EXECUTIVE INFORMATIONAL OVERVIEW

Gentium S.p.A
Piazza XX Settembre 2
Villa Guardia, Como (Italy) 22079
Phone: 39 031 385217
Fax: 39 031 385241
http://www.gentium.it

Drugs for Vascular Diseases Induced by Cancer & Cancer Treatments

Snapshot

June 26, 2006

Gentium S.p.A. ("Gentium" or "the Company") is a biopharmaceutical company engaged in researching, discovering, developing, and manufacturing drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. Gentium's most advanced candidate, Defibrotide, is in development to treat and prevent severe hepatic **veno-occlusive disease (VOD)**† with multiple organ failure (MOF)—a condition in which some of the veins in the liver are blocked as a result of toxic cancer treatments, such as **chemotherapy**. Defibrotide may protect the **vascular endothelial cells**, particularly those of small vessels, from damage and activation. Gentium's R&D program includes several ongoing clinical studies. Gentium also has several product candidates in preclinical development for use subsequent to **stem cell transplantation (SCT)**, to prevent **deep vein thrombosis (DVT)**, for **inflammatory bowel disease (IBD)**, and oral **mucositis**. Oral Defibrotide is in development to treat **multiple myeloma**, a cancer of the plasma cell. In 1986, one of Gentium's predecessor companies received approval to sell Defibrotide in Italy to treat DVT; later the indication was revised to treat and prevent all vascular disease with risk of **thrombosis** (also in Italy). The Company currently derives revenues from the manufacture and sale of active pharmaceutical ingredients, reporting €3.3 million (US$4 million) in total revenues for 2005. Gentium independently operates as a research facility as well as a production plant for these marketed substance pharmaceuticals in Villa Guardia, near Como, Italy. Effective May 16, 2006, Gentium's American Depository Shares (ADSs) were listed for trading on the NASDAQ National Market System (NMS-NASDAQ) under the symbol GENT, from its prior AMEX listing under the symbol GNT.

Recent Financial Data

Ticker (Exchange)	GENT (NASDAQ)*
Recent Price (06/22/06)	$14.00
52-Week Range	$6.75-20.10
Shares Outstanding	11.7 million
Market Capitalization	$163.8 million
Avg. 3-month volume	53,095
Insider Owners +5%	52%
Institutional Owners	55% (est.)
EPS (Quarter ended 03/31/06)	(€0.32)
Employees	60

** New ticker symbol effective May 16, 2006.*

Key Points

- Defibrotide has been granted **Orphan Drug** status, **Fast Track** designation, and is supported by grants from the **U.S. Food and Drug Administration's (FDA)** Office of Orphan Products Development—enabling market exclusivity for the treatment of VOD upon reaching the market. There are no approved drugs by the FDA or the **European Agency for the Evaluation of Medicinal Products (EMEA)** to treat or prevent this deadly disease.
- A severe form of VOD with MOF could be a devastating complication of cancer treatments with a survival rate after 100 days of about 20%. A multicenter Phase II clinical trial coordinated by the Harvard University's Dana-Farber Cancer Institute in patients with severe VOD after treatment with Defibrotide concluded in December 2005, reporting a survival rate after 100 days of approximately 39%.
- Treatment of severe VOD represents an estimated global market opportunity of $600 million. Prevention (**prophylaxis**) of VOD could replace treatment and become a $1 billion opportunity. Additional chemo-protective indications could represent larger market opportunities.
- Collaborations and/or agreements are in place to help develop and market Defibrotide and additional candidates with Sigma-Tau Pharmaceuticals and Axcan Pharma (AXCA-NASDAQ), among others.
- On May 6, 2006, Gentium announced the completion of a $22.1 million private placement of 1,943,525 of its American Depository Shares (ADSs) at a price of $11.39 per ADS. Investors in the financing also received warrants to purchase 388,705 ADSs at an exercise price of $14.50 per ADS. The net proceeds from the offering will be used to fund the continued development of the Company's product candidates and for general corporate purposes.

†**BOLD** WORDS ARE REFERENCED IN GLOSSARY ON PAGES 57-59.

Table of Contents

Executive Overview

Gentium S.p.A. ("Gentium" or "the Company") is an Italian-based biopharmaceutical company engaged in researching, discovering, developing, and manufacturing drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. The Company targets those pharmaceuticals that could be useful in the treatment of rare diseases—especially where there are no treatment alternatives. Gentium's current research and development (R&D) efforts are focused on agents that target, in particular, endothelial cell protection. Recently, endothelial cells and their associated adhesion molecules have been shown to play a crucial role in **coagulation**, inflammation, and cancer.

Gentium's most advanced candidate, Defibrotide, is in development to treat and prevent severe hepatic veno-occlusive disease (VOD) with multiple organ failure (MOF), 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 MOF (severe VOD), is a potentially devastating complication of cancer treatment with a survival rate after 100 days of only approximately 20%, according to a review of more than 200 published medical articles by Gentium. In 1986, a predecessor company to Gentium's received approval to sell Defibrotide in Italy to treat deep vein thrombosis (DVT); later the indication was changed to treat and prevent all vascular disease with risk of thrombosis (also in Italy). Gentium's experience with Defibrotide has contributed to its efforts in developing a variety of additional potential indications for Defibrotide beyond VOD, including a treatment for multiple myeloma (a cancer of the plasma cell).

Results from a multicenter Phase II clinical trial coordinated by the Harvard University's Dana-Farber Cancer Institute on patients with VOD with MOF were presented in December 2005, reporting a survival rate after 100 days of approximately 39% after treatment with Defibrotide (versus 20% with no treatment), with results based on the treatment of 142 patients. Importantly, there is currently no drug approved by the U.S. Food and Drug Administration (FDA) or the European Agency for the Evaluation of Medicinal Products (EMEA) to treat or prevent VOD.

The Company's VOD program includes several ongoing clinical studies in the U.S., Europe, and Israel, with data expected to be presented from the Phase III trial by the fourth quarter 2007. The stages of development and status of each intended use of Defibrotide, as well as the Company's preclinical candidates are outlined in Table 1 and further described within the Core Story section of this Executive Informational Overview® (EIO®) on pages 16-28.

Table 1
Gentium S.p.A.
PRODUCT PIPELINE

CANDIDATE	INTENDED USE	DEVELOPMENT STAGE
Defibrotide	Treat VOD with multiple-organ failure (MOF)	Phase III in the U.S./Orphan drug designation in the U.S. and Europe; Fast Track designation in the U.S.
Defibrotide	Prevent VOD	Phase II/III in Europe/Orphan drug designation in Europe
Defibrotide	Treat multiple myeloma	Phase I/II in Italy
Mesalazine	Treat inflammatory bowel disease (IBD)	Phase III in U.S. and Canada
Oligotide	Protect against damage (apoptosis) of cells of the blood vessel walls caused by fludarabine, a chemotherapy agent	Preclinical in Germany
Gen 301	Prevent and treat mucositis	Preclinical in England

Source: Gentium S.p.A.

In May 2003, the FDA designated Defibrotide as an orphan drug for use in treating VOD and made grants of $525,000 to Dana-Farber supporting research into the use of Defibrotide to treat VOD with MOF. Gentium has supported this research with a grant of $450,000 to Dana-Farber. In July 2004, the European Commission granted Gentium **orphan medicinal product designation** (medicinal products that have been designated as orphan due to the rarity of the diseases they treat) for the use of Defibrotide to both treat and prevent VOD.

Partnerships/Alliances

Gentium has relationships in place with industrial and academic institutions to combine its research expertise with those taking place at these institutions. These relationships are referenced in Figure 2 (page 6). Additionally, pages 29-30 describe Gentium's license and distribution agreements. The Company is also targeting the discovery of further beneficial effects of its products with the intent on creating pharmaceuticals with a broader range of treatment indications, specifically to increase its own marketing potential by licensing its products to international companies within U.S. and European markets.

History, Headquarters, and Employees

Research began in 1956 with substances derived from mammalian organs to treat coagulation and **fibrinolytic** disorders—the first being a mixture of glycosaminoglycans developed for potential anticoagulant and antithrombotic activity. In early 1960, research focused on developing compounds to correct coagulation and thrombotic disorders, where the focus was more on safety than current treatment (i.e. reduced hemorrhagic potential). This resulted in a novel fibrinolytic/antithrombotic compound, initially named fraction P (due to its phosphate rich content). The compound was later discovered to be a **polydeoxyribonucleotide** (i.e. a low molecular weight single stranded DNA), with advantages over other antithrombotic drugs due to negligible systemic anticoagulant properties. Fraction P is now known as Defibrotide and has been marketed in Italy in injectable form since 1986 and in oral form since 1992.

Gentium was formed in early 2001 from Crinos Industria Farmacobiologica SpA (Crinos), where the Company now incorporates the research and drug substances manufacturing divisions of Crinos as well as all Crinos' patents into its operations. Crinos has been restructured and now exists as a separate, independent marketing company in Italy. Crinos Industria S.p.A. was originally founded in 1944 and has expanded to become one of Italy's leading independent pharmaceutical companies.

In June 2005, Gentium closed an initial public offering (IPO) of 2.7 million American Depository Shares (1 ADS = 1 ordinary share) at $9 per share, including exercise of the underwriters' over-allotment option, raising $24.3 million in gross proceeds. A subsequent institutional private placement raised an additional $10.9 million (see also page 32). The Company further announced on June 6, 2006 that it had raised $22.1 million in a private placement of 1.9 million ADSs at a price of $11.39 per share. Investors in the financing also received warrants to purchase 388,705 ADSs at an exercise price of $14.50 per ADS. The net proceeds from the offering will be used to fund the continued development of the Company's product candidates and for general corporate purposes. The Company operates a research facility and production plant in Villa Guardia, near Como, Italy and employs approximately 60 individuals. Gentium owns its own land, buildings, laboratories, and equipment.

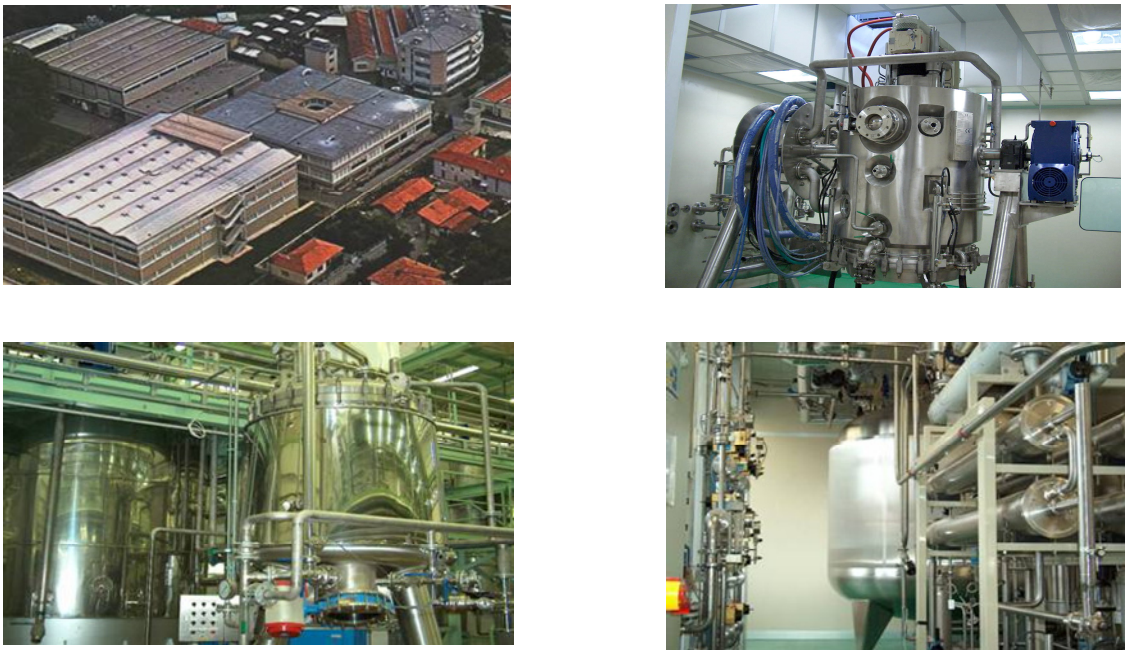
Manufacturing

Five drug substances (Defibrotide, heparin, urokinase, sulglicotide, and condroitins), are manufactured by Gentium and marketed in Italy and elsewhere by several different companies. Gentium has developed efficient manufacturing methods and controls in accordance with current **good manufacturing practices (GMPs)—**assuring a drug's potency, identity, strength, quality, and purity. Defibrotide is sold to the Company's affiliate, Sirton (a subsidiary of Gentium's majority shareholder, FinSirton, which currently owns 32% of its stock), who processes the compound for either oral or intravenous (IV) administration and sells the finished products to Crinos S.p.A. to treat and prevent vascular disease at risk of thrombosis.

The Company's facility, used for the production of Defibrotide, is dedicated to porcine (pig) product manufacture. This manufacturing process is unique in that it involves the extraction of DNA from pig intestinal mucosa. Gentium also manufactures and sells to Sirton two active pharmaceutical ingredients, urokinase (where Gentium is the European leader for this product) and calcium heparin, used by Sirton to make generic drugs, and sulglicotide, which is used to treat peptic ulcers. Sulglicotide is sold to unrelated third parties and the Company is actively working on developing other customers for these products.

In 2004, Gentium completed an upgrade to its manufacturing facilities at a cost of approximately €7.2 million (approximately $10 million), which is intended to facilitate the FDA and European regulatory approval process for its product candidates and enable future production. Select snapshots of the Company's manufacturing facility are provided in Figure 1.

Figure 1
Gentium S.p.A.
MANUFACTURING FACILITY



Source: Gentium S.p.A.

Growth Strategy

Gentium is engaged in researching, discovering, developing, and manufacturing pharmaceuticals to treat and prevent a variety of rare vascular diseases and conditions related to cancer and cancer treatments. The Company is also targeting the discovery of any further beneficial effects of its existing products, where its pharmaceuticals could offer a broader range of treatment indications. Gentium is focused on building solid relationships with industrial and academic institutions to combine its research expertise, manufacturing, and marketing capabilities with these institutions. Some of the institutions in which Gentium currently has relationships are depicted in Figure 2 and referenced throughout the Core Story section (pages 16-28).

Figure 2
Gentium S.p.A.
CLINICAL PARTNERSHIPS

Source: Gentium S.p.A.

The specific elements of the Company's growth strategy are outlined below:

- *Obtain regulatory approvals for advanced product candidates.* While clinical trials are being conducted for new uses of Defibrotide, the Company does not expect revenue from any potential new indications for Defibrotide, such as to treat VOD with MOF, until at least 2008, or revenue from Defibrotide to prevent VOD until at least 2009. In the meantime, the Company derives revenue from marketed products (Defibrotide, heparin, urokinase, sulglycotide, and condroitins), which are manufactured by Gentium and marketed in Italy and elsewhere by several different companies.

- *Discover and develop additional product candidates*. Gentium expects to continue to discover and develop, either internally or through collaborative arrangements, additional product candidates including:

  - Defibrotide for uses such as to treat multiple myeloma, to treat **renal** disorders, to increase the number of **stem cells** available for transplant, and to prevent DVT;

  - Other drugs, such as oligotide, to protect against damage to blood vessel wall cells from certain cancer treatments; and

- Gen 301 (a preclinical candidate), which may prevent and treat oral ulcers that develop during and after cancer treatments.

- *Enter into collaborative and strategic agreements to assist in developing and marketing products and product candidates*. Gentium has entered into a limited number of license and distribution agreements (detailed on pages 29-30) to date, including:

  - A license for the right to market Defibrotide to treat VOD in North America, Central America, and South America (upon regulatory approval) to Sigma-Tau Pharmaceuticals, Inc. (of Gaithersburg, Maryland). Sigma Tau markets drug treatments for rare conditions and diseases. Sigma-Tau Pharmaceuticals, Inc. is a U.S. subsidiary of Sigma Tau Finanziaria S.p.A., an international family of pharmaceutical companies (Gentium retains the right for VOD prevention in these markets);

  - A license to sell the rights to develop and sell the Company's formulation of mesalazine to treat inflammatory bowel disease (IBD) in Canada, upon Health Canada approval, and in the U.S. upon FDA approval, to Axcan Pharma, Inc., a specialty pharmaceutical company with offices in North America and Europe; and

  - To obtain a license for the right to distribute Gentium's formulation of mesalazine to treat IBD in Italy to Crinos, a subsidiary of Stada (a large European pharmaceutical company). Crinos also markets Defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement with Gentium.

Intellectual Property

Gentium possesses seven issued U.S. patents, four pending U.S. patent applications, 28 issued foreign patents, and 88 pending foreign patent applications. The Company's patent portfolio provides broad coverage and protection, including composition of matter, methods of use, and manufacturing. This is important since complex biological compounds are very difficult to duplicate and require new clinical trials for approvals. The Company's patent rights and other proprietary rights are crucial to protecting its intellectual property.

In particular, The United States Patent & Trademark Office (USPTO) issued a patent covering the Company's manufacturing process of Defibrotide in 1991. In April 2001, Gentium filed a patent application with the USPTO and corresponding patent applications in certain foreign countries regarding the use of Defibrotide in stem cell transplants. These U.S. patents expire between 2008 and 2024. Table 2 provides a depiction of certain key patents within Gentium's patent portfolio.

Table 2
Gentium S.p.A.
INTELLECTUAL PROPERTY

TITLE	OWNER
Formulation having mobilizing activity	Gentium S.p.A. / First Owner of EP00830293.7 and PCT/EP01/04105 Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: Method of increasing the amount of stem cells and progenitor cells in the peripheral blood of a mammal; the method is characterized by the administration of Defibrotide in combination or in temporal proximity with at least one hematopoietic factor (G-CSF) having the capacity to mobilize hematopoietic progenitors. The present inventions also refer to the related pharmaceutical formulations containing thereof.

TITLE	OWNER
A method for determining the biological activity of Defibrotide	Gentium S.p.A.

SUBJECT MATTER: An enzymatic method for determining the biological activity of Defibrotide is described. This method, which is based on the capacity of Defibrotide to potentiate the enzymatic activity of plasmin, comprises the steps of: (a) bringing into contact Defibrotide, plasmin, and a substrate specific for the plasmin which, by reaction with the plasmin, provides a measurable product and (b) measuring the amount of product formed at successive times.

TITLE	OWNER
DNA-based aptamers for human cathepsin G	Gentium S.p.A.

SUBJECT MATTER: Non-peptidic inhibitors of cathepsin G, characterized by high levels of selectivity and which can be efficaciously used in the treatment and prophylaxis of inflammatory occurrences and procoagulant conditions. The cathepsin G-inhibiting aptamers of the present invention consist of linear DNA or polynucleotide sequences having a chain length of at least 60 nucleotides and being substantially not subjected to undergo efficient base pairing.

