

Gentium S.p.A.
Form F-3
May 27, 2011

As filed with the Securities and Exchange Commission on May 27, 2011
Registration No. 333-_____

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

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

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

Republic of Italy
(State or other jurisdiction of
incorporation or organization)

Not Applicable
(I.R.S. Employer
Identification No.)

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

CT Corporation System
111 Eighth Avenue, 13th Floor
New York, New York 10011
(212) 894-8940
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:
Theodore L. Polin, Esq.
Adam D. So, Esq.
Epstein Becker & Green, P.C.
250 Park Avenue
New York, New York 10177
(212) 351-4500

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective as determined by market conditions.

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

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415, check the following box.

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Class of Securities To Be Registered (1)	Amount To Be Registered	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Ordinary shares, no par value per share (2)	(3)	(3)	(3)	N/A
Warrants (2)	(3)	(3)	(3)	N/A
Total for sale by Registrant	(3)	(3)	\$30,000,000	\$3483 (4)

(1) This Registration Statement covers ordinary shares and ordinary shares that may be issued upon exercise of warrants. In addition, securities registered hereunder may be sold separately or as units with other securities registered hereunder.

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

(3) An indeterminate number of securities is being registered as may at various times be issued at indeterminate prices, with an aggregate public offering price not to exceed \$30,000,000 or the equivalent thereof in one or more currencies.

(4) Computed in accordance with Rule 457(o) of the rules and regulations under the Securities Act.

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

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

SUBJECT TO COMPLETION DATED _____, 20__

PROSPECTUS

Gentium S.p.A.

\$30,000,000

American Depositary Shares Representing Ordinary Shares
Warrants

This prospectus relates to American Depositary Shares (“ADSs”), each representing one ordinary share of our company, Gentium S.p.A., and warrants that we may offer from time to time in one or more offerings up to a total public offering price of \$30,000,000 on terms to be determined at the time of the offer for subscription. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities

Our ADSs trade on the Nasdaq Global Market under the symbol “GENT.” As of May 26, 2011 the aggregate market value of our ordinary shares held by non-affiliates was \$98,570,714 based on 14,966,317 outstanding ordinary shares, of which 5,349,662 ADSs or ordinary shares were held by affiliates, and a per share price of \$10.25 which was the closing sale price of our ADS as quoted on the Nasdaq Global Market on May 26, 2011.

These securities may be offered for subscription directly by us, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See “Plan of Distribution” in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the offer for subscription of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any such offer for subscription will also be included in a prospectus supplement.

Our business and an investment in our ADSs involve significant risks. These risks are described under the caption “Risk Factors” beginning on page 4 of this prospectus.

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

_____, 20__

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form F-3 that we filed with the Securities and Exchange Commission (or the SEC) using a “shelf registration” process. Under this shelf process, we may from time to time, offer for subscription any combination of securities described in this prospectus in one or more offerings.

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

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

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

PROSPECTUS SUMMARY

This prospectus summary highlights selected information contained elsewhere in this prospectus and the documents incorporated by reference. You should read the following information together with the more detailed information regarding our company and the ADSs appearing elsewhere in this prospectus and in selected portions of our Annual Report on Form 20-F for the year ended December 31, 2010 and other documents filed with the SEC that we have incorporated by reference into this prospectus.

Our Business

We are a biopharmaceutical company focused on the development and manufacture of our primary product candidate, defibrotide, an investigational drug based on a mixture of single-stranded and double-stranded DNA extracted from pig intestines. Our development of defibrotide has been focused on the treatment and prevention of a disease called hepatic veno-occlusive disease, or VOD, a condition that occurs when veins in the liver are blocked as a result of cancer treatments, such as chemotherapy or radiation, that are administered prior to stem cell transplantation. Severe VOD is the most extreme form of VOD and is linked to multiple-organ failure and high rates of morbidity and mortality.

We have completed two clinical trials, a Phase III trial of defibrotide for the treatment of severe VOD in the U.S., Canada and Israel and a Phase II/III pediatric trial in Europe for the prevention of VOD. Defibrotide has been given “orphan” status by the U.S. Food and Drug Agency, or FDA, and the European Medicines Agency, or EMA, which means that we will have limited market exclusivity upon regulatory approval. The FDA has also granted “fast-track product” designation to defibrotide for the treatment of VOD. While we have not yet obtained regulatory approval to market defibrotide, we are authorized to distribute defibrotide on a pre-approval basis under a treatment Investigational New Drug, or IND, protocol, which we call our cost recovery program, in the U.S. and through a named-patient program throughout the rest of the world. We do not know of any FDA or EMA approved treatments for VOD.

