectus supplement and/or amendment to the registration statement of which this prospectus forms a part amending the list of selling security holders to include the pledgee, secured party or other successors in interest of the selling security holder under this prospectus.

The selling security holders may also sell their ADSs pursuant to Rule 144 under the Securities Act, which permits limited resale of ADSs purchased in a private placement subject to the satisfaction of certain conditions, including, among other things, the availability of certain current public information concerning the issuer, the resale occurring following the required holding period under Rule 144 and the number of shares being sold during any three-month period not exceeding certain limitations.

Sales through brokers may be made by any method of trading authorized by any stock exchange or market on which the ADSs may be listed or quoted, including block trading in negotiated transactions. Without limiting the foregoing, such brokers may act as dealers by purchasing any or all of the ADSs covered by this prospectus, either as agents for others or as principals for their own accounts, and reselling such ADSs pursuant to this prospectus. The selling security holders may effect such transactions directly, or indirectly through underwriters, broker-dealers or agents acting on their behalf, in effecting sales, broker-dealers or agents engaged by the selling security holders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling security holders, in amounts to be negotiated immediately prior to the sale (which compensation as to a particular broker-dealer might be in excess of customary commissions for routine market transactions).

The selling security holders and any broker-dealers or agents that are involved in selling the ADSs may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any profits received by the selling security holders or such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay certain fees and expenses incurred by us incident to the registration of the ADSs. We have agreed to indemnify the selling security holders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the ADSs may be resold by the selling security holders without registration and without regard to any volume limitations by reason of Rule 144(e) under the Securities Act or any other rule of similar effect or (ii) all of the ADSs have been sold pursuant to the prospectus or Rule 144 under the Securities Act or any other rule of similar effect.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to the ordinary shares or ADSs for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling security holders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of the ordinary shares or ADSs by the selling security holders or any other person.

## OFFERING EXPENSES

We will bear all costs, expenses and fees in connection with the registration of the ADSs offered by this prospectus. The selling security holders will bear brokerage commissions and similar selling expenses, if any, attributable to the sale of ADSs, as well as any fees and disbursements of counsel to the selling security holders.

The following table sets forth the estimated expenses payable by us in connection with the offering described in this registration statement. All amounts are subject to future contingencies other than the SEC registration fee.

| | | |
|---|---|---|
| Securities and Exchange Commission Registration Fee | $ | 3,675 |
| Depositary fees | | 97,000 |
| Legal Fees and Expenses | | 149,585 |
| Accounting Fees and Expenses | | 15,000 |
| Placement Agents Fees and Expenses | | 1,322,598 |
| Financial Advisor Fees and Expenses | | 75,000 |
| Escrow Agent Fees and Expenses | | 10,000 |
| Miscellaneous | | 25,000 |
| Total | $ | 1,697,858 |

## FINANCIAL STATEMENTS

Audited financial statements for the fiscal year ended December 31, 2005 are contained in our Annual Report on Form 20-F for the fiscal year ended December 31, 2005, which is incorporated by reference herein.

## EXPERTS

The financial statements of Gentium at December 31, 2003, 2004, 2005 and for each of the three years in the period ended December 31, 2005 appearing in this prospectus and in the registration statement of which this prospectus forms a part have been audited by Reconta Ernst & Young S.p.A., independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The address of Reconta Ernst & Young S.p.A. is Via della Chiusa, 2, 20123, Milan, Italy. Reconta Ernst & Young S.p.A. is registered with the Public Company Accounting Oversight Board.

## LEGAL MATTERS

The validity of the ordinary shares underlying the ADSs offered hereby have been passed upon for us by Gianni, Origoni, Grippo & Partners, Piazza Belgioioso, 2, 20121 Milan, Italy.

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