TITLE	OWNER
Formulation with anti-tumor action	Gentium S.p.A.

SUBJECT MATTER: A method for treating a mammalian affected by a tumor, said method comprising administering to said mammalian an effective amount of Defibrotide alone or in combination with at least an other active ingredient with anti-tumor action. The present invention also refers to the related pharmaceutical compositions containing Defibrotide and at least another active ingredient with an anti-tumor action (for example paclitaxel, monocrotaline, BCNU and/or cyclophosphamide).

Source: Gentium S.p.A.

Table 2

Gentium S.p.A.

INTELLECTUAL PROPERTY (CONTINUED)

TITLE	OWNER
A process for obtaining chemically defined and reproducible polydeoxyribonucleotides	Gentium S.p.A./ First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: By carrying out the depolymerization of stabilized solutions of highly polymerized and nicked polydeoxyribonucleotides, as obtained through stabilizing aggregation of raw nucleic acids, the depolymerization being carried out by heating at controlled temperature and being controlled as function of the variation of the reversible hyperchromicity, followed by the removal of the hydrogen bonds in the double stranded filaments and by thermal stabilization of the single stranded filaments, the polydeoxyribonucleotides, known as Defibrotide has the following formula of random sequence: P1-5,(dAp)12-24,(dGp)10-20,(dTo)13-26,(dCp)10-20, wherein P is phosphoric radical, dAp is deoxycytidylic monomer and has well defined chemical-physical properties, reproducible in the industrial production.

TITLE	OWNER
Pharmaceutical composition for the prevention and treatment of arteriosclerosis	Gentium S.p.A./First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: Use of Defibrotide for the prevention and treatment of arteriosclerosis. The present invention also refers to the related pharmaceutical compositions containing thereof.

TITLE	OWNER
Pharmaceutical composition for the treatment of ischemic ictus	Gentium S.p.A./First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: Use of Defibrotide in the treatment of the cerebral stroke, in particular in the acute stage and immediately post-critic of the ischemic ictus.

TITLE	OWNER
Stable aqueous suspension of Mesalazine	Gentium S.p.A./First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: A pharmaceutical composition in the form of an aqueous suspension, comprising Mesalazine colloidal cellulose in an amount between 1.2 to 1.6% w/w.

TITLE	OWNER
Cathepsin G - inhibiting aptamers	Gentium S.p.A./First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: Cathepsin G-inhibiting aptamers comprising oligonucleotides selected from the group consisting of the consensus sequences: GGN1-7GGN8-14GGN1-6GGN1-7GGN1-6GG, GGN10-13GGN1-5GGN1-5GGN3-6GGN2-7GG and the sequence GGGTTGAGGGTGGATTACGCCACGTGGAGCTCGGATCCACACATCCAGG, wherein N represents nucleotides and the figures represent the number of possible nucleotides at that site, said cathepsin G-inhibiting aptamers are suggested as medicament.

TITLE	OWNER
Use of Sulglicotide for the treatment of the mucositis	Gentium S.p.A.

TITLE	OWNER
Oligodeoxyribonucleotides having anti-ischemic activity and methods of preparation	Gentium S.p.A./First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: New oligodeoxyribonucleotides of animal origin, having a molecular weight comprised between 4,000 and 10,000 daltons, that can be obtained by fractionation of polydeoxyribonucleotides or otherwise by chemical or enzymatic depolymerization of high molecular weight deoxyribonucleic acids. The new compounds are endowed with a significant anti-ischemic activity.

TITLE	OWNER
Use of complex among cationic liposomes and polydeoxyribonucleotides as medicaments	Gentium S.p.A./ First Owner Crinos Industria Farmacobiologica S.p.A.

SUBJECT MATTER: Use as medicament, specifically as anti-inflammatory, of complexes formed by cationic liposomes and polydeoxyribonucleotides having a molecular weight in the range 7,000-60,000 daltons, obtainable by depolymerization of nucleic acids, wherein in said complexes the polydeoxyribonucleotides are located on an outer surface of the liposome.

TITLE	OWNER
Pharmaceutical formulation having anti-tumour activity	Gentium S.p.A.

Source: Gentium S.p.A.

Management, Board of Directors, and Scientific Advisory Board

Management

Table 3 summarizes Gentium's key executive management figures, followed by brief biographies.

Table 3
Gentium S.p.A.
EXECUTIVE MANAGEMENT

Dr. Laura Ferro	President and Chief Executive Officer
Cary M. Grossman	Chief Operating Officer
Gary Gemignani	Chief Financial Officer
Dr. Massimo Iacobelli	Senior Vice President, Scientific Director
Salvatore Calabrese	Vice President, Finance and Secretary

Source: Gentium S.p.A.

Dr. Laura Ferro, President and Chief Executive Officer

Dr. Laura Ferro has served as Gentium's president and chief executive officer (CEO) and one of the Company's directors since 1991. Dr. Ferro is also the president and CEO of the Company's largest shareholder, FinSirton. She also serves as vice president of Sirton, a subsidiary of FinSirton that specializes in manufacturing pharmaceutical products. Dr. Ferro is additionally a member of the Board of Directors of FinSirton, Sirton, and Foltene. From 1991 to 1997, Dr. Ferro held various executive positions at Sirton, including CEO and chairperson of the research and development unit. Prior to that, Dr. Ferro was a practicing physician for 15 years. Dr. Ferro is the chairperson of the research committee of Europharm, the European Association of Small and Medium-Sized Pharmaceutical Companies, and is a member of the executive committee of Farmindustria, an Italian pharmaceutical industry group. She is also the president of the Gianfranco Ferro Foundation, a not-for-profit Italian organization with the mission of stimulating research, education, and dissemination of information on the correct use of medications and adverse events of medicines. Dr. Ferro received her M.D. and Ph.D. degrees from the University of Milan, and a MBA from Bocconi University in Milan in 1994. Dr. Ferro is a licensed physician. She was certified in psychiatry at the University of Milan in 1981, and in Clinical Pharmacology at the University of Milan in 1994.

Cary M. Grossman, Chief Operating Officer

Mr. Cary M. Grossman is chief operating officer, a position he was appointed to on June 1, 2006. Prior to this, Mr. Grossman served as Gentium's executive vice president and chief financial officer (CFO) since August 2004. He is also the chairman and chief executive officer (CEO) of Coastal Bancshares Acquisition Corp., a special purpose acquisition company. Mr. Grossman is a director of Sand Hill IT Security Acquisition Corp., a special purpose acquisition company, and INX Inc., which provides network infrastructure and Internet protocol telephony solutions. From 2002 until 2003, he served as the executive vice president and CFO of US Liquids, Inc., an environmental services company. Mr. Grossman left US Liquids, Inc. in 2003 as a result of the acquisition of three of its businesses by a private equity firm and was president and CEO of the acquiring company, ERP Environmental Services, until November 2003. From 1997 until 2002, Mr. Grossman served Pentacon, Inc., a provider of inventory management services and distributor of components to Fortune 50 original equipment manufacturers, as a board member and in several senior executive positions including chairman of the Board of Directors (2001-2002), acting CFO (2001-2002), and lead director (1998-2001). Pentacon and substantially all of its subsidiaries filed a Joint Chapter 11 Plan of Debtors in 2002. From 1991 until 2002, Mr. Grossman was the managing partner of McFarland, Grossman & Company, Inc., an investment banking and financial advisory firm he co-founded in 1991. Prior to that, Mr. Grossman practiced public accounting for 15 years. He earned a bachelor of business administration in accounting from the University of Texas, and is a certified public accountant (CPA).

Gary Gemignani, Chief Financial Officer

Mr. Gary Gemignani was appointed chief financial officer on June 1, 2006. He began his career in public accounting, joining Arthur Andersen in 1986, where he was employed for approximately seven years. His subsequent experience includes approximately six years in the pharmaceutical industry with Wyeth (WYE-NYSE) and Novartis AG (NVS-NYSE) and approximately six years with Prudential Financial, Inc. (PRU-NYSE) in various senior finance, financial reporting, and accounting roles.

Dr. Massimo Iacobelli, Senior Vice President, Scientific Director

Dr. Massimo Iacobelli has served as Gentium's senior vice president, scientific director since 2002 and as Gentium's vice president, clinical development and chief medical officer from 1995 to 2002. From 1990 to 1994, he was the senior vice president, medical marketing, at Sirton. From 1988 to 1989, Dr. Iacobelli directed the Drug Safety Department at Bayer S.p.A. He received a medical degree from Universit`a degli Studi, Napoli, Italy.

Salvatore Calabrese, Vice President, Finance and Secretary

Mr. Salvatore Calabrese has served as Gentium's vice president, finance and secretary since February 2005. From December 2003 until February 2005, he was an accounting and finance manager for Novuspharma, S.p.A., a development-stage biopharmaceutical company focused on the discovery and development of cancer drugs and a subsidiary of Cell Therapeutics, Inc. (CTIC-NASDAQ). He reported to the CFO of Cell Therapeutics and was responsible for cost containment, budgeting, financial reporting, and the implementation of Sarbanes-Oxley compliance. From September 1996 until November 2003, Mr. Calabrese was employed by PricewaterhouseCoopers as an accountant and was a manager in Assurance Business Advisory Services at the time of departure. From October 2000 to June 2003, Mr. Calabrese worked in the Boston office of PricewaterhouseCoopers. He earned a Bachelors' Degree in economics at the University of Messina and a Masters Degree in accounting, audit and financial control at the University of Pavia. He is also a chartered accountant in the Republic of Italy.

Board of Directors

Decisions regarding strategic deployment of Gentium's assets are made by its Board of Directors and are based upon information and advice presented by management and advisors to the Board. Table 4 provides a summary of Gentium's board members, followed by brief biographies.

Table 4
Gentium S.p.A.
BOARD OF DIRECTORS

Dr. Laura Ferro	Chairman of the Board
Luca Breveglieri	Director
Gigliola Bertoglio	Director
Dr. Lee M. Nadler	Director
Dr. Andrea Zambon	Director
Dr. Kenneth Anderson	Director
Marco Codella	Director
David E. Kroin	Director

Source: Gentium S.p.A.

Dr. Laura Ferro

Biography on page 10.

Luca Breveglieri

Mr. Luca Breveglieri joined Gentium's Board in April 2006. Mr. Breveglieri is an Italian-qualified attorney and has been a partner of Breveglieri Verzini e Soci, an Italian law firm, since 2000. From 1982 to 2000, Mr. Breveglieri was the founding partner of Breveglieri e Associati. Mr. Breveglieri is an Italian certified public accountant. Mr. Breveglieri received a degree in law from Universita degli Studi, Pisa, Italy, in 1977.

Gigliola Bertoglio

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

Dr. Lee M. Nadler

Dr. Lee M. Nadler has served as one of Gentium's directors since June 2005. Dr. Nadler is the senior vice president of experimental medicine at Harvard University's Dana-Farber Cancer Institute and a professor of Medicine at Harvard University. He joined the staff of the Dana-Farber Cancer Institute in 1977, and was promoted to the faculty in 1980. He served as chief and chair of several departments, including serving as the first chairperson of the Dana-Farber Cancer Institute's Department of Adult Oncology. Dr. Nadler received a medical degree from Harvard Medical School in 1973.

Dr. Andrea Zambon

Dr. Andrea Zambon has served as one of Gentium's directors since June 2005. Dr. Zambon was a co-founder and president of a web-based company, OKSalute S.p.A., serving the medical community from 2000 until 2002. From 2000 until 2004, he was president of Zambon, S.p.A, the holding company of Zambon Group, S.p.A., an Italian pharmaceutical and chemical company that operates in 19 countries in Europe, North and South America, and Asia. From 1989 until 1999, he served in various capacities at Zambon Group S.p.A., including president and CEO from 1993 to 1999, managing director from 1991 to 1993, managing director of Zambon Research, S.p.A. in 1990, a research subsidiary of Zambon Research S.p.A., and manager of the international regulatory affairs unit in 1989. From 1988 to 1989, Dr. Zambon was employed by Smith Kline & Beckman in various departments, including clinical development, regulatory affairs, and market research, for three new chemical businesses. From 1986 to 1987, he was employed by Zambon Group, S.p.A., where he helped establish its research and development division. He has served on numerous corporate and industry association boards. Dr. Zambon earned a medical degree from the University of Milan Medical School.

Dr. Kenneth Anderson

Dr. Kenneth Anderson has served as one of Gentium's directors since June 2005. Dr. Anderson has been a professor at the Dana-Farber Cancer Institute, Cancer Research and Clinical Care, since 1980, a professor of medicine at Harvard Medical School since 2000 and a Kraft Family professor of medicine at

Harvard Medical School since 2002. He has been the chief of the Division of Hematologic Neoplasia at the Dana-Farber Cancer Institute since 2002, the vice chair of the Joint Program in Transfusion Medicine at Harvard Medical School since 2000, the director of the Jerome Lipper Multiple Myeloma Center at the Dana-Farber Cancer Institute since 2000, the associate medical director of Brigham and Women's Hospital Blood Bank since 1998, and an attending physician at the Bone Marrow Transplantation Service at Brigham and Women's Hospital since 1997. Dr. Anderson is a member of 11 medical and scientific societies and on the editorial boards of 11 medical and scientific journals. He received a bachelors' degree, summa cum laude, from Boston University in 1973, a M.D. from Johns Hopkins University School of Medicine in 1977, and a masters degree in Art from Harvard University in 2000.

Marco Codella

Mr. Marco Codella has served as one of Gentium's directors since June 2005. He has been the CFO of Sigma Tau Industrie Farmaceutiche Riunite S.p.A., since May 1999 and was a professor of economics and management accounting at University of Rome, La Spienza since 2001. From 1997 to 1999, Mr. Codella was the finance, IT, and Logistics Director of Crown Cork & Seal Italy S.p.A., an Italian subsidiary of Crown Holdings, Inc., a manufacturer of packaging products to consumer marketing companies. From 1994 to 1997, Mr. Codella was the finance and IT director of Crown Cork & Seal 95 Italy S.p.A. From 1990 to 1994, Mr. Codella held various finance positions at Digital Equipment Italia S.p.A., an Italian subsidiary of Digital Equipment Corporation, a computer company. From 1987 to 1990, Mr. Codella was the finance manager of an Italian subsidiary of Ampex Corporation, a provider of technology for acquisition, storage, and processing of visual information. From 1984 to 1987, Mr. Codella was an auditor at Deloitte, Haskins & Sells, an accounting firm. Mr. Codella is a director of Eubiotina Research S.p.A., Biosint S.p.A., Avantgarde S.p.A., SigmaTau Health Science S.p.A., Techogen S.p.A. and Kenton S.r.l., each of which is a subsidiary of Sigma Tau Finanziaria S.p.A., and Fonchim, a pension fund for chemical industry workers. Mr. Codella is an Italian certified public accountant. He graduated summa cum laude from Rome University in 1984 with a degree in economics.

David E. Kroin

David Kroin has served as a member of Gentium's Board of Directors since December 2005. Mr. Kroin has been the managing director of Great Point Partners, LLC, an asset management firm focusing in the healthcare industry, with an emphasis on life sciences, since September 2003. From December 1998 to September 2003, Mr. Kroin was a senior member of the healthcare group at J.H. Whitney & Co., an alternative-asset-management firm. From June 1997 to December 1998, Mr. Kroin worked as an analyst in the corporate finance and mergers and acquisitions group at Merrill Lynch & Co., Inc. Mr. Kroin graduated from the University of Michigan with a B.S. in actuarial mathematics in May 1997.

Scientific Advisory Board

Table 5 provides a summary of Gentium's Scientific Advisory Board, followed by biographies.

Table 5
Gentium S.p.A.
SCIENTIFIC ADVISORY BOARD

Dr. Lee M. Nadler	Chairman of the Board
Dr. Alessandro M. Gianni	Member
Professor Cy Stein, M.D. Ph.D.	Member
Peter Levitch	Member
Dr. Ralph B. D'Agostino, Sr. Ph.D.	Member
Dr. Stephen Fredd, M.D.	Member
Dr. Richard E. Champlin, M.D	Member
Dr. Kenneth Anderson	Member

Source: Gentium S.p.A.

Dr. Lee M. Nadler

Biography on page 12.

Dr. Alessandro M. Gianni

Dr. Alessandro M. Gianni is the head of the Bone Marrow Transplant Unit at The National Institute of Tumors of Milan, Italy. Dr. Gianni has been the director of the Department of Leukemias and Lymphomas of the Milan Cancer Institute since February 2004. Since 1998, he has been the director of the chair of Medical Oncology at the University of Milan and has been a professor at the University of Milan since 1978. Since 1992, he has been the director of several different units of the Division of Medical Oncology at the Milan Cancer Institute. He is a member of the European Group for Bone Marrow Transplantation, the American Association for Cancer Research, the American Society of Clinical Oncology, the Italian Society of Experimental Hematology, the European Hematology Association, and the International Society of Hematotherapy and Graft Engineering. He has authored or co-authored more than 250 publications in peer-reviewed journals. Dr. Gianni graduated from the Liceo Classico Alessandro Manzoni, Milan in 1962 and obtained his medical degree, magna cum laude, from the University of Milan in 1968.

Professor Cy Stein, M.D. Ph.D.

Professor Cy Stein, M.D. Ph.D., is the head of Medical Genitourinary Oncology and professor of Medicine, Urology, and Molecular Pharmacology at the Albert Einstein College of Medicine, New York. He also serves as an attending physician at the Montefiore Medical Center and is a Diplomate of nearly 20 years standing of both the American Board of Internal Medicine and the American Board of Oncology. Professor Stein has been a director of CytoGenix, Inc. (CYGX.OB-OTC.BB), a biomedical research and development company, since 2003. Professor Stein has been involved for the past 15 years with preclinical and clinical trials of nucleic acid therapies for cancers, with increasing emphasis in recent years on RNA interference. Professor Stein received a bachelor of arts from Brown University in 1974, a Ph.D. in organic chemistry in 1978 from Stanford University, and a Medical Degree from Albert Einstein College of Medicine in 1982.