We have recently filed a marketing authorization application to EMA and we anticipate filing for regulatory approval for defibrotide with the FDA by the end of our second quarter in 2011. We are also working on our U.S. regulatory strategy with our commercial partner, Sigma-Tau Finanziaria S.p.A. and its affiliate, Sigma-Tau Pharmaceuticals, Inc., to which we have licensed our commercial rights to use defibrotide for both the treatment and prevention of VOD in the Americas. We are currently establishing our European sales force, as we intend to commercialize defibrotide in the major European countries on our own.

We have a manufacturing plant in Italy where we produce active pharmaceutical ingredients, which are subsequently used to make the finished forms of various drugs. We believe that we are the sole worldwide producer of defibrotide. In addition to defibrotide, we manufacture urokinase and sulglicotide, both of which are sold to third parties. All of the Company’s operating assets are located in Italy.

We are subject to a number of risks, including our ability to successfully obtain regulatory approval for defibrotide, the uncertainty that defibrotide will become a successful commercial product, our ability to generate projected revenue through our named-patient and cost recovery programs, our dependence on corporate partners, our ability to obtain financing, if necessary, and potential changes in the health care industry. Before making an investment decision, you should carefully consider the risks described under “Risk Factors” in our Annual Report on Form 20-F for our most recent fiscal year (together with any material changes thereto contained in subsequent filed reports on Form 6-K) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus and any accompanying prospectus supplement, in light of your particular investment objectives and financial circumstances. The risks so described are not the only risks facing us. Additional risks not presently known to us or that we currently

deem immaterial may also impair our business operations. Our business, financial condition and results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus.

Corporate Information and Executive Offices

We started as a group of pharmaceutical businesses founded in Italy in 1944 and have been involved in the research and development of drugs derived from DNA and DNA molecules since the 1970s. In 1993, we were formed by FinSirton S.p.A. as Pharma Research S.r.L., an Italian private limited company, for the purpose of pursuing research and development activities of prospective pharmaceutical specialty products. FinSirton has historically been our largest shareholder and is currently one of our two largest shareholders, with the other shareholder being Sigma-Tau Finanziaria S.p.A. together with its affiliates. FinSirton may be deemed to be controlled by Dr. Laura Ferro, our former Chief Executive Officer and President and currently one of our directors, and her family. In December 2000, Crinos Industria Farmacobiologica S.p.A., a subsidiary of FinSirton, contributed its plants, equipment and patents relating the development of biological pharmaceutical products, including all of its rights relating to defibrotide, to us in return for 98% of our ordinary shares. FinSirton continued to own the remaining 2% of our ordinary shares. At that time, we changed from a private limited company to a corporation and in July 2001, we changed our name to Gentium S.p.A. Under our current bylaws, the duration of our company will expire on December 31, 2050. We are governed by the Italian Civil Code.

In May 2002, Crinos Industria Farmacobiologica S.p.A. sold its commercial division, including its products, licenses and patents relating to pharmaceutical products in Italy, including the brand name “Crinos,” to a newly formed subsidiary, Crinos S.p.A., of Stada, a leader in the generic pharmaceutical industry in Europe, and Crinos Industria Farmacobiologica S.p.A. changed its name to Sirton Pharmaceuticals S.p.A. In 2003 and 2004, Sirton distributed its 98% ownership interest in our ordinary shares to FinSirton as dividends, and FinSirton became our sole shareholder. In January 2005 and April 2005, FinSirton sold portions of its ownership interest to third parties. In June 2005, we conducted an initial public offering of 2,400,000 ADSs, each representing the right to receive one ordinary share, and listed the ADSs on the American Stock Exchange. FinSirton remains one of our largest shareholders, owning approximately 17% of our outstanding ordinary shares at May 27, 2011.

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

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

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

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our Annual Report on Form 20-F for our most recent fiscal year (together with any material changes thereto contained in subsequent filed reports on Form 6-K) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus and any accompanying prospectus supplement.

