Gentium S.p.A.
Form F-3
December 15, 2006

As filed with the Securities and Exchange Commission on December 15, 2006
Registration No. 333-_____

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

FORM F-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

GENTIUM S.p.A.
(Exact name of Registrant as specified in its charter)

Republic of Italy	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

Piazza XX Settembre 2
22079 Villa Guardia (Como), Italy
+39 031 385111
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

CT Corporation System
111 Eighth Avenue, 13th Floor
New York, New York 10011
(12) 894-8940
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:
Theodore L. Polin, Esq.
Christopher M. Locke, Esq.
Epstein Becker & Green, P.C.
250 Park Avenue
New York, New York 10017
(212) 351-4500

Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes effective.

If only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this Form are offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. **x**

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a registration statement pursuant to General Instruction I.C. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ¨

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.C. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title of Class of Securities To Be Registered	Amount To Be Registered (1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Ordinary shares, par value €1.00 per share (2)	151,200 (3)	$19.825 (4)	$2,997,540 (4)	$321

(1) Includes such additional ordinary shares as may become issuable by reason of stock splits, stock dividends or similar transactions.

(2) American Depositary Shares ("ADSs") evidenced by American Depositary Receipts issuable upon deposit of the ordinary shares registered hereby are being registered under a separate registration statement. Each ADS represents one ordinary share.

(3) Consists of 151,200 ordinary shares issuable upon exercise of warrants.

(4) Computed in accordance with Rule 457(h) of the Securities Act of 1933, as amended, solely for the purpose of calculating the registration fee. The computation is based on $19.825 per share, the average of the high and low sales prices of the Registrant's ADSs on December 13, 2006, as reported by the Nasdaq Global Market.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall after that become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this Registration Statement shall be come effective on such date as the Commission, acting pursuant to Section 8(a), may determine.

THE INFORMATION IN THIS PRELIMINARY PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THESE SECURITIES MAY NOT BE SOLD UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PRELIMINARY PROSPECTUS IS NOT AN OFFER TO SELL NOR DOES IT SEEK AN OFFER TO BUY THESE SECURITIES IN ANY JURISDICTION WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION DATED DECEMBER 15, 2006

PRELIMINARY PROSPECTUS

Gentium S.p.A.

151,200 American Depositary Shares
Representing 151,200 Ordinary Shares

The selling security holders identified in this prospectus are offering up to 151,200 American Depositary Shares ("ADSs"), each representing one ordinary share of our company, Gentium S.p.A. The ADSs offered hereby represent ordinary shares that may be issued upon exercise of warrants that were issued to the selling security holders listed herein. Our ADSs are listed on the Nasdaq Global Market under the symbol "GENT." The lasted reported sale price for our ADSs on the Nasdaq Global Market on December 14, 2006 was $20.36 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 $1,701,000. See "Selling Security Holders" beginning on page 23 for a list of the selling security holders. See "Plan of Distribution" beginning on page 24 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.

[_____], 2006

TABLE OF CONTENTS

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 151,200 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.

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 September 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 2008 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 41% after treatment with defibrotide, although those results were based on the treatment of only 150 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 Phase II clinical trial of defibrotide in patients with VOD with multiple-organ failure was completed in December 2005. Results show that the survival rate after 100 days for the 150 patients treated was approximately 41% 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. We intend to start a Phase II/III clinical trial in Europe and the United States in 2007 for both the prevention of VOD and the prevention of transplant associated microangiopathy in adults. 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 “Obligotide” 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. If 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