Peter Levitch

Mr. Peter Levitch has been president of Peter Levitch & Associates (PLA), an independent consulting firm to health professionals, since 1981, providing guidance in the development of pharmaceuticals, medical devices, biologics, and diagnostics. The primary focus of PLA is bringing products through the clinical evaluation and FDA regulatory approval phases. Mr. Levitch has participated in over 250 FDA applications as well as a number of marketing applications for drugs, biologicals, and medical devices. Mr. Levitch has worked with such companies as Amgen Inc. (AMGN-NASDAQ), Genentech Inc. (DNA-NYSE), Centocor, Inc., Cytogen Hybritech/Eli Lilly & Company (LLY-NYSE), Baxter International Inc. (BAX-NYSE), Monsanto Co. (MON-NYSE), Becton, Dickenson, Company (BDX-NYSE), and Seragen, among many others. From 1980 to 1981, Mr. Levitch was vice president, clinical and regulatory affairs for Oxford Research International Corp. From 1969 to 1980 he was employed by Ortho Diagnostics, Inc., a division of Johnson & Johnson (JNJ-NYSE), first as manager of clinical research and, from 1973 to 1980, as director of regulatory and clinical affairs. Mr. Levitch has authored or co-authored numerous articles and abstracts, including “Preparing an IND for New Drugs,” “Phase I Clinical Study of Gamma Interferons”, and “Gaining FDA Approval of Biotechnology Derived Products.” He has conducted lectures on such topics as “Preparing INDs and NDAs and Managing Clinical Research,” “Good Clinical Practices,” “Conducting FDA Meetings,” and “FDA Approvable Indications,” among many others. Mr. Levitch earned a B.A. in Zoology-Chemistry from Hofstra University in 1954 and a M.A. in physiology from Hofstra University in 1957.

Dr. Ralph B. D’Agostino, Sr., Ph.D.

Dr. Ralph B. D’Agostino, Sr., Ph.D. has been a professor of mathematics/statistics at Boston University since 1977 and a professor of public health at Boston University, School of Public Health, Department of Epidemiology and Biostatistics since 1982. He has been the editor of statistics in medicine since 1998. Dr. D’Agostino is also an associate editor of *American Journal of Epidemiology*, and on the editorial board

of *Current Therapeutic Research* and the *Journal of Hypertension*. He has been the director of the Statistics and Consulting Unit at Boston University and director of Data Management and Statistics at the Framingham Study. Dr. D'Agostino has served as an expert consultant to the FDA since 1974. He is a fellow of the American Statistical Association and the Cardiovascular Epidemiology section of the American Heart Association. He has twice, in 1981 and 1995, received the FDA Commissioner's Special Citation. He received an A.B. in Mathematics, summa cum laude, from Boston University in 1962, a A.M. in Mathematics from Boston University in 1964, and a Ph.D. in Mathematical Statistics from Harvard University in 1968.

Dr. Stephen Fredd, M.D.

Dr. Stephen Fredd, M.D. has been a consultant to the pharmaceutical industry since 2002. From 1980 to 2002, Dr. Fredd was the deputy director of the Division of Cardi-Renal Drugs of the Center for Drug Evaluation and Research at the FDA. From 1987 to 1997, he was the director and founder of the Division of Gastrointestinal and Coagulation Drugs of the Center for Drug Evaluation and Research (CDER) at the FDA. From 1982 to 1987, Dr. Fredd was a medical officer and the acting director of the Officer of Orphan Products Development of the Office of the Commissioner at the FDA. From 1980 to 1982, he was a medical officer at the Division of Antinflammatory, Oncological, and Radiopharmaceutical Drugs of the Center for Drug Evaluation and Research at the FDA. From 1965 to 1980, Dr. Fredd was a privately practicing doctor of internal medicine. From 1977 to 1980, he was an assistant professor of medicine at George Washington University Medical Center, and from 1965 to 1977, he was an instructor in Medicine at New York University Medical Center. Dr. Fredd received FDA Awards of Merit in 1989 and 1997, FDA Commendable Service Awards in 1987 and 1998, and the FDA Commissioner's Special Citation in 1989. Dr. Fredd received an A.B., magna cum laude, from Princeton University in 1955 and a M.D. from New York University Medical Center in 1959.

Dr. Richard E. Champlin, M.D

Dr. Champlin is professor of medicine and chairman of the department of Blood and Marrow Transplantation at the University of Texas M.D. Anderson Cancer Center. He graduated from the University of Chicago's Pritzker School of Medicine, before completing post-graduate training at the UCLA School of Medicine, Los Angeles. Professor Champlin has been an assistant and associate professor of medicine and directed the Transplantation Biology Program at the UCLA Center for the Health Sciences before assuming his current post. He chairs the Working Committee on Alternative Donors and Cell Sources of the International Bone Marrow Transplant Registry. He was the founding president of the American Society of Blood and Marrow Transplantation and past president of the Council for Donor, Transplant, and Collection Centers for the National Marrow Donor Program. He is vice president of the Foundation for Accreditation of Hematocellular Therapy and a member of the Biologic Response Modifiers Advisory Board for the FDA and the Hematology Board, American Board of Internal Medicine. Dr. Champlin is a member of several scientific societies and serves on the editorial boards of *Blood*, *Bone Marrow Transplantation*, and *Journal of Hematotherapy*. His research interests include the investigation of non-myeloablative conditioning prior to allogeneic transplantation and the use of allogeneic and autologous hematopoietic transplantation for hematologic malignancies and selected solid tumors.

Dr. Ken Anderson, M.D.

Biography on pages 12-13.

Core Story

Gentium S.p.A. ("Gentium" or "the Company") is a biopharmaceutical company focused on the research, discovery, development, and manufacturing of drugs to treat and prevent a variety of vascular diseases and conditions related to cancer and cancer treatments. Gentium's founding company received approval in 1986 to sell a drug called Defibrotide in Italy to treat deep vein thrombosis (DVT); the indication was changed in 1993 to both treat and prevent vascular disease with risk of thrombosis.

Currently, Gentium is developing Defibrotide for a variety of uses, including to treat and prevent hepatic veno-occlusive disease (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 multi-organ failure (MOF) is a potentially devastating complication with a survival rate after 100 days of only approximately 20%. There is no drug approved by the U.S. FDA or European regulators to treat or prevent VOD; thus Defibrotide could become an important product should it receive approval and reach the market.

Due to the historically low survival rate and lack of treatments for this condition, there is an immediate need for a drug to treat VOD with MOF. Gentium's application for FDA Fast Track designation for Defibrotide to treat VOD with MOF occurring after stem cell transplantation (SCT) by means of injection was approved in May 2005. The Fast Track designation program is designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Reasons for Gentium being granted Fast Track are summarized in Table 6. At this point, the approval process for Defibrotide for this use remains dependent upon the successful completion of clinical trials.

Table 6
Gentium S.p.A.
REASONS GRANTED FAST TRACK

- Veno-occlusive disease (VOD) of the liver following bone marrow transplantation is a serious disease
- There have been no drugs approved in the U.S. for treatment of severe hepatic VOD in hemotopoetic stem cell recipients
- Clinical studies suggest that Defibrotide may be useful for the treatment of VOD in hemotopoetic stem cell recipients

Source: Gentium S.p.A.

Additional potential indications for Defibrotide may include treatment of multiple myeloma, treatment of renal disorders, and prevention of DVT. Gentium is also developing other drugs, such as oligotide, which may protect against damage to blood vessel wall cells caused by a particular cancer treatment, and Gen 301, which may prevent and treat oral ulcers that often develop during and after cancer treatments.

In order to achieve its development goals, the Company intends to enter into collaborative and strategic agreements to assist in its development, manufacturing, and marketing efforts. To date, Gentium has licensed the right to market Defibrotide in North America, Central America, and South America (upon regulatory approval to treat VOD) to Sigma-Tau Pharmaceuticals, Inc. Additionally, the Company sold the rights to develop and sell its formulation of mesalazine in Canada, (upon approval by Health Canada), and the U.S. (upon FDA approval), to Axcan Pharma, Inc. Furthermore, the Company licensed the right to distribute mesalazine in Italy to Crinos. Crinos also markets Defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement with Gentium. Details of each of these strategic alliances are provided on pages 29-30.

Gentium currently manufactures Defibrotide, calcium heparin, and sulglicotide at its manufacturing facility near Como, Italy. Gentium also leases affiliate Sirton's facility to manufacture urokinase. Urokinase and calcium heparin are active pharmaceutical ingredients used to make other drugs. Sulglicotide is used to treat peptic ulcers. The Company has also developed a formulation of the drug, mesalazine, to treat inflammatory bowel disease (IBD). Almost all of Gentium's revenues during the past three years have been generated from sales of these products to Sirton.

MARKET OVERVIEW

Cancer is an abnormal cell produced by the body that engages in uncontrolled growth by escaping the body's immune system. If the spread is not controlled, it can result in death. Since abnormal cells are originally produced from within the body, they are not recognized as foreign. This means that the body does not respond through the typical immune response of destroying this foreign substance. Cancer cells that escape the body's immune system can proliferate in a variety of ways, invading and destroying healthy human tissue and eventually causing cell death.

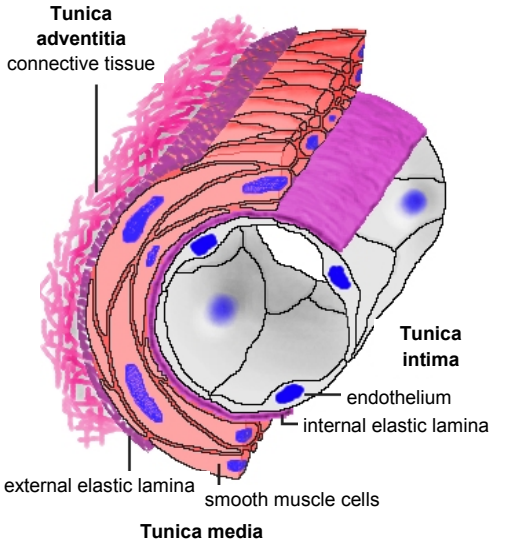
Most cancer patients receive one or more of the following therapies: chemotherapy, radiation therapy, and hormone therapy. These treatments are used to target and kill cancer cells. In some cases, the therapy treats the cancer directly; in other cases, it is administered to prepare the patient for a stem cell or bone marrow transplant, which is another method used to treat cancer or other diseases. While therapies are designed to kill off the cancer cells, they can unfortunately carry significant negative side effects, including damage to the cells that line the blood vessel walls, which can lead to various disorders of the vascular system. So much damage, in fact, that some patients may not be able to continue with cancer treatments because they develop these vascular system complications. Other patients believed to be at "high risk" for developing these vascular system complications may not receive optimal cancer treatments or any treatment at all due to these complications.

The American Cancer Society estimates that in 2006, approximately 1.4 million new patients in the U.S. will be diagnosed with cancer and that there will be approximately 564,830 deaths attributable to cancer. New cases and deaths due to specific types of cancer are illustrated in Table 7 (page 18).

Veno-Occlusive Disease (VOD)

Veno-occlusive disease (VOD) is a disorder of the vascular system that can result from commonly used cancer therapies such as chemotherapy, radiation therapy, and hormone therapy. Specifically, the aggressive pre-conditioning regimen that precedes stem-cell transplantation can expose a patient to high levels of various chemotherapies, which travel to the microvessels of the liver with the intent of being filtered out though circulation. These microvessels in turn experience extreme concentrations of **cytotoxic** drugs, which cause extensive damage to the endothelial lining of these vessels. Figure 3 provides an illustration of the vascular system.

Figure 3
VASCULAR SYSTEM DISORDERS



Source: Gentium S.p.A.

The natural response by the body is to clot the sites of injury. Such a response results in **occlusion** of these small-diameter vessels and, ultimately, liver failure. Liver failure allows for the buildup of toxins in the blood, compromising the function of the kidneys, lungs, and heart, leading to multi-organ failure (MOF) and death. The prognosis for patients with severe VOD with MOF is grim, where VOD typically occurs within 30 days of stem cell transplantation, and the survival rate for patients with VOD is 20% or less following 100 days.

The International Bone Marrow Transplant Registry has estimated that approximately 45,000 people in the U.S. and Europe received blood and bone marrow transplants in 2002. May of these patients are being treated for hematologic cancers. Based on Gentium's review of more than 200 published papers, it is estimated that up to 20% of patients who receive blood and bone marrow transplants develop VOD. Approximately one-third of these patients progress to severe VOD and approximately 80% of the patients who develop severe VOD die within 100 days of stem cell transplantation without treatment. Thus, VOD is considered one of the most important and challenging complications of stem cell transplantation.

Table 7
ESTIMATED NEW CANCER CASES AND DEATHS FOR ALL SITES, 2006*

	Estimated New Cases			Estimated Deaths		
	Both Sexes	**Male**	**Female**	**Both Sexes**	**Male**	**Female**
All Sites	1,399,790	720,280	679,510	564,830	291,270	273,560
Oral cavity & Pharynx	30,990	20,180	10,810	7,430	5,050	2,380
Tongue	9,040	5,870	3,170	1,780	1,150	630
Mouth	10,230	5,440	4,790	1,870	1,100	770
Pharynx	8,950	6,820	2,130	2,110	1,540	570
Other oral cavity	2,770	2,050	720	1,670	1,260	410
Digestive System	263,060	137,630	125,430	136,180	75,210	60,970
Esophagus	14,550	11,260	3,290	13,770	10,730	3,040
Stomach	22,280	13,400	8,880	11,430	6,690	4,740
Small Intestine	6,170	3,160	3,010	1,070	560	510
Colon	106,680	49,220	57,460	55,170	27,870	27,300
Rectum	41,930	23,580	18,350	0	0	0
Anus, anal canal, & anorectum	4,660	1,910	2,750	660	220	440
Liver & intrahepatic bile duct	18,510	12,600	5,910	16,200	10,840	5,360
Gallbladder & other billiary	8,570	3,720	4,850	3,260	1,280	1,980
Pancreas	33,730	17,150	16,580	32,300	16,090	16,210
Other digestive organs	5,980	1,630	4,350	2,320	930	1,390
Respiratory System	186,370	101,900	84,470	167,050	93,820	73,230
Larynx	9,510	7,700	1,810	3,740	2,950	790
Lung & bronchus	174,470	92,700	81,770	162,460	90,330	72,130
Other respiratory organs	2,390	1,500	890	850	540	310
Bones & Joints	2,760	1,500	1,260	1,260	730	530
Soft Tissue (including heart)	9,530	5,720	3,810	3,500	1,830	1,670
Skin (excluding basal & squamous)	68,780	38,360	30,420	10,710	6,990	3,720
Melanoma-skin	62,190	34,260	27,930	7,910	5,020	2,890
Other nonepithelial skin	6,590	4,100	2,490	2,800	1,970	830
Breast	214,640	1,720	212,920	41,430	460	40,970
Genital system	321,490	244,240	77,250	56,060	28,000	28,060
Uterine cervix	9,710	0	9,710	3,700	0	3,700
Uterine corpus	41,200	0	41,200	7,350	0	7,350
Ovary	20,180	0	20,180	15,310	0	15,310
Vulva	3,740	0	3,740	880	0	880
Vaginal & other genital, female	2,420	0	2,420	820	0	820
Prostate	234,460	234,460	0	27,350	27,350	0
Testis	8,250	8,250	0	370	370	0
Penis & other genital, male	1,530	1,530	0	280	280	0
Urinary System	102,740	70,940	31,800	26,670	17,530	9,140
Urinary bladder	61,420	44,690	16,730	13,060	8,990	4,070
Kidney & renal pelvis	38,890	24,650	14,240	12,840	8,130	4,710
Ureter & other urinary organ	2,430	1,600	830	770	410	360
Eye & orbit	2,360	1,230	1,130	230	110	120
Brain & other nervous system	18,820	10,730	8,090	12,820	7,260	5,560
Endocrine	32,260	8,690	23,570	2,290	1,020	1,270
Thyroid	30,180	7,590	22,590	1,500	630	870
Other endocrine	2,080	1,100	980	790	390	400
Lymphoma	66,670	34,870	31,800	20,330	10,770	9,560
Hodgkin's disease	7,800	4,190	3,610	1,490	770	720
Non-Hodgkin's	58,870	30,680	28,190	18,840	10,000	8,840
Multiple myeloma	16,570	9,250	7,320	11,310	5,680	5,630
Leukemia	35,070	20,000	15,070	22,280	12,470	9,810
Acute lymphocytic leukemia	3,930	2,150	1,780	1,490	900	590
Chronic lymphocytic leukemia	10,020	6,280	3,740	4,660	2,590	2,070
Acute myeloid leukemia	11,930	6,350	5,580	9,040	5,090	3,950
Chronic myeloid leukemia	4,500	2,550	1,950	600	300	300
Other leukemia	4,690	2,670	2,020	6,490	3,590	2,900
Other & unspecified primary sites‡	2,680	13,320	14,360	45,280	24,340	20,940

** Rounded to the nearest 10; excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. About 58,490 carcinoma in situ of the breast and 46,170 melanoma in situ will be newly diagnosed in 2005.*

‡ Estimated deaths for colon and rectum cancers are combined. More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificates.

Source: American Cancer Society, Inc. (2006).

Due to the suffering caused by VOD, large pharmacoeconomic costs, and high mortality rates, it is likely that doctors, with the appropriate and available treatment, would intervene at the earliest point possible should such a treatment become available for use as a prophylaxis for VOD (an indication for which Gentium currently retains all worldwide rights).

Risk Factors

In addition to being caused by cancer treatments, other risk factors that could contribute to the development of VOD due to stem cell transplantation, according to the Mayo Foundation for Medical Education and Research, are outlined in Table 8.

Table 8

RISK FACTORS FOR VOD

PRE-TRANSPLANTATION FACTORS
– Preexisting liver dysfunction (elevated transaminases, fibrosis or cirrhosis, low pseudocholinesterase level or low albumin level pretransplantation)
– Presence of hepatic metastases
– Advanced age
– Prior radiation treatment of the liver
– Use of vancomycin or acyclovir in the pretransplantation period
– Previous stem cell transplantation
– Prior therapy with gemtuzumab ozogamicin (Mylotarg)
– Viral hepatitis C
– Decreased protein C
– Factor V Leiden mutation, prothrombin 20210 mutation
– Busulfan for conditioning, especially when area under the curve is >1500 µmol · min−1· L−1 and combined with cyclophosphamide
TRANSPLANTATION-RELATED FACTORS
– High-dose conditioning regimens
– Allogeneic transplantation (compared with autologous transplantation)
– Use of norethisterone
– Grafts from unrelated donors or related HLA mismatched transplants
– Methotrexate as part of graft-vs-host disease prophylaxis
– Cytomegalovirus infection
– Total body irradiation, especially combined with cyclophosphamide (depending on total dose and fractionation)

Source: Mayo Clin Proc. 2003;78:589-598, 2003 Mayo Foundation for Medical Education and Research.

Symptoms

Symptoms of VOD may begin suddenly, where blockage of the small veins causes the liver to swell with blood, making the abdomen tender to the touch. Fluid may leak from the surface of the swollen liver and accumulate in the abdomen, producing a condition called **ascites**. **Jaundice** (a yellowish discoloration of the skin and the whites of the eyes) may also occur.