The prospectus supplement applicable to each type or series of securities we offer may contain a discussion of risks applicable to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the caption “Risk Factors” in the applicable prospectus supplement, together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus. These risks could materially affect our business, results of operations or financial condition and cause the value of our securities to decline. You could lose all or part of your investment.

WARNING REGARDING FORWARD-LOOKING STATEMENTS

This prospectus may contain forward-looking statements that involve substantial risks and uncertainties regarding future events or our future performance. When used in this prospectus, the words “anticipate,” “believe,” “estimate,” “may,” “intent,” “continue,” “will,” “plan,” “intend,” and “expect” and similar expressions identify forward-looking statements. You should read statements that contain these words carefully because they discuss our future expectations contain projections of our future results of operations or of our financial condition or state other “forward-looking” information. We believe that it is important to communicate our future expectations to our investors. Although we believe that our expectations reflected in any forward-looking statements are reasonable, these expectations may not be achieved. The factors listed in the section captioned “Risk Factors,” as well as any cautionary language included in this prospectus or incorporated by reference, provide examples of risks, uncertainties and events that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. Before you invest in our ordinary shares or ADSs, you should be aware that the occurrence of the events described in the “Risk Factors” section and elsewhere in this prospectus could have a material adverse effect on our business, performance, operating results and financial condition. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements set forth in this prospectus. Except as required by federal securities laws, we are under no obligation to update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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

REASONS FOR THE OFFER AND USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the subscription of these securities for general corporate and working capital purposes, which include funding strategic initiatives that we may undertake from time to time. We have not yet determined the amount of net proceeds to be used for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the subscription of these securities. Our plans to use the estimated net proceeds from the subscription of these securities may change, and if they do, we will update this information in a prospectus supplement.

PLAN OF DISTRIBUTION

We may offer for subscription the securities described by this prospectus to one or more underwriters or dealers for public offering, through agents, directly to investors or through a combination of any such methods of placement. The name of any such underwriters, dealers or agents involved in the offer of the securities, the amounts underwritten and the nature of their obligation to take the securities will be specified in the applicable prospectus supplement. We have reserved the right to offer for subscription the securities directly to investors on our own behalf in those jurisdictions where we are authorized to do so. The offer for subscription of the securities may be effected in transactions (a) on any national or international securities exchange or quotation service on which the securities may be listed or quoted at the time of subscription, (b) in the over-the-counter market, (c) in transactions other than on such exchanges or in the over-the-counter market or (d) through the writing of options.

We and our agents and underwriters, may offer the securities for subscription at a fixed price or prices that may be changed, at market prices prevailing at the time of subscription, at prices related to such prevailing market prices or at negotiated prices. The securities may be offered on an exchange, which will be disclosed in the applicable prospectus supplement. We may, from time to time, authorize dealers, acting as our agents, to offer the securities for subscription upon such terms and conditions set forth in the applicable prospectus supplement.

If we use underwriters to place securities, we will enter into an underwriting agreement with them at the time of the subscription by them. In connection with the placement of the securities, underwriters may receive compensation from us in the form of underwriting discounts or commissions and may also receive commissions from investors for whom they may act as agents. Any underwriting compensation paid by us to underwriters or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers, will be set forth in the applicable prospectus supplement to the extent required by applicable law. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions (which may be changed from time to time) from the investors for whom they may act as agents.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase debt securities as a principal, and may then resell the debt securities at varying prices to be determined by the dealer.

If so indicated in the prospectus supplement, we will authorize underwriters, dealers or agents to solicit offers by certain specified institutions to subscribe offered securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject to any conditions set forth in the applicable prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts. The underwriters and other persons soliciting such contracts will have no responsibility for the validity or performance of any such

contracts.

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Underwriters, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution toward certain civil liabilities, including any liabilities under the Securities Act.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. These may include over-allotment, stabilization, syndicate short covering transactions and penalty bids. Over-allotment involves sales in excess of the offering size, which creates a short position. Stabilizing transactions involve bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate short covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the underwriters to reclaim selling concessions from dealers when the securities originally sold by the dealers are purchased in covering transactions to cover syndicate short positions. These transactions may cause the price of the securities sold in an offering to be higher than it would otherwise be. These transactions, if commenced, may be discontinued by the underwriters at any time.