Prognosis and Treatment

The prognosis for patients with VOD depends on the extent of damage and whether the injury (exposure to a toxin) recurs. Typically, in a blockage that disappears quickly, the person recovers regardless of any treatment. However, approximately 25% of people with VOD die of liver failure and/or MOF within about three months. There is no specific treatment for the blocked veins. In cases caused by the ingestion of a toxic substance, such as a chemotherapeutic agent, the only treatment is to discontinue taking that substance. There currently are no approved therapies to specifically treat or prevent VOD.

ADVANCED PIPELINE CANDIDATES

Gentium has experience developing and manufacturing pharmaceuticals derived from DNA extracted from natural sources as well as pharmaceuticals which are synthetic oligonucleotides. The Company's most advanced pipeline candidates utilize Defibrotide to treat and prevent VOD as well as to treat multiple myeloma. An illustration of the Company's current product pipeline is provided in Table 9 followed by detailed descriptions of each of the key areas of focus for the Company.

Table 9
Gentium S.p.A.
PRODUCT PIPELINE

Candidate and Indication	Development/Preclinical	Phase I	Phase II	Phase III
Mesalazine for treatment of IBD				
Defibrotide for treatment of VOD (US)				
Defibrotide to prevent VOD in children (EU)				
Defibrotide to prevent VOD/TMA in adults (EU)				
Defibrotide to treat of Multiple Myeloma (EU)				
Defibrotide (oral) for Deep Vein Thrombosis (EU)				

Source: Gentium S.p.A.

Defibrotide to Treat VOD with Multiple-Organ Failure (MOF) — Lead Product

Gentium's lead product candidate is Defibrotide to treat VOD—specifically VOD with multiple-organ failure (MOF). Defibrotide is a single-stranded polydeoxyribonucleotide that may protect the vascular endothelial cells, particularly those of small vessels, from damage and activation. After binding to endothelial cells, Defibrotide has shown to decrease cell adhesion and pro-coagulant activity of activated endothelial cells, and increase the fibrinolytic potential of endothelial cells. The effects of the drug have shown to be predominately local within the vascular bed, with no significant effect on systemic coagulation.

It is believed that the extensive beneficial pharmacological effects of Defibrotide are due to its anti-thrombotic, anti-inflammatory, and anti-ischemic properties. Given the rare nature of VOD, the FDA has designated Defibrotide as an orphan drug to treat VOD in May 2003 and in July 2004, the Commission of the European Communities as well designated Defibrotide to treat and prevent VOD as an orphan medicinal product (similar to orphan drug status by the FDA).

The British Journal of Hematology (2000)

In 2000, the *British Journal of Hematology* published results of a 40 patient "compassionate use" study of Defibrotide to treat VOD conducted in 19 centers across Europe from December 1997 to June 1999. In this study, 19 patients, or 47.5%, survived more than 100 days. The publication indicated that four of the 19 patients who survived more than 100 days subsequently died. 28 patients were judged likely to die or had evidence of MOF. The 100 day survival rate is a milestone generally used to determine transplant success. This publication stated that Defibrotide was generally administered safely with no significant side-effects.

The Journal of the American Society of Hematology (2002)

In 2002, results from 88 patients with VOD with MOF following stem cell transplants who were treated with Defibrotide from March 1995 to May 2001 were published in *Blood*, the *Journal of the American Society of Hematology*. This publication reported data on 19 patients treated under individual Investigational New Drug Applications (IND) and on a subsequent 69 patient multi-center Phase I/II clinical trial that was conducted under an IND filed by a Dana-Farber investigator.

The primary goal of the trial was to assess the potential effectiveness of Defibrotide and its side effects (if any). All patients in the trial received Defibrotide on an emergency basis. This publication stated that 31 patients, or 35.2%, of those patients survived at least 100 days after stem cell transplant with minimal adverse side effects, primarily transient mild hypotension. 13 of those 31 patients who had survived more than 100 days had died by October 2001 (the latest date for which survival information was available). No mortality from VOD or other toxicity related to the cancer treatment was seen more than 134 days after treatment with Defibrotide, with the most common cause of later death being relapse.

Phase II Clinical Trial (U.S.)

The Dana-Farber investigator also sponsored, under its IND, a Phase II clinical trial in the U.S. of Defibrotide. This trial enrolled 145 stem cell transplant patients with VOD with MOF at eight cancer centers. Funded by Gentium and $525,000 in grants from the orphan drug division of the FDA, the purpose of this trial was to evaluate the effectiveness of Defibrotide, including the effect of the drug on the survival rate of patients with VOD with MOF, the effective dosage, and potential adverse side effects.

The Dana-Farber investigator presented the results from this multicenter Phase II clinical trial at the 47th Annual Meeting of the American Society of Hematology on December 12, 2005. Results show that the survival rate after 100 days for the 142 patients for whom that information was available was approximately 39% after 100 days with minimal adverse events as compared to the historical 100 day survival rate of approximately 20%. Survival rate information after 100 days is not available.

Phase III Clinical Trial (U.S.)

As of April 2006, The Institutional Review Board (IRB) of the Dana-Farber/Harvard Cancer Center of Boston, Mass., which is also the IRB for Dana-Farber Cancer Institute, Massachusetts General Hospital, Beth Israel Deaconess Medical Center, and The Children's Hospital, has given its approval to participate in a Phase III trial. All four of these institutions are expected to participate in the trial, which is expected to be open for enrollment of patients by the end of May 2006.

Fast Track Process

The FDA has approved Gentium's application for "Fast Track" designation for Defibrotide to treat VOD with MOF occurring after stem cell transplantation. The FDA approval process for Defibrotide for this use remains dependent upon the successful completion of clinical trials. Gentium is sponsoring and expects to conduct the Phase III clinical trial and any additional clinical trials required by the FDA under its own IND (which was submitted to the FDA in December 2003).

A summary of the Company's clinical experience in treating severe VOD in patients with MOF using Defibrotide is provided in Table 10 (page 22), followed by an expected timeline, as made available by Gentium, of the development both in the U.S. as well as Europe in Table 11 (page 22).

Table 10
Gentium S.p.A.
DEFIBROTIDE DATA: TREATMENT OF VOD
Clinical Experience in Severe VOD/MOF

Study	No. of Patients	% Surviving 100+ days
British Journal of Hematology, 2000	40	47.5%
Blood, the Journal of the American Society of Hematology, 2002	88	35.2%
Phase II, dose finding study in the U.S.	140	40.0%
Phase III trial in U.S. to treat severe VOD (20+ centers expected)	80	N/A

– Defibrotide increases chance for complete response and full recovery
– No significant toxicity
– Supported by grants from FDA Office of Orphan Products Development
– Fast track designation – May 2005
– Final U.S. Phase II data and analysis: presentation at ASH-Dec '05
– U.S. Phase III study of 80 patients blinded to historical control open for enrolment Q2 '06

Source: Gentium S.p.A.

Table 11
Gentium S.p.A.
ESTIMATED DEVELOPMENT TIMELINE FOR DEFIBROTIDE (U.S. AND EU)

VOD IN THE U.S.	
Q4 '05	Final U.S. Phase II Data Presented at ASH
Q2 '06	Initiated U.S. Phase III Trial to Treat Severe VOD
2H '07	Complete Enrollment of U.S. Phase III Trial
2H '07	Phase III Data Available
2H '07	Begin VOD Prevention Trial
Q4 '07	Submit File for NDA
1H '08	Approval of Defibrotide to Treat of Severe VOD
Q4 '08	Prevention Trial Data Available
Q4 '08	File for Prevention Approval
VOD IN THE EU	
Q1 '06	Initiated EU Phase II/III Trial to Prevent VOD in Children
Q2 '06	Begin Enrollment of EU Phase II/III Trial in Adults-VOD/TAM Prevention
1H '08	Complete Enrollment of Pediatric Study in EU
1H '08	Post U.S. Approval to Treat Severe VOD, File for EU Approval to Treat Severe VOD
2H '08	Complete Enrollment of EU Adult Study
2H '08	Pediatric Trial Complete and Data Available
2H '08	Adult Trial Complete and Data Available
Q4 '08	File for EU Approval to Prevent VOD in Children
Q1 '09	File for EU Approval to Prevent VOD/TAM in Adults
1H '09	EU Approval of Defibrotide to Prevent VOD in Children and Adults

Source: Gentium S.p.A.

Financial Implications

It is estimated that the cost of stem cell transplantation approximates $100,000-$250,000, though costs can reach up to $400,000 or more should complications arise. Developing VOD clearly impedes the success of treatments. The average cost of treating a patient with VOD without Defibrotide is approximately $40,000 (which includes supportive care only). This includes the initial hospital stay, an estimated additional hospital stay of 3-14 days; as well as 7-14 days should a patient need to be readmitted. Having a treatment that could avoid VOD could potentially save between $11,400-$46,000 for severe cases (*Source: AHA Hospital Statistics, 2006*).

Since severe VOD is a disease with a high and critical unmet need, a treatment which holds the potential to improve patient outcomes creates high social and economic value. Other high priced drugs can only offer the promise to extend life. These treatments include therapies such as Avastin from Genentech Inc., Erbitux from Imclone Systems (IMCL-NASDAQ), and Campath from Genzyme Corp. (GENZ-NASDAQ) and distributed by Berlex Laboratories.

Defibrotide to Prevent VOD

In addition to treating VOD with MOF as described on pages 20-22, Gentium is also developing Defibrotide to prevent VOD (prophylaxis) for patients who are at risk for developing VOD. Based on research for VOD, many recipients of high doses of chemotherapy, radiation therapy, or hormone therapy or taking therapies to prepare for stem cell transplants, have an elevated risk of developing VOD. There is currently no FDA or European regulatory approved drugs to prevent patients from contracting VOD at this time.

A preliminary pilot clinical study in Switzerland by the University Hospital of Geneva on Defibrotide in patients at high risk of VOD suggested that Defibrotide may effectively and safely prevent VOD. The study tested patients who received stem cell transplants. Of the 52 transplant patients who received Defibrotide as a preventative agent, none of these patients developed VOD. This compares to 10 of 52 patients who underwent transplants in the same center before the study who developed VOD, and where three patients died.

Potential Side Effects

The study indicated that mild to moderate toxicity, such as mild nausea, fever, and abdominal cramps was documented, although the report stated that it was difficult to determine whether the toxicity was directly attributable to the Defibrotide, the chemotherapy preceding the stem cell transplants, or other drugs used during the stem cell transplants. Furthermore, it was not indicated how many patients experienced this toxicity.

Phase II/III Clinical Trial (Europe)

Gentium is sponsoring a Phase II/III clinical trial in Europe on Defibrotide to prevent VOD in children with the European Group for Blood and Marrow Transplantation (http://www.ebmt.org/), a not-for-profit scientific society. This study, which was initiated in January 2006, is expected to include 270 patients undergoing stem cell transplantation at 30 clinical sites in Europe and Israel and is to evaluate the ability of Defibrotide to prevent VOD. As of early April 2006, 11 centers were open for patient admission and 15 patients were enrolled.

The Company is also co-sponsoring with the European Group for Blood and Marrow Transplantation a second Phase II/III clinical trial in Europe on Defibrotide to prevent VOD and transplant associated **microangiopathy** in adults. This trial is expected to include approximately 370 patients enrolled by several centers in Europe beginning by the second quarter of 2006 who are to randomly receive either Defibrotide or a placebo. Gentium expects to initiate development of Defibrotide to prevent VOD in the U.S. by starting a clinical trial of this product candidate in early 2007. Table 12 (page 24) summarizes the development status of Defibrotide to prevent VOD.

Table 12
Gentium S.p.A.
DEFIBROTIDE DATA: PREVENTION OF VOD

Study	No. of Patients	No. of VOD	No. of Deaths
Defibrotide*	52	0	0
Control Group	52	10	3
Q4 '05 - Phase II/III in EU to prevent VOD in children	270 (30 centers, 12 open in May)		
Q2 '06 - Phase II/III in EU to prevent VOD and TAM in adults	370 (enrollments expected July '06)		

**NOTE: Study at University Hospital of Geneva 2004*

- Defibrotide demonstrated efficacy in preventing VOD
- Control Group matched historical control data
- Adult trial also addresses prevention of Transplant Associated Microangiopathy (TAM)
- Planning U.S. prevention trial for 2007

Source: Gentium S.p.A.

Case Study (Sara's Story)

Sara Shuckhart, an 18-year-old with Hodgkin's Disease received a bone-marrow transplant from the Fred Hutchinson Cancer Research Center at the Seattle Cancer Care Alliance (SCCA). Shortly after the transplant, Sara developed VOD. She was able to get involved in a clinical study with Defibrotide. For the next four weeks following her diagnosis, she received four intravenous doses of Defibrotide per day. Following the drug's administration, Sara's condition improved significantly. Sara's story is further described at http://www.fhcrc.org/patient/patient_stories/sara.html?&&printfriendly=yes 8/30/2005 my life.

Multiple Myeloma

Multiple myeloma is a rare form of cancer characterized by excessive production (**proliferation**) and improper function of certain cells (**plasma cells**) found in the bone marrow. Plasma cells, which are a type of white blood cell, are produced in the bone marrow and eventually enter the bloodstream. Excessive plasma cells may eventually mass together to form a tumor or tumors in various sites of the body, especially within the bone marrow. With a single tumor, it is called solitary plasmocytoma; when multiple tumors are present, it is called multiple myeloma.

Plasma cells are a key component of the immune system and secrete a substance known as myeloma proteins (M-proteins), a type of antibody. Antibodies are special proteins that the body produces to combat invading microorganisms, toxins, or other foreign substances. Too many plasma cells produced in affected individuals can result in abnormally high levels of these proteins within the body. The American Cancer Society estimates that in the U.S. during 2006, approximately 16,570 new cases of multiple myeloma will be diagnosed and approximately 11,310 deaths will occur (illustrated in Table 7, page 18), with a 5-year survival rate of approximately 32%. There are an additional approximately 19,000 patients in the EU, making the U.S. and European patient size of 34,000.

Existing Treatments

While low doses of oral Melphalan (a cancer [**antineoplastic**] medication that interferes with the growth of cancer cells and slows their growth and spread within the body, and used specifically to treat multiple myeloma, cancer of the ovary, and breast cancer) with Prednisone (a drug used to reduce swelling though a decrease in the body's ability to fight infections) has extended the median survival of multiple myeloma to three years from six months, the response rates to Melphalan and Prednisone have been only about 50% to 60%. Since complete remissions are rare, and myeloma remains incurable with conventional chemotherapy, survival has not been significantly improved with vincristine, adriamycin, and dexamethasone (VAD), or other forms of infusional chemotherapy, over Melphalan and Prednisone.

Bone marrow toxicity due to conventional chemotherapy is dose-limiting. Hematopoietic cell transplantation, or marrow transplantation, with either a patient's own marrow (**autologous**) or a family member (**allogenic**) has been explored extensively as a means to increase doses of conventional chemotherapy.

Allogeneic transplantation has been associated with a very high treatment-related mortality of up to 40%. It is therefore performed infrequently. Autologous transplantation has been shown much safer, with a treatment-related mortality of <3%. This method of transplantation has shown to be superior to conventional chemotherapy for the treatment of multiple myeloma, and has been associated with a median survival to 55-72 months. However, only approximately 50% of patients aged 60 or under, and fewer than 20% of patients between 60 and 70, receive transplantation due to early death, co-morbidity, poor response to therapy, and failed peripheral blood stem cell harvests (*Source: Business Briefing, U.S. Oncology Review, 2004*).

Symptoms

Symptoms of multiple myeloma may include bone pain, especially in the back and the ribs; low levels of circulating red blood cells (**anemia**) resulting in weakness, fatigue, and lack of color (**pallor**); and kidney (renal) abnormalities. In most cases, affected individuals are more susceptible to bacterial infections such as pneumonia. The exact cause of multiple myeloma is unknown.

Oral Defibrotide to Treat Multiple Myeloma

Preclinical studies conducted by the Myeloma Center of the Dana-Farber Cancer Institute at Harvard University on human multiple myeloma in rodents suggests that Defibrotide's effect on the cells of blood vessel walls may help increase the effectiveness of other treatments for multiple myeloma. In particular, the overall survival rate of rodents with human multiple myeloma increased and tumor volume decreased when the animals were administered Defibrotide in combination with other chemotherapy agents.

Phase I/II Study by Myeloma Center of Dana-Farber

The Myeloma Center of Dana-Farber is conducting additional preclinical studies on the effects of Defibrotide on multiple myeloma. An independent Phase I/II clinical study of Defibrotide to treat multiple myeloma, combined with Melphalan, Prednisone, and Thalidomide (used to treat and prevent the debilitating and disfiguring skin sores associated with erythema nodosum leprosum [ENL], an inflammatory complication of leprosy) commenced in December 2005.

This study is expected to 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. Gentium has stated that it intends to pay part of the costs of this trial, which is scheduled to be a dose-escalating, multi-center, non-comparative, open label study designed to assess the safety and the efficacy of Defibrotide with Melphalan, Prednisone, and Thalidomide (MPT) regimen as a salvage treatment in advanced refractory multiple myeloma patients.

The Phase I component of the trial is to combine oral MPT with escalating doses of Defibrotide to determine the maximum tolerated dosage of Defibrotide combined with MPT in 24 patients (three cohorts of eight patients). In the Phase II component of the trial, the oral MPT regimen is to be combined with the maximum tolerated dosage of Defibrotide and administered to 50 consecutive patients to assess response rate and clinical efficacy. As of early April 2006, three centers have Institutional Review Board (IRB) approval and are open for patient enrollment and five patients are enrolled. A depiction of the expected timeline for development of oral Defibrotide to treat multiple myeloma, as made available by Gentium, is provided in Table 13 (page 26).

Table 13

Gentium S.p.A.

ESTIMATED DEVELOPMENT TIMELINE FOR ORAL DEFIBROTIDE FOR MULTIPLE MYELOMA

Q4 '05	Initiated Phase I/II Trial in Italy
Q3 '06	Enrollment of Phase I Study in Italy Complete
Q4 '06	Phase I Data Available
Q1 '07	Initiate Phase II Study in Italy
2H '07	Initiate U.S./EU Phase II Study
2H '08	U.S./EU Phase II Study Complete
1H '09	Initiate Two Separate Phase III studies in U.S. & EU
1H '11	Phase III Studies Complete

Source: Gentium S.p.A.

EARLY STAGE PIPELINE CANDIDATES

Gentium as well as other unrelated industrial and academic institutions have conducted preclinical studies on additional uses of Defibrotide as well as other drugs in the Company's pipeline. Gentium intends to continue to develop its own product candidates with the hope of expanding its target markets. If successful in bringing its advanced product candidates to market, which are described on pages 20-26, Gentium could use this cash to continue to fund expenses associated with developing its earlier stage product candidates.

Defibrotide to Prevent Deep Vein Thrombosis

Defibrotide has been marketed since 1986 by both Gentium as well as its predecessors in Italy to treat deep vein thrombosis (DVT), and to both treat and prevent all vascular disease with risk of thrombosis since 1993. DVT is a blockage of the veins in the legs that can have many causes, including hip surgery, pregnancy, cancer and cancer therapies, and injuries. DVT can lead to **pulmonary embolism**, the dislodging and migration of blood clots to the lungs, which is often fatal. These uses of Defibrotide both involve intravenous injection and oral administration. In 2002, Gentium licensed the right to sell Defibrotide to treat and prevent all vascular disease with risk of thrombosis in Italy to Crinos, noting that vascular disease with risk of thrombosis refers to several serious cardiovascular conditions.

Phase I/II Clinical Trial

Gentium has stated its intent to develop an orally administered formulation of Defibrotide to prevent DVT for markets outside of Italy. The Company concluded a 69-patient Phase I/II clinical trial of Defibrotide to prevent DVT after hip surgery in Denmark in 2002. In this clinical trial, Defibrotide was administered through intravenous infusion for up to two days followed by oral administration for a further three to six days. This trial was discontinued after three patients receiving Defibrotide through intravenous infusion experienced **hypotension**, a serious adverse event. No serious adverse events were noted in patients receiving Defibrotide orally. Based on the results of this trial and prior use of Defibrotide to prevent DVT in Italy, Gentium believes that the compound may be safe and effective in preventing DVT. It is possible that the most significant market opportunity for this use involves administering it orally, as this would allow patients to take the drug at home instead of a hospital. Additional clinical trials must be conducted outside of Italy to explore the safety and effectiveness of oral administration of Defibrotide for this use, noting that in a recent study with the oral form of Defibrotide, the rate of DVT was 6% (3/50)—comparable to low molecular weight heparin.

Defibrotide (For Use Subsequent to Stem Cell Transplantation)

Gentium may be able to expand the market for Defibrotide to include its use to mobilize and increase the number of stem cells available for transplant. A stem cell transplant is a medical procedure that involves collecting stem cells from the blood of a patient before chemotherapy, radiation therapy, hormone therapy, or through a compatible donor intravenously, and then re-administering them to the patient after treatment. Stem cell transplants are used to treat side effects of certain cancer therapies—one being the

permanent damage to bone marrow, which inhibits or halts the production of blood cells and can be life threatening.

While there are many different types of blood cells, which all develop from stem cells, the majority of stem cells are found in the bone marrow (the soft inside part of the bone). Some are also found in blood (peripheral blood stem cells). Doctors may use stem cell transplants to regenerate bone marrow after certain cancer therapies. Stem cell transplants can further be used to treat some cancers directly, as well as to treat side effects of some cancer treatments.

Peripheral blood stem cell transplants are less invasive than bone marrow transplants, which require a surgical procedure to remove bone marrow from a patient's or donor's bones. However, since blood is not as rich in stem cells as bone marrow, the availability of adequate amounts of peripheral blood stem cells from the patient or a compatible donor is critical to the effectiveness of a peripheral blood stem cell transplant.

Gentium also has several product candidates in preclinical development for use subsequent to stem cell transplantation (SCT), such as additional uses of Defibrotide, for example, to mobilize and increase the number of stem cells available in patients' and donors' blood for subsequent stem cell transplantation, to prevent deep vein thrombosis in markets outside of Italy, and to develop other drugs, such as oligotide (which Gentium believes may protect against damage to blood vessel wall cells caused by a particular cancer treatment) and Gen 301 (which Gentium believes may prevent and treat oral ulcers that often develop during and after cancer treatments).

Mesalazine (For Inflammatory Bowel Disease)

Inflammatory bowel disease (IBD) or **ulcerative colitis**, is a disease that causes inflammation and lesions in the large intestine. Gentium has created a gel formulation of mesalazine, an anti-inflammatory product intended to treat the disease. In 2002, the Company sold the exclusive rights to develop and market this product in Canada to Axcan Pharma, upon Health Canada approval, and the U.S., upon FDA approval. Axcan is a Canadian pharmaceutical company that specializes in gastrointestinal therapies and markets its products through its own sales force in North America and Europe. Details of this arrangement are provided on page 30.

Phase III Study

Axcan completed an open-label, randomized 180-patient Phase III study to assess the evolution of the clinical symptoms of IBD during the induction of remission by Gentium's formulation of mesalazine in 2005. This study was supported by two 50-patient placebo-controlled studies. Axcan has reported that it expects to launch the product this year if approved by Health Canada and/or the FDA.

Oligotide (To Reduce Toxic Effects of Chemotherapeutics)

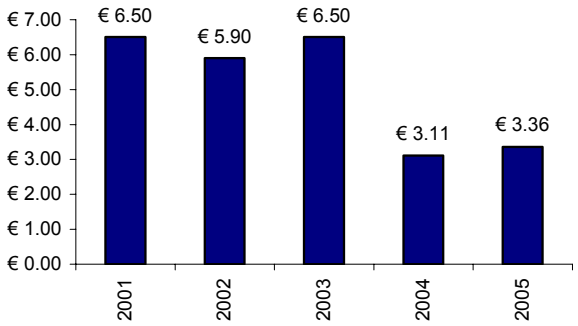
Gentium is developing oligotide, another product derived from natural DNA. One particular chemotherapy agent, **fludarabine**, is used to treat **chronic lymphocytic leukemia (CLL)**. Fludarabine interferes with the growth of cancer cells, but it also causes damage, specifically **apoptosis** (a series of events in a cell that leads to its death) to blood vessel wall cells which oligotide seems to prevent.

Preclinical Studies (University of Regensburg, Germany)

Researchers at the University of Regensburg, Germany, performed preclinical studies showing that oligotide, when used in combination with fludarabine, reduced the level of apoptosis in the cells of blood vessel walls to approximately the same level normally found in cells that have not been treated with fludarabine. Gentium believes that oligotide could be used in conjunction with fludarabine and other cancer therapies to reduce the toxic effects of these cancer therapies. Gentium may conduct further research on oligotide to investigate its effectiveness in protecting blood vessel cell walls against cancer therapies.

MARKETED PRODUCTS

Figure 4
Gentium S.p.A.
ANNUAL REVENUES (MM's of €'s)



Source: Gentium S.p.A.

Gentium and its predecessors have manufactured Defibrotide since 1986 using a patented manufacturing process on which the Company holds both a U.S. patent and a European patent (granted in 1991), as well as licenses for others to sell the product in Italy. Besides Defibrotide to both treat and prevent vascular disease with risk of thrombosis, Gentium manufactures and sells urokinase and calcium heparin in Italy (active pharmaceutical ingredients used to make other drugs); sulglicotide (to treat peptic ulcers); as well as other pharmaceutical products. Revenues from the sales of the Company's currently marketed products (described below) are depicted in Figure 4.

- *Defibrotide.* Gentium currently manufactures Defibrotide for Sirton, an affiliate of Gentium. Sirton focuses on processing the Defibrotide for either oral administration or intravenous administration and sells the finished products to Crinos. Crinos markets Defibrotide in Italy to both treat and prevent vascular disease with risk of thrombosis under a semi-exclusive license agreement.

- *Urokinase*. Urokinase has the potential to dissolve fibrin clots and, as such, is used to treat various vascular disorders, such as DVT and pulmonary embolisms. The Company sells urokinase to Sirton, who uses it as an ingredient in the manufacture of generic drugs. Sirton sells the final formulated generic drugs to other companies, which then sell the drugs to hospitals and pharmacies.

- *Heparin Calcium.* Heparin calcium is used to prevent blood from clotting. Decreasing clot formation diminishes the likelihood of strokes and heart attacks. Heparin calcium has numerous uses including the treatment of certain types of lung, blood vessel, and heart disorders, and administration during or after certain types of surgery, such as open heart and bypass surgeries. Other uses include the flushing of catheters and other medical equipment. Gentium sells heparin calcium to Sirton, who uses it as an ingredient in the manufacture of generic drugs. Sirton sells the final formulated generic drugs to other companies, which then sell the drugs to hospitals and pharmacies.

- *Sulglicotide.* Sulglicotide appears to have ulcer healing and gastrointestinal protective properties. The effects of this drug have prompted Gentium to commission a preclinical investigation by a UK-based **contract research organization (CRO)** specializing in studies of mucositis caused by anticancer or radiation therapies, into its function in potential prevention, and treatment of mucous membrane damage. Gentium also sells sulglicotide to Sirton for use in contract manufacturing of Gliptide, a drug marketed in Italy to treat peptic ulcers, and to Samil, a Korean company, for use in manufacturing a product of Samil's for sale in Korea.

Strategic Alliances

License and Distribution Agreements

Rights to market Defibrotide for different indications are shared between two companies based on geography. Crinos, a subsidiary of Stada Arneimittel AG, has marketing rights for Defibrotide in its only approved market, which is the prevention and treatment of vascular disease with risk of thrombosis in Italy, and the right of first refusal for this and other uses approved going forward in all European countries. In the Americas, Gentium has licensed rights for the treatment of VOD to Sigma-Tau Pharmaceuticals, which also has the right of first refusal for VOD prophylaxis and stem cell mobilization if Gentium chooses to partner these programs. Details of these agreements (as depicted in Figure 5) are provided below.

Figure 5
Gentium S.p.A.
STRATEGIC ALLIANCES

Source: Gentium S.p.A.

Sigma-Tau

On December 7, 2001, Gentium entered into a License and Supply Agreement with Sigma-Tau Industrie Pharmaceutiche Reunite S.p.A., which markets drug treatments for rare conditions and diseases. Sigma-Tau Industrie Pharmaceutiche Reunite S.p.A. and Sigma-Tau Pharmaceuticals, Inc. are subsidiaries of Sigma Tau Finanziaria S.p.A., an international family of pharmaceutical companies. Under this agreement, Gentium has licensed the right to market Defibrotide in the Americas to treat VOD to Sigma-Tau Pharmaceuticals in the U.S. This license expires on the earlier of the eighth year of Gentium's launch of the product or the expiration of the U.S. patent regarding the product, which expires in 2010. In return for the license, Sigma-Tau Pharmaceuticals agreed to pay Gentium an aggregate of $4.9 million—of which it has paid to Gentium $4.1 million to date, owing an additional $550,000 within 30 days of the end of a Phase III pivotal study, and $350,000 within 30 days of obtaining an FDA New Drug Application (NDA) or Biologic License Application (BLA) and other approvals necessary for the marketing of Defibrotide in the U.S.

Sigma-Tau Pharmaceuticals must purchase all of its Defibrotide for this use from Gentium at a price equal to the higher of €50.00 per unit or 31% of its net sales of Defibrotide, and must also pay Gentium a royalty equal to 7% of its net sales of Defibrotide. Gentium has also granted Sigma-Tau Pharmaceuticals an exclusive, irrevocable right of first refusal to market Defibrotide to prevent VOD, to mobilize and increase the number of stem cells available in patients' and donors' blood for subsequent stem cell transplantation, and in non-intravenous forms for these indications.

Stada

On May 17, 2002, Sirton, SFS Stada Financial Services Ltd., and Crinos S.p.A. entered into an Umbrella Agreement. Under this Umbrella Agreement, Sirton spun off its marketing and sales division, including the brand-name "Crinos" to Crinos S.p.A., a newly formed subsidiary of Stada Arzneimittel AG. As part of the sale, Gentium granted Crinos S.p.A. a semi-exclusive license to market Defibrotide in Italy to treat and prevent vascular disease at risk of thrombosis. Gentium has the right to grant a second license in Italy but only to a third party that has been expressly approved by Crinos.

This agreement remains valid until the later of the expiration of the patent on Defibrotide in Italy in 2009, and the date there is no market remaining for Defibrotide, as determined in good faith by the parties. Gentium also granted Crinos S.p.A. a right of first refusal for an exclusive or semi-exclusive license to market Defibrotide in Italy for additional uses approved in the future, as well as for all uses in all European

countries. Crinos S.p.A. can exercise this right of first refusal free of charge within 45 days of Gentium sending written notice of an offer to market or co-market Defibrotide for a new use or in a new European country.

As a further part of the sale, Gentium granted Crinos S.p.A. a semi-exclusive license to market mesalazine in Italy. This agreement remains valid until the later of the expiration of the patent on mesalazine in Italy in 2015, and the date there is no market remaining for mesalazine, as determined in good faith by the parties. Gentium also granted Crinos a right of first refusal for an exclusive or semi-exclusive license to market mesalazine in Italy for additional uses approved in the future, as well as for all uses in all other European countries. Crinos can exercise this right of first refusal free of charge within 45 days of Gentium sending written notice of an offer to market or co-market mesalazine for a new therapeutic use or in a new European country.

Axcan Pharma

On October 9, 2002, Gentium entered into a Purchase Agreement with Sirton and Axcan, where Gentium and Sirton sold the rights to develop, make, use, and sell Gentium's formulation of mesalazine in the U.S., upon FDA approval, and Canada, upon Health Canada approval, to Axcan in consideration for Axcan paying Gentium $1.5 million upfront plus 4% royalty on sales. Gentium and Sirton have also granted Axcan a right of first refusal to purchase or license the rights to exploit, register, promote, or commercialize Gentium's formulation of mesalazine in territories outside of substantially all European countries.

Additional Sales and Marketing Opportunities

Gentium is also involved in direct marketing of certain indications where a small, dedicated sales force is sufficient to attain market penetration. The Company has retained all rights for the prevention of VOD worldwide and has multiple license and development opportunities for other indications.

Clinical Trial Agreements

European Blood and Marrow Transplantation Group

On February 26, 2004, Gentium entered into a Trial Agreement with the European Blood and Marrow Transplantation Group. Under this agreement, the European Blood and Marrow Transplantation Group is cosponsoring a clinical trial of Defibrotide to prevent VOD in children after stem cell transplants.

MDS Pharma Services S.p.A.

In December 2005, Gentium entered into a letter of intent with MDS Pharma Services S.p.A., an international contract research organization (CRO), in which MDS will manage the clinical and regulatory aspects of Gentium's clinical trials of Defibrotide to prevent VOD in children and adults that Gentium is co-sponsoring with the European Blood and Marrow Transplantation Group.

Bradstreet Clinical Research & Associates, Inc.

On March 19, 2004, Gentium entered into a General Consulting Agreement with Bradstreet Clinical Research & Associates, Inc., a New Jersey-based CRO. Under this agreement, Bradstreet provides Gentium with clinical and regulatory consulting services. Bradstreet provides estimated project budgets to Gentium to determine the manner in which the services are to be provided and the number of hours required to provide the services.

KKS-UKT, GmbH

On April 20, 2004, Gentium entered into a Consulting Agreement with KKS-UKT, GmbH, a German CRO. Under this agreement, KKS provided Gentium with clinical and regulatory consulting services. KKS provides estimated project budgets for Gentium to determine the manner in which the services will be performed. This agreement expired on April 20, 2005 and Gentium renewed it for a subsequent six month period.

Competition

There currently are no approved therapies to specifically treat or prevent VOD. Several approaches have been attempted to treat VOD, though none has demonstrated to be fully and uniformly effective. The most commonly used treatment for patients who develop the condition is heparin (or low-molecular weight heparin). Due to its radical (and potentially deadly) anti-coagulation effects, this treatment's use is limited by its marginally positive risk-benefit profile. Low molecular weight heparin, made by Aventis (AVE-NYSE) and others, competes with calcium heparin, which is one of the active pharmaceutical ingredients that the Gentium sells to Sirton, which makes it into a finished product for sale by Crinos.

With a lack of well-defined treatments, supportive care remains the cornerstone of care for patients affected by VOD. Maintaining intravascular volume and renal perfusion without causing fluid overload by optimizing sodium restriction and diuretics is extremely important. Patients should receive transfusions to keep their **hematocrit** levels higher than 40%, optimizing perfusion and helping to maintain intravascular volume.

It is noteworthy that many organizations, including large pharmaceutical and biopharmaceutical companies, as well as academic and research organizations and government agencies, may be interested in pursuing the research and development of drug therapies that target the blood vessel wall.

Recent Milestones

- Announced the completion of a $22.1 million private placement of 1,943,525 of its American Depository Shares (ADSs) at a price of $11.39 per ADS. Investors in the financing also received warrants to purchase 388,705 ADSs at an exercise price of $14.50 per ADS. Net proceeds from the offering will be used to fund the continued development of the Company's product candidates and for general corporate purposes.

- Completed a private placement of 1,115,125 American Depository Shares (1 ADS = 1 share), raising gross proceeds of $10.9 million. Investors in the financing also received warrants to purchase 650,452 ADSs at an exercise price of $9.69 per ADS.

- Completed plans to initiate U.S. Phase III clinical trial of Defibrotide for the treatment of severe VOD with MOF as a result of a FDA meeting held in September 2005;

- Completed plans to initiate two Phase II/III clinical trials in Europe for the prevention of VOD, both of which are with the European Group for Blood and Marrow Transplantation;

- Initiated an independent Phase I/II study of Defibrotide to treat advanced and refractory multiple myeloma patients in combination with Melphalan, Prednisone, and Thalidomide (MPT) at approximately 10 cancer centers in Italy;

- Initiated a review of existing published clinical data with experts in their respective fields regarding the use of an oral form of Defibrotide for the prevention of deep vein thrombosis (DVT) and for the use of Defibrotide to treat certain chronic renal conditions;

- Oral presentation of final Phase II severe VOD trial at American Society of Hematology (ASH) – December 2005

- Initiated a Phase III trial in the U.S. with Defibrotide to treat severe VOD (Q2 '06)

    - $900,000 in additional future milestone payments

    - $800,000 expected grant to Dana Farber from FDA's Office of Orphan Drug Development Grant

- Initiated Phase II/III pediatric trial in EU with Defibrotide to prevent VOD in collaboration with European Group for Blood and Marrow Transplant (Q1 '06)

- Added Richard Champlin, M.D. to the Scientific Advisory Board. Dr. Champlin is professor of Medicine and chairman of the Department of Blood and Marrow Transplantation at the University of Texas M.D. Anderson Cancer Center.

- Announced that effective May 16, 2006, the Company's American Depository Shares (ADSs) were listed for trading on The NASDAQ National Market System (NMS-NASDAQ) under the symbol GENT.

Potential Future Milestones

- Initiate a second Phase II trial in Europe with Defibrotide to prevent VOD and transplant associated microangiopathy in adults (July 2006)
- Complete enrollment of Italian Phase I study of Defibrotide to treat multiple myeloma (Q3 '06)
- Axcan to file mesalazine NDA for irritable bowel disease (IBD)
    - Receive $300,000 milestone payment upon filing
- Italian Phase I study in multiple myeloma available for presentation (Q4 '06)
- Start U.S. VOD prevention trial (2H '07)

Key Points to Consider

- *Gentium is seeking to obtain FDA approval to use Defibrotide to treat veno-occlusive disease (VOD) with multiple-organ failure (MOF) as the drug has been found to double survival rates in this untreatable, fatal disease.* The Dana-Farber investigator presented results from its Phase II clinical trial of Defibrotide in patients with VOD with MOF at the 47th Annual Meeting of the American Society of Hematology held on December 12, 2005. Results showed that the survival rate after 100 days for the 142 patients for whom that information was available was approximately 39% versus the historical survival rate of approximately 20%.