Any securities other than our ADSs hereunder may be new issues of securities with no established trading market. Any underwriters or agents by or through whom such securities are subscribed may make a market in such securities, but such underwriters or agents will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any such securities. The amount of expenses expected to be incurred by us in connection with any issuance of securities will be set forth in the applicable prospectus supplement. Certain of the underwriters, dealers or agents and their associates may engage in transactions with, and perform services for, us and certain of our affiliates in the ordinary course of business.

During such time as we may be engaged in a distribution of the securities covered by this prospectus we are required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes us, any affiliated purchasers, and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase, any security which is the subject of the distribution until the entire distribution is complete. Regulation M also restricts bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of our ADSs.

EXPERTS

The financial statements of Gentium at December 31, 2010 and 2009 and for each of the three-year periods ended December 31, 2010, incorporated by reference in this registration statement and related prospectus have been audited by Reconta Ernst & Young S.p.A., independent registered public accounting firm, as set forth in their report thereon appearing elsewhere therein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

LEGAL MATTERS

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

DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

Description of American Depositary Shares

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

10286.

Each ADS represents one ordinary share. Holders of ADSs will not be able to exercise voting rights attaching to the ordinary shares evidenced by the ADSs on an individual basis; rather, holders of ADSs will have the right to instruct the depositary as the holders' representative to exercise these voting rights. The depositary will mail to all record holders of ADSs a notice containing a summary of all information included in any notice of a shareholders' meeting received by the depositary and will solicit proxies from ADS holders for instructions on how to vote its ordinary shares at our shareholder meetings. Owners of ADSs representing our ordinary shares are subject to additional limitations as to their rights as explained in our risk factors entitled Risks Related to Ownership of the American Depositary Shares “–You may not be able to participate in rights offerings and may experience dilution of your holdings as a result” and “–You may be subject to limitations on transfer of your ADSs,” found in our Annual Report on Form 20-F for the fiscal year ended December 31, 2010.

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

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

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

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Description of Warrants

We may issue warrants for the subscription of shares that are then converted into ADSs. Warrants may be issued independently or together with ADSs and may be attached to or separate from any offered securities. Any issue of warrants will be governed by the terms of the applicable form of warrant and any related warrant agreement which we will file as an exhibit to our registration statement at or before the time we issue any warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies (including composite currencies) in which the price of such warrants may be payable;
- the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;
 - the price at which the securities purchasable upon exercise of such warrants may be subscribed;
- the date on which the right to exercise such warrants will commence and the date on which such right shall expire;
 - if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
 - information with respect to book-entry procedures, if any; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to subscribe ordinary shares (which may be converted into ADSs) may also include, if applicable, a discussion of certain U.S. federal income tax and ERISA considerations.

Each warrant will entitle its holder to subscribe ordinary shares (which may be converted into ADSs) at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised warrants will become void. We will specify the place or places where, and the manner in which, warrants may be exercised in the applicable prospectus supplement.

Prior to the exercise of any warrants to subscribe ordinary shares (which may be converted into ADSs), holders of the warrants will not have any of the rights of holders of ADSs.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

- (i) our Annual Report on Form 20-F for the fiscal year ended December 31, 2010, filed with the SEC on March 31, 2011; and
- (ii) all of our Reports on Form 6-K furnished to the SEC between the date of filing our Annual Report on Form 20-F with the SEC and the date of this prospectus.

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

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

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

WHERE YOU CAN FIND MORE INFORMATION

We file and submit reports, including annual reports on Form 20-F, and other information with the Securities and Exchange Commission pursuant to the rules and regulations of the SEC that apply to foreign private issuers. You may read and copy any materials filed with the SEC at its Public Reference Room at 100 F Street N.E., Washington, D.C. 20459. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The registration statement of which this prospectus is a part, and other public filings with the SEC, are also available on the website maintained by the SEC at <http://www.sec.gov>. Our website is located at www.gentium.it. The information contained on our website is not part of this prospectus.

INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

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

SERVICE OF PROCESS AND ENFORCEABILITY OF CIVIL LIABILITIES

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

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 8. Indemnification of Directors and Officers.