    - A Phase II trial for Defibrotide was supported by two grants from the FDA's Orphan Drug Division and the FDA has granted Fast Track status to Defibrotide to treat severe VOD. The U.S. Phase III trial is expected to be supported by a third grant.

    - The FDA has approved Gentium's application for Fast Track designation for Defibrotide to treat VOD with MOF 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.

- *The Company could receive an expanded approval of Defibrotide to include prevention of VOD in Europe and the U.S.* A preliminary study indicated that Defibrotide may be safe and effective in protecting against VOD. Gentium is co-sponsoring a Phase II/III clinical trial for this use 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.

    - The Company may initiate a Phase II/III clinical trial in the U.S. for Defibrotide by early next year. If the clinical trials confirm the preliminary indications, Gentium could pursue further development in Europe and the U.S., and ultimately apply for FDA and European regulatory approval for this use.

- *The Company's expanded approval of Defibrotide could also 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 commenced in December 2005, which could include 10 cancer centers in Italy.

- *Treatment of severe VOD represents an immediate estimated global market opportunity of more than $600 million.* The Company believes the prevention of VOD could eventually replace treatment and represent a $1 billion market opportunity. Additional chemo-protective indications represent potentially much larger market opportunities. In addition, the Company recently initiated a Phase I/II trial to treat multiple myeloma, which could be a $440 million market opportunity.

- *Gentium has gained support from world-renowned cancer institutes.* The principal investigators and trial centers involved in Defibrotide trials include the world's leading oncologists and transplantation specialists. Trials are being conducted at Dana-Farber Cancer Institute, M.D. Anderson, Memorial Sloan-Kettering, Fred Hutchinson Cancer Research Center and The Johns Hopkins Hospital and Health System, and others, which are shown in Figure 2 (page 6).

- *Gentium and its partners have conducted preclinical studies on other uses for Defibrotide and additional drugs in its pipeline.* The Company plans to continue to develop these product candidates and to further expand the possible markets for its products and product candidates. If successful in bringing initial product candidates to market, cash flow from operations could be used to fund some of the costs needed to develop its pipeline candidates.

- *Increase marketing capacity through strategic partnerships.* Gentium has 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 has granted Sigma-Tau Pharmaceuticals 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. Gentium could pursue similar agreements with Sigma-Tau Pharmaceuticals and other strategic partners to market Defibrotide in other jurisdictions and to market other product candidates.

- *The Company's state-of-the-art manufacturing facility at headquarters in Como, Italy is currently used for active pharmaceutical ingredients and Defibrotide.* This facility underwent a $10 million upgrade in 2004 and is FDA GMP-compliant. Gentium owns the land, buildings, laboratories, and equipment.

- *The Company holds 30 U.S. and EU patents with 70 applications pending*. Defibrotide's Orphan Drug designation in the U.S. and Europe provides additional market exclusivity for the treatment of VOD. Gentium continues to build on its core patents to provide additional protection.

- *With proforma cash of approximately $32 million as of March 31, 2006*, Gentium has approximately one to two years of cash remaining.

Historical Financial Results

Tables 14, 15, and 16 provide a summary of Gentium's key historical financial statements, including its Statement of Operations, Consolidated Balance Sheets, and Statements of Cash Flows in Euros (€'s), for the quarter ending March 31, 2006.

Table 14
GENTIUM S.p.A.
STATEMENT OF OPERATIONS
(Unaudited, in thousands of Euros, except per share data)

	Three Months Ended March 31,	
	2005	**2006**
Revenues:		
Sales to affiliates	€ 500	€ 912
Third party product sales	93	3
Total product sales	593	915
Other income and revenues	70	35
Total Revenues	663	950
Operating costs and expenses:		
Cost of goods sold	502	763
Charges from affiliates	271	215
Research and development	644	1,623
General and administrative	412	1,296
Depreciation and amortization	23	42
	(1,852)	(3,939)
Operating loss	(1,189)	(2,989)
Foreign currency exchange gain (loss), net	(55)	(168)
Interest income (expense), net	(2,148)	52
Pre-tax loss	(3,392)	(3,105)
Income tax expense:		
Current	(16)	—
Total tax expenses	(16)	—
Net loss	€ (3,408)	€ (3,105)
Net loss per share:		
Basic and diluted net loss per share	€ (0.68)	€ (0.32)
Weighted average shares used to compute basic and diluted net loss	5,000,000	9,610,630

Source: Gentium S.p.A.

Table 15
GENTIUM S.p.A.
BALANCE SHEETS
(in thousands of Euros)

(000's omitted)	March 31, 2006 Actual (Unaudited)	Proforma
Assets:		
Cash and cash equivalents	€ 9,746	€ 26,556
Receivables	2,006	2,006
Inventory	1,779	1,779
Other current assets	732	732
Total current assets	14,263	31,073
Property, net	8,653	8,653
Other assets, net	510	510
	€ 23,426	€ 40,236
Liabilities and Shareholders' Equity:		
Payables, accruals and other current liabilities	€ 5,126	€ 5,126
Current maturities of long-term debt	797	797
Convertible notes payable, net of discount	—	—
Total current liabilities	5,923	5,923
Long-term debt	2,203	2,203
Termination indemnities	715	715
Total liabilities	8,841	8,841
Shareholders' equity	14,585	31,395
	€ 23,426	€ 40,236

Proforma adjustment:

1. Assumes receipt of estimated net proceeds from private placement of 1,943,525 ADSs-definitive agreements 5/31/06.
2. Assumed conversion rate on March 31 of $1.00 = .824 euros

Source: Gentium S.p.A.

Table 16
GENTIUM S.p.A.
STATEMENTS OF CASH FLOWS
(Unaudited, in thousands of Euros)

	Three Months Ended March 31,	
	2005	2006
Cash flows from operating activities:		
Net loss	€ (3,408)	€ (3,105)
Adjustments to reconcile net income to net cash used in operating activities:		
Unrealized foreign exchange loss	118	—
Depreciation and amortization	360	219
Non cash interest expense	1,750	—
Stock based compensation	66	213
Changes in operating assets and liabilities:		
Accounts receivable	(262)	(131)
Inventories	(504)	(152)
Prepaid expenses and other assets	212	188
Accounts payable and accrued expenses	(428)	629
Deferred income	(73)	(35)
Termination indemnities	(17)	8
Net cash used in operating activities	(2,186)	(2,165)
Cash flows from investing activities:		
Capital expenditures	(244)	(198)
Intangible expenditures	(18)	(274)
Net cash used in investing activities	(262)	(472)
Cash flows from financing activities:		
Repayments of long-term debt	(162)	(401)
Proceeds from issuance of series A convertible notes	1,465	—
Capital contribution by shareholder	1,600	—
Repayment of affiliate's loan	(700)	—
Repayment from bank overdrafts and short term borrowings	(2,199)	—
Net cash provided/(used) by/in financing activities	4	(401)
Decrease in cash and cash equivalents	(2,444)	(3,039)
Cash and cash equivalents, beginning of period	2,461	12,785
Cash and cash equivalents, end of period	€ 17	€ 9,746
Supplemental disclosure of cash flow information:		
Cash paid for interest, net of capitalized amount	€ 61	€ 50
Income taxes paid	€ —	€ —

Source: Gentium S.p.A.

Risks

Some of the information in this report relates to future events or future business and financial performance. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in Gentium's Risk section on Forms 20-F, 6-K, and other forms filed with the Securities and Exchange Commission ("SEC") from time to time. The content of this report with respect to Gentium has been compiled primarily from information available to the public and released by Gentium through news releases and SEC filings. Gentium is solely responsible for the accuracy of that information. Information about other companies has been prepared from publicly available documents and has not been independently verified by Gentium. For more complete information about Gentium, refer to the Company's website at www.gentium.it.

The risks and uncertainties described below are not the only ones the Company faces. Additional risks and uncertainties not presently known or those it currently considers immaterial may also have an adverse effect on its business. If any of the matters discussed in the accompanying risk factors were to occur, Gentium's business, financial condition, results of operations, cash flows, or prospects could be materially adversely affected. Investors should carefully consider the risks described below, in conjunction with the other information and financial statements and related notes included in its SEC filings, before making an investment decision.

Investors should pay particular attention to the fact that Gentium S.p.A. conducts its operations in Italy and is governed by a legal and regulatory environment that in some respects differs significantly from the environment that prevails in other countries with which investors may be familiar. The Company's 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 its ADSs could decline and investors could lose all or part of their investment.

RISKS RELATING TO GENTIUM'S BUSINESS

The Company has generated limited revenues from commercial sales of its products to date, its revenues have declined significantly since 2003, and Gentium does not know whether it will ever generate significant revenues or achieve profitability.

The Company is focused on product development and has generated limited revenue from commercial sales of its products to date since 2003 because Sirton, its primary customer, has a decrease in demand for some of the products Gentium sells to it, as discussed below. In 2004, the Company had revenues of €3.113 million and in 2005 had revenues of €3.361 million.

Gentium does not expect its revenues to materially increase unless it is able to sell its product candidates, and the Company will continue to incur significant expenses as it researches, develops, tests, and seeks regulatory approval for these product candidates. While Gentium was profitable in 2002 and 2003, it incurred a net loss of €581,000 in 2001, a net loss of €7.0 million in 2004, and a net loss of €12.4 million in 2005. The Company's general and administrative expenses have increased as it added personnel to support its operations in connection with the development of its product candidates, internalized certain administrative services that were performed for the Company by its largest shareholder, FinSirton, and its affiliate, Sirton, and supported its operations in connection with being a public company. As a result, Gentium anticipates incurring substantial and increasing losses for the foreseeable future. The Company cannot assure investors that it will ever become profitable. If it fails to achieve profitability within the time frame expected by investors, the market price for Gentium's ADSs may decline.

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

Substantially all of Gentium's product sales in 2001, 2002, and 2003, (approximately 92% of its product sales in 2004 and approximately 97% of its product sales in 2005) have been from the sale of its 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. The Company's 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 Gentium and Sirton develop new customers. If the Company and Sirton are unsuccessful at developing new customers and the demand for its products continues to decrease, it could increase Gentium's need for additional capital, and its business could be adversely affected.

The Company currently does not have any regulatory approvals to sell Defibrotide to treat or prevent VOD or Defibrotide to treat multiple myeloma or any of its other product candidates and cannot guarantee that it will ever be able to sell any of these products anywhere in the world.

Gentium must demonstrate that its 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. The Company 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 costly, and Gentium cannot guarantee whether they will be successful.

Currently, the only regulatory approvals the Company has relate to the use of Defibrotide to prevent vascular disease with risk of thrombosis in Italy. It does not have approval to sell Defibrotide to treat or prevent VOD, Defibrotide to treat multiple myeloma, or any of its other product candidates anywhere in the world. Gentium will need to conduct significant additional research, preclinical testing, and clinical testing before it can file applications with the FDA, the European Commission, and other regulatory authorities for approval of its product candidates. In addition, to compete effectively, its future products must be easy to use, cost-effective, and economical to manufacture on a commercial scale. The Company may not meet any of these objectives, and, as a result, may not be able to sell any of its product candidates anywhere in the world.

The FDA and other regulatory authorities may require Gentium to conduct a new clinical trial of Defibrotide to treat VOD with MOF using a control group.

The Dana-Farber Cancer Institute at Harvard University conducted a Phase II clinical trial in the U.S. for the use of Defibrotide to treat VOD with MOF that concluded in December 2005. Based on the Company's review of more than 200 articles in the medical literature, it believes that the survival rate for this disease is only approximately 20%. As a result of this fact and the fact that Gentium 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.

The Company's Phase III clinical trial of Defibrotide to treat VOD with MOF that is currently underway uses historical control only. The FDA, upon reviewing this trial, may require it 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. Gentium believes 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 its ability to generate revenue from this product candidate.

The Company's additional product candidates are at early stages of development and will require clinical trials which may not be successful.

Gentium intends to apply for FDA and other regulatory agency approval for its additional product candidates, including other uses of Defibrotide, in the future, and these additional product candidates will require that it conducts clinical trials and undergoes 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.

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

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

The Company's clinical trials may be suspended at any time for a number of safety-related reasons. For example, it may voluntarily suspend or terminate its clinical trials if at any time it believes that its 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 Gentium's 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 MOF 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 MOF. Also, Gentium 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 MOF, 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 the Company's current products and many of its product candidates utilize or will utilize Defibrotide, any problems that arise from the use of this drug would severely harm its business operations since most of its 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.

Gentium is 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. The Company may have difficulty enrolling participants in these trials as patients may be reluctant to take the risk of not receiving treatment with Defibrotide. Gentium's other clinical trials may also be discontinued if it or the sponsors are not successful in enrolling participants.

The Company's products could be subject to restrictions or withdrawal from the market and it may be subject to penalties if it fails to comply with regulatory requirements, if and when any of its product candidates are approved.

Any product for which Gentium obtains 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 its 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 the Company is slow to adapt, or unable to adapt to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, it may lose marketing approval for its products when and if any of them are approved.

Gentium's 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 the Company to stop manufacturing its products if they determine that it is not complying with applicable regulations or require Gentium to complete further costly alterations to its facility.

Although the Company's main business is discovering, researching, and developing drugs, it also manufactures drugs, active pharmaceutical ingredients, and other products at its 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 the Company's 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 its facility. The Company is committed to complete appropriate corrective action prior to the next bi-annual inspection, and has kept the Italian Health Authority current with respect to the progress of its corrective actions, the majority of which have been completed. No penalties were imposed, its facility was not shut down, and its manufacturing activities was not otherwise limited or curtailed as a result of the Italian Health Authorities' notation of these deficiencies.

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

These regulators may require Gentium to stop manufacturing its products and product candidates if they determine that it is not complying with applicable regulations or require it to complete costly alterations to its facility. The Company spent approximately €292,000 in 2004 to correct the deficiencies noted by the Italian Health Authority and spent approximately €200,000 in 2005 to complete these corrective actions. Gentium spent approximately €7.2 million ($10 million) in 2004 to substantially upgrade its facility in anticipation of the FDA and European regulatory approval process for its product candidates.

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

Gentium does not have the personnel capacity to conduct or manage all of the clinical trials that it intends for its product candidates. The Company relies on third parties to assist it in managing, monitoring, and conducting most of its clinical trials. Gentium expects to enter into clinical trial agreements with numerous centers in the U.S. and Canada regarding its Phase III clinical trial of Defibrotide to treat VOD with MOF. The Company has entered into arrangements with the European Group for Blood and Marrow Transplantation, which is co-sponsoring with it 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.

Gentium has 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 U.S. and agreements with KKS-UKT, GmbH and MDS Pharma Services Italy SpA to provide such services for its 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 its agreements with them, the Company may not be able to enter into alternative arrangements without undue delay or additional expenditures, and therefore the clinical trials for its product candidates may be delayed or unsuccessful.

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

The Company's failure to raise additional funds in the future may delay the development of certain of its product candidates and sale of its products.

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

- the successful and continued development of its existing product candidates in preclinical and clinical testing;
- the costs associated with protecting and expanding its 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 its product candidates; and

- market acceptance of its products.

The Company will need additional funds before it can complete the development of its product candidates. The Company cannot assure investors that funds will be available to it in the future on favorable terms, if at all. If adequate funds are not available to Gentium on terms that it finds acceptable, or at all, the Company may be required to delay, reduce the scope of, or eliminate research and development efforts or clinical trials on any or all of its product candidates. The Company may also be forced to curtail or restructure its operations, obtain funds by entering into arrangements with collaborators on unattractive terms, or relinquish rights to certain technologies or product candidates that it would not otherwise relinquish in order to continue independent operations.

Gentium is currently dependent on third parties to market and distribute its products in finished dosage form, and may continue to be dependent on third parties to market and distribute its products and product candidates.

The Company's internal ability to handle the marketing and distribution functions for its current products and product candidates is limited and it does not expect to develop the capability to provide marketing and distribution for all of its future products. Gentium's long-term strategy includes having alliances with third parties to assist in the marketing and distribution of its product candidates. The Company has entered into an agreement with Sigma-Tau Pharmaceuticals, Inc. to market Defibrotide to treat VOD in North America, Central America, and South America and it may need to enter into similar agreements to market and distribute its other product candidates or develop these capabilities internally. Gentium faces, 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 clinical trials and for licenses of proprietary technology. These arrangements are complex to negotiate and time-consuming to document. The Company's future profitability will depend in large part on its ability to enter into effective marketing agreements and its product revenues will depend on those marketers' efforts, which may not be successful.

If Gentium is unable to attract and retain key personnel, it may be unable to successfully develop and commercialize its product candidates or otherwise manage its business effectively.

The Company is highly dependent on its senior management, especially Dr. Laura Ferro, its president and chief executive officer, and Dr. Massimo Iacobelli, its senior vice president and scientific director, whose services are critical to the successful implementation of its product acquisition, development, and regulatory strategies. If Gentium loses their services or the services of one or more of the other members of its senior management or other key employees, its ability to successfully commercialize its product candidates or otherwise manage its business effectively could be seriously harmed. Dr. Ferro's employment agreement with the Company is for a period of three years with a two year renewal option and prohibits her from competing with Gentium 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 the Company.

Replacing key employees may be difficult and may take an extended period of time because of the limited number of individuals in Gentium's 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 the Company may be unable to hire, train, retain, or motivate these additional key personnel. In addition, under Italian law, Gentium must pay its employees a severance amount based on their salary and years of service if they leave their employment, even if Gentium terminates them for cause or they resign. In order to expand its operations, the Company will need to hire additional personnel and add corporate functions that it currently does not have. Its ability to manage its operations and growth will require it to continue to improve its operational, financial, and management controls and reporting system and procedures, or contract with third parties to provide these capabilities for Gentium.

The Company's independent registered public accounting firm reported a material weakness in its internal controls and it may not be able to remedy this material weakness or prevent future weaknesses. If Gentium fails to maintain effective internal controls, it may not be able to accurately report its financial results or prevent fraud. As a result, potential shareholders could lose confidence in the Company's financial reporting, which would harm its business and the trading price of its ordinary shares.

Prior to its initial public offering in June 2005, Gentium was a relatively small, family run Italian business. It had not been required to close its accounting records on a monthly or even quarterly basis. A very small accounting team handled the accounts for not only the Company, but also its parent, FinSirton S.p.A., and sister companies, Sirton S.p.A. 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 U.S. Also, the financial reporting environment in Italy for private companies is significantly different than for public companies in the U.S.

As an Italian company publicly listed in the U.S., Gentium is required by Italian law to keep its books according to the local statutory accounting methods, as well as prepare U.S. GAAP-based financial statements for its Securities Act registration statements and Exchange Act reports. The preparation of the Company's U.S. GAAP-based financial statements is a manual process which involves the transformation of its 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 its senior accounting personnel. Moreover, U.S. GAAP accounting adjustments tend to result in large differences between its Italian statutory and U.S. GAAP based financial statements.

When Gentium started the process of preparing for its initial public offering, one of the first needs it identified to solve these issues was that of a full time, dedicated finance professional with knowledge of both U.S. and Italian accounting principles. The Company believes it satisfied that need by hiring Mr. Salvatore Calabrese, vice president, finance in February 2005.

Mr. Calabrese was not with Gentium during the 2004 fiscal year. As a result, its independent registered public accounting firm, during the course of auditing the 2004 financial statements for its initial public offering registration statement, informed Gentium that its financial statement close process and the transformation of its Italian statutory financial statements into U.S. GAAP did not reduce to an acceptably low level. Thus, 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. The Company's independent registered public accounting firm considered these deficiencies in determining the nature, timing, and extent of their procedures in their audit of its 2004 financial statements, and those deficiencies did not affect their report on its 2004 financial statements. Gentium did include a risk factor in its prospectus for its initial public offering explaining these deficiencies.

Although the Company hoped to remedy the material weakness designation during 2005, it was not able to do so due to the need to simultaneously (i) create an independent accounting department, including Mr. Calabrese, at Gentium, separate from the accounting team that handled the finances of FinSirton S.p.A., Sirton S.p.A., and Foltene Pharmaceuticals S.p.A., (ii) consummate the initial public offering, including the Securities Act registration statement and prospectus, and (iii) consummate a PIPE transaction in October 2005. The Company's auditors also raised additional structural issues that remained at the end of 2005. The following highlights the issues identified and the steps that Gentium is taking to remedy these items. The Company believes that all material weakness issues will be resolved during 2006.

Issue: For the first six months of 2005, Gentium still relied on FinSirton S.p.A. for most of the data processing related to its significant processes, such as inventory costing, payroll, and general ledger. The Company also had limited control over FinSirton S.p.A.'s information technology system related to the input or output of data. Additionally, it 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, Gentium established its own six (6) person accounting, controlling, and reporting department, separate from FinSirton S.p.A., which includes not only Mr. Calabrese but also Roberta Grandini as controller. Ms. Grandini is experienced in U.S. GAAP and was previously the controller for a U.S. public biotechnology company. In addition, the Company purchased, and is in the process of installing, its own information technology system which will allow it to have full control, including information security control, over data processing, including its underlying books and records. Gentium expects that this transition from FinSirton S.p.A.'s accounting department and information technology system to its accounting department and information technology system will be complete by the end of the second quarter of 2006.

Issue: The Company's process for budgeting, awarding, tracking, and verifying research and development contracts and costs has historically been handled outside of the general accounting system. Gentium has 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, the Company established and expanded its 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. Gentium 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 its medical director before any purchase requests or contracts may be signed. Furthermore, on a quarterly basis, Gentium performs an analysis of actual expenses versus budgeted expenses, and such analysis is presented and discussed with its management, its Audit Committee, and the Board of Directors as a whole.

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

Remedy: Gentium believes that its establishment of and expansion of its own, independent accounting department, including Mr. Calabrese and Ms. Grandini, and the acquisition of its own independent information technology system, will solve points (i) and (ii) above. In addition, although the Company will continue to need to prepare both Italian statutory financial statements and U.S. GAAP based financial statements, it believes that the expansion of its accounting department will help it close its records efficiently and that the establishment of a 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 Gentium's operating results or cause it to fail to meet its reporting obligations. Inferior internal controls could also cause investors to lose confidence in the Company's reported financial information, which could have a negative effect on the trading price of its ordinary shares.

Gentium's revenues, expenses, and results of operations have been and will continue to be subject to significant fluctuations, which makes it difficult to compare its operating results from period to period.

Since 2003, the Company's revenues have fluctuated significantly due to the need to temporarily cease operations at its 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. Gentium's revenues have also fluctuated due to changes in the amounts of each of its products that it sells in different periods. Due to the fact that the Company does not sell directly to the end-user, the timing of manufacturer orders can cause variability in sales. In 2005, Gentium experienced higher sales volume in the second and in the fourth quarter; however the Company cannot predict if such fluctuation will happen

in future years. Until it has successfully developed and commercialized a product candidate, Gentium expects that substantially all of its revenues will result from the sale of its existing products. The Company expects that operating results will vary significantly from quarter to quarter and year to year as a result of the timing and extent of:

- its research and development efforts;
- the revenues generated from the sale or licensing of its products;
- the execution or termination of collaborative arrangements;
- the receipt of grants;
- the initiation, success, or failure of clinical trials; and
- the manufacture of its product candidates, or other development related factors.

Some of Series A senior convertible promissory notes the Company issued in the fourth quarter of 2004 and the first quarter of 2005 were converted into its ordinary shares upon the closing of its initial public offering in June 2005 and the remainder were repaid in June and July 2005.

Gentium's results of operations in 2004 and 2005 reflect the interest expense 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 its initial public offering), was less than the fair value of its ordinary shares at the time of issuance of the notes, which was $10.00. During 2004 and 2005, the Company 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, Gentium's interest expense, pre-tax income (loss) and net income (loss) for those periods was less than it would have been otherwise. Accordingly, the Company's 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 Gentium's manufacturing capability is located in one facility that is vulnerable to natural disasters, telecommunication and information system failures, terrorism and similar problems, and it is not insured for losses caused by all of these incidents.

The Company conducts most of its 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. Gentium's insurance covers losses to its facility, including the buildings, machinery, electronic equipment and goods, for approximately €16 million, but does not insure against all of the losses listed above, including terrorism and some types of flooding. Although the Company believes that its insurance coverage is adequate for its current and proposed operations, there can be no guarantee that it will adequately compensate Gentium for any losses that may occur. The Company is not insured for business interruption and has no replacement manufacturing facility readily available.

Gentium obtains 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 Gentium.

The Company's largest shareholder is FinSirton, which owns approximately 32% of its ordinary shares. Dr. Ferro, who is Gentium's chief executive officer and president and one of its directors, together with members of her family, controls FinSirton. FinSirton provides some of the Company's office space, and corporate, payroll, and information technology services. Sirton, which is a wholly-owned subsidiary of FinSirton, has been and currently is Gentium's principal customer. Sirton also provides the Company with

a number of business services such as, quality control and regulatory services, and leases Gentium office and manufacturing space.

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

Gentium's industry is highly competitive and subject to rapid technological changes. As a result, it may be unable to compete successfully or to develop innovative products, which could harm its business.

Gentium's 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 the Company is unaware of any other products or product candidates that treat or prevent VOD or the apoptosis that its product candidate oligotide is designed to treat, it believes that other companies have products or are currently developing products to treat some of the same disorders and diseases that its other product candidates are designed to treat.

These companies include AnorMED Inc. (AOM-AMEX), AstraZeneca International (AZN-NYSE), British Biotech plc, Abbott Laboratories (ABT-NYSE), The Bayer Group, GlaxoSmithKline plc (GSK-NYSE), Bristol-Myers Squibb Company (BMY-NYSE), Eli Lilly Company, Boehringer Ingelheim, Axcan Pharma Inc., The Proctor & Gamble Company (PG-NYSE), Solvay Pharmaceuticals, Inc., Millennium Pharmaceuticals, Inc. (MLMN-NASDAQ), ARIAD Pharmaceuticals, Inc. (ARIA-NASDAQ), Celgene Corp. (CELG-NASDAQ), Titan Pharmaceuticals, Inc. (TTP-AMEX), Cell Genesys, Inc. (CEGE-NASDAQ), Human Genome Sciences, Inc. (HSGI-NASDAQ), Chugai Pharmaceutical Co., Ltd., The National Cancer Institute, Seattle Genetics, Inc. (SGEN-NASDAQ), EntreMed, Inc. (ENMD-NASDAQ), NeoRx Corporation (NERX-NASDAQ), Xcyte Therapies, Inc., Amgen, Inc. (AMGN-NASDAQ), CuraGen Corporation (CRGN-NASDAQ), Aesgen, Inc. and Endo Pharmaceutical Holdings Inc. (ENDP-NASDAQ).

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 Gentium sells 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 the Company. In addition, these companies' products and product candidates are in more advanced stages of development than Gentium's 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 Gentium can or establish their products in the market before it can. Their products may also prove to be more effective, safer, or less costly than the Company's product candidates. This could hurt Gentium's ability to recognize any significant revenues from its 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 Gentium intends to file before approving a New Drug Application filed by anyone else for this use of Defibrotide, the orphan drug status will provide the Company with limited market exclusivity for seven years from the date of the FDA's approval of its New Drug Application. However, a marketing authorization may be granted for the same therapeutic indications to a similar medicinal product if the Company gives its consent to the second applicant.

If it is 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. Gentium's product would not have market exclusivity. Additionally, while Gentium is 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 its 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 the Company's 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 the Company a marketing authorization for those uses of Defibrotide, the Company 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 Gentium gives its consent to the second applicant, it is 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, the Company's product would not have market exclusivity.

If Gentium is unable to adequately protect its intellectual property, its ability to compete could be impaired.

The Company's long-term success largely depends on its ability to create and market competitive products and to protect those creations. The Company's pending patent applications, or those it 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 it may not obtain adequate patent protection. As a result, Gentium may face unanticipated competition, or conclude that without patent rights the risk of bringing products to the market is too great, thus adversely affecting its 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 Gentium's product candidates can be approved for sale and commercialized, its relevant patent rights may expire or remain in force for only a short period following commercialization.

Gentium's issued U.S. patents expire between 2008 and 2016, and its U.S. patents for which it has submitted applications will expire between 2008 and 2025.

The Company's U.S. patent covering Defibrotide expires in 2010, and its U.S. patent covering the chemical process for extracting Defibrotide expires in 2008. Gentium's 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 the Company could face increased competition for its products that are derived from Defibrotide. Patent expiration could adversely affect Gentium's ability to protect future product development and, consequently, its operating results and financial position.

The Company also relies on trade secrets to protect its technology, especially where it does not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While it uses reasonable efforts to protect its trade secrets, its employees, consultants, contractors, outside scientific collaborators, and other advisors may unintentionally or willfully disclose Gentium's information to competitors. Enforcing a claim that a third party illegally obtained and is using the Company's trade secrets is costly and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets. Gentium intends to eventually license or sell its products in China, Korea, and other countries which do not have the same level of protection of intellectual property rights as exists in the U.S. and Europe. Moreover, the Company's competitors may independently develop equivalent knowledge, methods, and know-how.

RISKS RELATED TO OWNERSHIP OF THE ADSs

Gentium's largest shareholder exercises significant control over it, which may make it more difficult for investors to elect or replace directors or management and approve or reject mergers and other important corporate events.

The Company's largest shareholder, FinSirton, owns approximately 32% of its outstanding ordinary shares. Dr. Laura Ferro, who is Gentium's chief executive officer and president and one of its 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 the Company's shareholders, including the election of directors and the approval of mergers or other important corporate events. They may exercise this ability in a manner that advances their best interests and not necessarily an investors. In particular, Dr. Ferro may use her control over FinSirton's shareholdings in the Company

to resist any attempts to replace her or other members of Gentium's board of directors or management or approve or reject mergers and other important corporate events. Also, the concentration of the Company's beneficial ownership may have the effect of delaying, deterring, or preventing a change in its control, or may discourage bids for the ADSs or its 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 Gentium's business is doing well.

The Company's executive officers (other than Cary Grossman, its chief operating officer), directors and current largest shareholder, FinSirton, have agreed with the underwriters of its initial public offering to a lock-up of their ordinary shares for a period of 18 months after the effective date of the registration statement relating to its initial public offering of securities, provided, however, that if the average price per ADS of its ADSs equals or exceeds 200% of the initial public offering price of the ADSs in Gentium's 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 any shares that underlie options that the Company may grant to these officers and directors in the future. Gentium's chief operating officer, Cary Grossman, has agreed with the underwriters to a lock-up of 85,000 ordinary shares issuable upon exercise of certain of his options for a period of 365 days after the effective date of the registration statement relating to its initial public offering of securities. 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 the Company's 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 its officers, directors, and existing shareholders subject to these lockup agreements. Gentium's other outstanding ordinary shares and ordinary shares issuable upon exercise of warrants are not subject to lock-up agreements. The Company has filed a registration statement registering the resale of 2,001,125 outstanding ordinary shares and ADSs and 1,143,482 ordinary shares and ADSs issuable upon exercise of warrants by certain selling security holders. Further, it has agreed to register (upon request) 1,159,505 outstanding ordinary shares currently held by two of its shareholders, 73,334 shares issuable upon conversion of warrants issued in connection with its Series A senior convertible promissory notes held by one of its security holders, and 151,200 ordinary shares issuable upon exercise of purchase options Gentium granted to the underwriters of its initial public offering for resale in the market. The Company intends to register ADSs representing such ordinary shares in addition to the ordinary shares themselves, and 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 Gentium's bylaws and applicable law, and may require prior approval of its shareholders at an extraordinary meeting of shareholders.

The Company was incorporated under the laws of the Republic of Italy. The principal laws and regulations that apply to its operations, those of Italy and the European Union, are different from those of the U.S. In order to issue new equity or debt securities convertible into equity, with some exceptions, Gentium must increase its authorized capital. In order to do so, the Company's board must meet and resolve to recommend to its shareholders that they approve an amendment to its bylaws to increase its capital. Gentium's shareholders must then approve that amendment to its 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. These meetings take time to call. In addition, a notary public must verify the compliance of the capital increase with the Company's bylaws and applicable Italian law. Further, under Italian law, Gentium's existing shareholders and any holders of convertible securities sometimes 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 the Company. Also, Gentium's shareholders can authorize the board of directors to increase its capital, but the board may exercise such power for only five years. If the authorized capital is not issued by the

end of those five years, the authorized capital expires, and Gentium's board and shareholders would need to meet again to authorize a new capital increase.

Italian law also provides that if the shareholders vote to increase the Company's capital, dissenting, abstaining, or absent shareholders representing more than 5% of the outstanding shares of the Company may, for a period of 90 days following the filing of the shareholders' approval with the Registry of Companies, challenge such capital increase if the increase was not in compliance with Italian law. In certain cases (if, for example, a shareholders' meeting was not called), any interested person may challenge the capital increase for a period of 180 days following the filing of the shareholders' approval with the Registry of Companies. Finally, once the shareholders authorize a capital increase, Gentium must issue all of those authorized shares before the shareholders may authorize a new capital increase, unless the shareholders vote to cancel the previously authorized shares. These restrictions could limit the Company's ability to issue new equity or convertible debt securities on a timely basis.

The Company is restricted under Italian law as to the amount of debt securities that it may issue relative to its equity.

Italian law provides that Gentium may not issue debt securities for an amount exceeding twice the amount of the sum of the aggregate par value of its ordinary shares (which it calls its capital), its legal reserve, and any other disposable reserves appearing on its latest Italian GAAP balance sheet approved by its shareholders. The legal reserve is a reserve to which the Company allocates 5% of its net income each year until it equals at least 20% of its capital. One of the other reserves that Gentium maintains on its balance sheet is a "share premium reserve", meaning amounts paid for its ordinary shares in excess of the capital.

At December 31, 2005, the sum of its capital, legal reserves and other reserves on its Italian GAAP balance sheet was €29.6 million. If the Company issues debt securities in the future, until such debt securities are repaid in full, it may not voluntarily reduce its capital or its 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 Gentium's equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of its equity, some legal scholars are of the opinion that the ratio must be restored by a recapitalization of the Company. If Gentium's equity is reduced, it could recapitalize by issuing new shares or having its shareholders contribute additional capital to the Company, although there can be no assurance that it would be able to find purchasers for new shares or that any of its current shareholders would be willing to contribute additional capital.

If Gentium suffers losses that reduce its capital to less than €120,000, it would need to either recapitalize, change its form of entity, or be liquidated.

Italian law requires the Company to reduce its shareholders' equity and, in particular, its capital (aggregate par value of its ordinary shares) to reflect on-going losses. Gentium is also required to maintain a minimum capital of €120,000. At December 31, 2005, the Company's capital was approximately €9.611 million. If Gentium suffers losses from operations that would reduce its capital to less than €120,000, then either it must increase its capital (which it could do by issuing new shares or having its shareholders contribute additional capital to the Company) or convert the form of the Company into an S.r.l., which has a lower capital requirement of €10,000. If Gentium did not take these steps, a court could liquidate the Company.

Investors may not be able to participate in rights offerings and may experience dilution of their holdings as a result.

Gentium may from time to time distribute rights to its shareholders, including rights to acquire its securities. Under the Company's deposit agreement for the ADSs with its 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. Gentium is 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, the Company may not be able to take advantage of any exemptions from registration under the Securities Act. Accordingly, holders of its

ADSs may be unable to participate in rights offerings and may experience dilution in their holdings as a result.

Investors may be subject to limitations on transfer of their ADSs.

An investors 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 Gentium's books or the books of the depositary are closed, or at any time if the Company 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 an investor's behalf) may have fewer rights as a shareholder than an investor would if the investor was a shareholder of a U.S. company.

Gentium is incorporated under the laws of the Republic of Italy. As a result, the rights and obligations of its shareholders are governed by Italian law and its 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 an investor's behalf) having fewer rights as a shareholder than investors would if they were a shareholder of a U.S. corporation.

Italian labor laws could impair the Company's flexibility to restructure its business.

In Italy, Gentium's 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 the Company is subject could impair its flexibility if it needs to restructure its business.

Recent Events

06/06/2006—Announced that it has completed its previously announced $22.1 million private placement of 1,943,525 of its American Depository Shares (ADSs) at a price of $11.39 per ADS. Investors in the financing also received warrants to purchase 388,705 ADSs at an exercise price of $14.50 per ADS. Investors participating in the financing were large U.S. and Italian institutional investors. The net proceeds from the offering will be used to fund the continued development of the Company's product candidates and for general corporate purposes.

05/31/2006—Announced that it has entered into definitive agreements for a $22.1 million private placement of 1,943,525 of its ADSs at a price of $11.39 per ADS. Investors in the financing will also receive warrants to purchase 388,705 ADSs at an exercise price of $14.50 per ADS.

05/25/2006—Announced that effective June 1, 2006, Cary Grossman, the Company's current chief financial officer, will become chief operating officer and Gary Gemignani will join the Company as the chief financial officer. Mr. Gemignani will be based in a newly established office in New York City. Mr. Grossman will continue to be involved with Mr. Gemignani in the Company's corporate finance and investor relations activities but will assume a more active role in day-to-day business management.

05/13/2006—Announced that its ADSs will be listed and begin trading on the NASDAQ National Market System under the symbol GENT. Gentium ADSs will no longer be listed on the American Stock Exchange.

05/05/2006—Announced that effective May 16, 2006, the Company's ADSs will be listed for trading on The NASDAQ National Market System under the symbol GENT. The Company's ADSs will continue to trade on the American Stock Exchange until they are de-listed from the American Stock Exchange after the market closes on May 15, 2006.

04/16/2006—The Company reported its financial condition and operating results using U.S. Generally Accepted Accounting Principles (GAAP). The Company's manufacturing facility was closed from February through August 2004 for a major upgrade; therefore, comparison of 2005 operating results with 2004 results may not be meaningful. The Company's financial statements are prepared using the Euro (€), its functional currency. On December 31, 2005, €1.00 = $1.18.

- For the fourth quarter ended December 31, 2005 compared with the prior year's fourth quarter: total revenues were €1.44 million, compared to €1.23 million; operating costs and expenses were €3.59 million, compared to €2.97 million; operating loss was €2.15 million, compared to €1.73 million; pre-tax loss was €1.92 million, compared to €4.00 million; net loss was €2.51 million, compared to €4.00 million; basic and diluted net loss per share was €0.27, compared to €0.80.

- For the year ended December 31, 2005 compared with the prior year: total revenues were €3.64 million versus €3.70 million; operating costs and expenses were €11.02 million versus €8.45 million; operating loss was €7.38 million versus €4.75 million; interest expense, net, was €4.15 million versus €2.20 million; pre-tax loss was €11.78 million versus €7.0 million; net loss was €12.43 million versus €7.03 million; basic and diluted net loss per share was €1.79 versus €1.41; cash used in operating activities was €8.7 million versus €4.1 million; cash and cash equivalents amounted to €12.8 million as of December 31, 2005.

03/28/2006—Received its first Institutional Review Board (IRB) approval to initiate a U.S. Phase III clinical trial with Defibrotide for the treatment of veno-occlusive disease (VOD) with multiple organ failure (severe VOD) as a complication of stem cell transplantation. Data from this 80-patient, multi-center trial will be compared to an historical control group of 80 patients, with survival at day 100 as the primary endpoint. The Company believes that approximately 80% of patients with severe VOD die within 100 days of stem cell transplantation without treatment.

02/02/2006—Reported that on February 7, 2006, Guenther Eisser, chief of biology research for Gentium, will present a poster entitled, "Defibrotide, an endothelium stabilizing drug, has anti-angiogenic properties *in vitro* and *in vivo*," at the Angiogenesis in Cancer and Vascular Disease Congress being held in Miami, FL from February 4-8, 2006.

01/30/2006—Reported that an independent study of Defibrotide was the subject of a published paper titled "Successful Treatment with Defibrotide for Sinusoidal Obstruction Syndrome (also known as veno-occlusive disease or "VOD") after Hematopoietic Stem Cell Transplantation (SCT)," which appeared in the December 2005 issue of *Kobe Journal of Medical Science*. The lead author of the paper was Kimikazu Yakushijin, Division of Endocrinology/Metabolism, Neurology and Hematology/Oncology, Department of Clinical Molecular Medicine, Kobe University Graduate School of Medicine, Japan.

01/21/2006—Announced the initiation of a Phase II/III trial with Defibrotide to prevent VOD, a complication of bone marrow and stem cell transplantation, in pediatric patients. The randomized study will include 270 pediatric patients undergoing stem cell transplantation at 30 clinical sites in Europe and Israel and will evaluate the ability of Defibrotide to prevent VOD. Secondary endpoints are measuring the severity of VOD and the occurrence of transplant-associated microangiopathy in each group. The European Group for Blood and Marrow Transplantation (EBMT) is co-sponsoring the study with additional support from the Deutsche Krebshilfe (German Cancer Aid).

12/08/2005—Announced that the outcome from an International Working Group, formed with the goal of developing a consensus formulation of the diagnostic criteria necessary for the diagnosis of microangiopathy following stem cell transplantation, will be the subject of an Oral Session to be presented on December 12, 2005 at 11:45 a.m., at the 2005 Annual Meeting of the American Society of Hematology (ASH). Massimo Iacobelli, Gentium's chief scientific officer, participated in the International Working Group formed as an initiative of the EBMT with 15 international experts in microangiopathic disorders and/or transplantation. The purpose was to identify rigorous, consistent, and feasible criteria applicable to future clinical trials.

12/07/2005—Announced that positive data from the Phase II trial with Defibrotide for the treatment of VOD and MOF as a complication of bone marrow and stem cell transplantation will be presented by Paul G. Richardson, M.D. in a paper entitled, "*Defibrotide for the Treatment of veno-occlusive disease (VOD) and Multi-System Organ Failure (MOF) Post SCT: Analysis of Response and Survival According to Degree and Type of MOF*." Dr. Richardson, clinical director of Dana Farber Cancer Institute's Jerome Lipper Multiple Myeloma Center, assistant professor of medicine at Harvard Medical School and principal investigator in the Phase II trial, will present the paper in a Simultaneous Oral Session at the 2005 Annual Meeting of the American Society of Hematology (ASH).

11/29/2005—Announced that David E. Kroin has been elected to Gentium's Board of Directors. Mr. Kroin is a co-founder and managing director of Great Point Partners, LLC, an asset management firm focused on the healthcare industry, with an emphasis on life sciences. Mr. Kroin's biography is provided on page 13.

11/15/2005—The Company reported its financial condition and operating results using U.S. Generally Accepted Accounting Principles (GAAP). The Company's manufacturing facility was closed from February through August 2004 for a major upgrade; therefore, comparisons of 2005 operating results with 2004 results may not be meaningful. The Company's financial statements are prepared using the Euro (€), its native currency. On September 30, 2005, €1.00 = $1.21.

- For the third quarter ended September 30, 2005, compared with the prior-year's third quarter: total revenues were €0.37 million versus €0.71 million; operating costs and expenses were €2.69 million versus €2.03 million; operating loss was €2.32 million versus €1.32 million; interest expense, net of other income was €0.05 million, compared to €0.03 million in 2004; pre-tax loss was €2.19 million versus €1.30 million; net loss was €2.20 million versus €1.32 million; and basic and diluted net loss per share was €0.28 versus €0.26.

10/17/2005—Announced that it has completed its previously announced $10.9 million private placement of 1,551,125 of its American Depository Shares (ADSs) at a price of $7.05 per ADS. Subject to shareholder approval, investors in the financing will also receive warrants to purchase 620,452 ADSs at an exercise price of $9.69 per ADS. The purchase price is subject to reduction of 20% if the Company's shareholders do not approve the issuance of the warrants within 180 days.

10/04/2005—Announced that it has entered into definitive agreements for a $10.9 million private placement of 1,551,125 million of its ADSs at a price of $7.05 per ADS. Subject to shareholder approval, investors in the financing will also receive Warrants to purchase 620,452 ADSs at an exercise price of $9.69 per share. The closing is subject to certain conditions precedent to the closing. The purchase price is subject to reduction of 20% if the Company's shareholders do not approve the issuance of the Warrants within 180 days. Funds managed by Great Point Partners, LLC were the lead investors in the transaction. Rodman & Renshaw LLC acted as the lead placement agent for the offering, and Maxim Group LLC and I-Bankers Securities Incorporated were co-placement agents.

10/21/2005—Announced that Defibrotide will be the subject of an independent Phase I/II study to treat multiple myeloma (MM) in combination with Melphalan, Prednisone, and Thalidomide (MPT) at approximately 10 cancer centers in Italy. The principal investigator for this study is Dr. Mario Boccadoro, M.D., Division of Hematology, University of Turin, Italy.

09/15/2005—Announced that Richard Champlin, M.D., has joined Gentium's Scientific Advisory Board. Dr. Champlin is professor of medicine and chairman of the Department of Blood and Marrow Transplantation at the University of Texas M.D. Anderson Cancer Center. Dr. Champlin's biography is provided on page 15.

09/07/2005—Announced that on September 6, 2005, representatives of the Company, including members of management and the scientific advisory board, met with officials at the U.S. FDA to discuss the Company's proposed Phase III clinical trial for the use of Defibrotide for the treatment of hepatic VOD with MOF. At that meeting, the FDA encouraged the Company to conduct further studies of Defibrotide to treat VOD, including severe VOD. The FDA also provided the Company with constructive comments regarding certain aspects of the trial protocol.

06/30/2005—Reported financial results for the three- and six-month periods ended June 30, 2005. The Company reports its financial condition and operating results using U.S. Generally Accepted Accounting Principles (GAAP). The Company's financial statements are prepared using the Euro (€), its native currency. On June 30, 2005, €1.00 = $1.21.

- For the second quarter ended June 30, 2005, compared with the prior-year's second quarter: total revenues were €1.2 million versus €1.0 million; operating costs and expenses were €2.9 million versus €2.1 million; operating loss was €1.7 million versus €1.1 million; interest expense was €2.11 million versus €0.03 million; pre-tax loss was €4.3 million versus €1.1 million; net loss was €4.3 million versus €1.2 million; and basic and diluted net loss per share was €0.81 and €0.80 versus €0.23 and €0.23.

08/09/2005—Announced that Dr. Guenther Eissner, Ph.D., chief of the Molecular Biology Research Laboratory for Gentium, presided over a poster presentation at the XXth Annual Congress of the International Society on Thrombosis and Hemostasis. The poster presentation, "Defibrotide and Oligotide, Two DNA-Based Drugs, Protect Human Microvascular Endothelial Cells Against Chemotherapy-Induced Damage and Activation," reports that data showed the drugs' potential ability to protect human endothelial cells from chemotherapy-induced activation, transendothelial migration, and apoptotic damage and may eliminate the increased allogenicity of cytotoxic T-cells (CTL). In laboratory studies, Defibrotide showed anti-thrombotic, anti-ischemic, and pro-fibrinolytic activity with endothelium protective effects.

07/27/2005—Announced that the underwriters of its initial public offering of June 16, 2005 have exercised their over-allotment option to purchase an additional 300,000 of the Company's ADSs at a price of $9.00. Gentium received gross proceeds of $2.7 million from the exercise of this option. To date, the underwriters have purchased a total of 2,700,000 ADSs. Maxim Group LLC and I-Bankers Securities Incorporated served as co-managers of the offering.

07/13/2005—Announced that the U.S. FDA has agreed that Gentium's Chemistry, Manufacturing & Controls ("CMC") submission provides adequate characterization of Defibrotide for the Company's planned Phase III clinical trial for the treatment of hepatic VOD with MOF. An adequate CMC submission is one of the pre-requisites to commencing Phase III clinical trials.

06/16/2005—Announced that its initial public offering (IPO) of 2.4 million of ADSs representing 2.4 million of its ordinary shares has been priced at $9.00 per ADS. The Company has granted the underwriters a 45-day option to purchase up to 360,000 additional ADSs to cover over-allotments. The ADSs will be listed on the American Stock Exchange under the symbol "GNT" and will begin trading on June 16, 2005. A registration statement relating to these securities was filed with and declared effective by the Securities and Exchange Commission on June 15, 2005.

06/16/2005—The American Stock Exchange® (Amex®) listed American Depositary Shares (ADS) representing ordinary shares of Gentium S.p.A under the ticker symbol GNT.

Glossary of Lesser-Known Terms

Allogenic—Being genetically different although belonging to or obtained from the same species.

Anemia—A pathological deficiency in the oxygen-carrying component of the blood, measured in unit volume concentrations of hemoglobin, red blood cell volume, or red blood cell number.

Antineoplastic—Inhibiting or preventing the growth or development of malignant cells.

Apoptosis—Programmed cell death; this physiological process is necessary for the elimination of superfluous, diseased, or damaged cells and the formation of new cells. Also known as programmed cell death.

Ascites—An effusion and accumulation of serious fluid in the abdominal cavity.

Autologous—Derived or transferred from the same individual's body.

Chemotherapy—A chemical that binds to and specifically kills microbes or tumor cells. In oncology, a drug therapy for cancer.

Chronic lymphocytic leukemia (CLL)—The most common form of leukemia in adults, in which the lymphocytes may look fairly normal but are not fully mature and do not deal effectively with infection. The malignant cells are found in the blood and bone marrow, collect in and enlarge the lymph nodes, and may crowd out other blood cells in the bone marrow, resulting in a shortage of red blood cells (producing anemia) and platelets (producing easy bruising and bleeding).

Coagulation—The process of clot formation.

Contract Research Organization (CRO)—An organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions. CROs are independent companies carrying out specialized functions of Pharmaceutical Research and Development such as Phase I, Phase II, Phase III, or Phase IV clinical trial.

Cytotoxic—Having a deleterious effect upon cells.

Deep vein thrombosis (**DVT**)**—**A blood clot (thrombus) in a deep vein in the thigh or leg. The clot can break off as an embolus and make its way to the lung, where it can cause respiratory distress and respiratory failure. DVT is sometimes called the "economy-class syndrome". Even in young, healthy travelers, long stretches of time spent immobilized in the cramped seat of an aircraft with very low humidity sets the stage for formation of a blood clot in the leg. Abbreviated as DVT.

Endothelial—Pertaining to or made up of endothelium.

Endothelial Cells—A thin, flattened cell, a layer of them lines the inside surfaces of body cavities, blood vessels, and lymph vessels, making up the endothelium.

European Agency for the Evaluation of Medicinal Products (EMEA)—A decentralized body of the European Union, with headquarters in London since January 1995. Its main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use.

Fast Track—A formal mechanism to interact with the FDA using approaches that are available to all applicants for marketing claims.

Fibrinolytic—Pertaining to, characterized by, or causing the dissolution of fibrin by enzymatic action.

Fludarabine—A chemotherapy drug used in the treatment of hematological malignancies.

Good Manufacturing Practices (GMPs)—The quality system regulation overseen by the Food and Drug Administration (FDA), which includes requirements related to the methods used in, and the facilities and controls used for designing, manufacturing, packaging, labeling, storing, installing, and servicing of medical devices intended for human use.

Hemocrit—The percentage by volume of packed red blood cells in a given sample of blood after centrifugation.

Hypotension—Abnormally low blood pressure.

Inflammatory Bowel Disease (IBD)—A group of chronic intestinal disorders characterized by inflammation of the large intestine.

Jaundice—Yellowish discoloration of the whites of the eyes, skin, and mucous membranes caused by deposition of bile salts in these tissues. It occurs as a symptom of various diseases, such as hepatitis, that affect the processing of bile.

Microangiopathy—Any disease of the capillaries, often applied to vascular changes in diabetes mellitus.

Mucositis—An inflammation of mucous membranes.

Multiple Myeloma—A malignancy of the plasma cells that affects multiple sites within the bone marrow and secretes all or part of a monoclonal antibody.

Occlusion—An obstruction or a closure of a passageway or vessel.

Orphan drug—Designation given to either a rare disease that affects fewer than 200,000 people, or a common disease that has been ignored because it is less prominent in the U.S. compared with developing nations. According to the NIH, there are approximately 6,000 of these diseases.

Orphan Medicinal Product Designation—Medicinal products that have been designated as orphan due to the rarity of the diseases they treat. Measures were first put in place to create incentives for developing orphan medicinal products in America in 1983. Incentives are required, as there are more than 5,000 identified diseases that affect less than 0.05% of the population for which there are currently no satisfactory treatments. This U.S. initiative has proved so successful in stimulating research that Japan, Singapore, and Australia have introduced similar regimes as has the EU in the form of Regulation 141/2000/EC on orphan medicinal products (Orphan Regulation).

Pallor—Extreme or unnatural paleness.

Plasma cell—Any of the antibody-secreting cells found in lymphoid tissue and derived from B-cells upon lymphokine stimulation and reaction with a specific antigen. Also called *plasmacyte.*

Polydeoxyribonucleotide—A group of 13 or more deoxyribonucleotides in which the phosphate residues of each deoxyribonucleotide act as bridges in forming diester linkages between the deoxyribose moieties.

Proliferation—To grow or multiply by rapidly producing new tissue, parts, cells, or offspring.

Prophylaxis—Prevention of or protective treatment for disease.

Pulmonary Embolism—The lodgment of a blood clot in the lumen of a pulmonary artery, causing a severe dysfunction in respiratory function.

Renal—Of, relating to, or in the region of the kidneys.

Stem Cell—Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost.

Stem Cell Transplantation (SCT)—The use of stem cells as a treatment for cancer or other diseases. In this procedure, the stem cells are removed (or obtained) from a donor; before a transplant is done for cancer, the patient receives high-dose chemotherapy and/or radiation to destroy the malignant cells; the stem cells are then given to the patient in whom they can produce new blood and immune cells and replace the cells destroyed by the treatment; the stem-cell preparation is infused into a vein and, once in the bloodstream, the stem cells head straight for the bone marrow space.

Thrombosis—Blood cells reacting to a foreign object by clotting and blocking the artery.

Ulcerative Colitis—Inflammation of the colon and rectum. The cause is unclear although there are often antibodies to colonic epithelium and E. Coli strain 0119 B14.

U.S. Food and Drug Administration (FDA)—The U.S. Agency responsible for regulation of biotechnology food products. The major laws under which the agency has regulatory powers include the Food, Drug, and Cosmetic Act, and the Public Health Service Act.

Vascular—Pertaining to blood vessels or indicative of a copious blood supply.

Veno-Occlusive Disease (VOD)—A disease that sometimes occurs following high-dose chemotherapy or radiation, in which the blood vessels that carry blood through the liver become swollen and clogged.

Jeffrey J. Kraws and Karen B. Goldfarb
Phone: (609) 306-2274
Fax: (609) 395-9339
Email: eio@crystalra.com
Web: www.crystalra.com

Legal Notes and Disclosures: This report has been prepared by Gentium S.p.A., (the "Company") with the assistance of Crystal Research Associates, LLC. ("CRA") based upon information provided by the Company. CRA has not independently verified such information. In addition, CRA has been compensated by the Company in cash of US$35,000 and 15,000 warrants for its services in creating this report, for updates, and for printing costs.

Some of the information in this report relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can be only predictions and the actual events or results may differ from those discussed due to, among other things, the risks described in Gentium's, reports on Forms 20-F, 6-K, and other forms filed with the Securities and Exchange Commission ("SEC") from time to time. The content of this report with respect to Gentium has been compiled primarily from information available to the public released by Gentium. Gentium is solely responsible for the accuracy of that information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Gentium or CRA. Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding. For more complete information about Gentium, the reader is directed to the Company's website at www.gentium.it This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Free additional information about Gentium, and its public filings, as well as free copies of this report can be obtained in either a paper or electronic format by calling (39) 031-385217.