We have procured and intend to maintain a directors' and officers' liability insurance policy that insures such persons against the costs of defense, settlement or payment of a judgment under certain circumstances. We have also entered into indemnification agreements with our directors and executive officers for the indemnification of and advancement of expenses to these persons to the fullest extent permitted by law.

Item 9. Exhibits.

Exhibit
Number

Description of Documents

- 3(i) Articles of Association of Gentium S.p.A., formerly known as Pharma Research S.r.l. dated November 11, 1993, incorporated by reference to Exhibit 3(i) to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 3(ii) Amended and Restated Bylaws of Gentium S.p.A., as amended on April 30, 2010., incorporated by reference to Exhibit 3(ii) to the Registration Statement on Form F-3, Registration No. 333-171443, previously filed with the Securities and Exchange Commission on December 28, 2010.
- 4.1 Form of Deposit Agreement among Gentium S.p.A., The Bank of New York and the owners and beneficial owners from time to time of American Depositary Receipts (including as an exhibit the form of American Depositary Receipt), incorporated by reference to Exhibit 4.6 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on June 9, 2005.
- 4.2 Form of American Depositary Receipt (see Exhibit 4.1).
- 4.3 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto dated as of May 31, 2006, incorporated by reference to Exhibit 4.9.1 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 4.4 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto, dated as of February 6, 2007, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 7, 2007.
- 4.5 Form of warrant (regarding Series A financing), incorporated by reference to Exhibit 4.2.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.

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- 4.6 Form of Representatives' Purchase Option between Gentium S.p.A. and Maxim Group LLC and I-Bankers Securities Inc., incorporated by reference to Exhibit 1.2 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on June 9, 2005.
 - 4.7 Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated October 14, 2005, incorporated by reference to Exhibit 4.8.2 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
 - 4.8 Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.2 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
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Exhibit Number	Description of Documents
4.9	Form of Ordinary Share Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
4.10	Form of Investors' Rights Agreement between Gentium S.p.A. and holders of the Series A senior convertible promissory notes and warrants dated October 15, 2004, incorporated by reference to Exhibit 4.2.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
4.11	Amendment No. 1 to Gentium S.p.A. Series A Senior Convertible Promissory Notes, Warrants, Subscription Agreements and Investor Rights Agreements among Gentium S.p.A. and the other parties thereto dated May 27, 2005, incorporated by reference to Exhibit 4.2.6 to Amendment No. 4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 31, 2005.
4.12	Investors' Rights Agreement by and among Gentium S.p.A., Alexandra Global Master Fund Ltd. And Generation Capital Associates made as of January 10, 2005, incorporated by reference to Exhibit 4.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
4.13	Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of October 14, 2005, incorporated by reference to Exhibit 4.8.3 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
4.14	Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of June 6, 2006, incorporated by reference to Exhibit 4.9.4 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
4.15	Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of February 9, 2007, incorporated by reference to Exhibit 4.10.3 to the Registration Statement on Form F-3, Registration No. 333-141198, previously filed with the SEC on March 9, 2007.
4.16.1	Amended and Restated 2004 Equity Incentive Plan, incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-8, Registration No. 333-137534, previously filed with the SEC on September 22, 2006.
4.16.2	Amendment No. 1 to Amended and Restated 2004 Equity Incentive Plan, made as of March 26, 2007, incorporated by reference to Exhibit 4.1.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
4.17	Amended and Restated Nonstatutory Share Option Plan and Agreement dated March 23, 2006, incorporated by reference to Exhibit 4.2 to the Annual Report on Form

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20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.

- 4.18 Amendment No. 1 to Amended and Restated Nonstatutory Share Option Plan and Agreement, made as of March 26, 2007, incorporated by reference to Exhibit 4.2.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.19 2007 Stock Option Plan, dated March 26, 2007, incorporated by reference to Exhibit 4.42 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 5.1 Opinion of Gianni, Origoni, Grippo & Partners, dated May 27, 2011, as to the legality of the ordinary shares underlying the American Depositary Shares being offered by the prospectus forming a part of this Registration Statement, filed herewith.

Exhibit Number	Description of Documents
10.1	Ministry for Universities, Scientific and Technological Research Loan granted to Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., by Sanpaolo Imi S.p.A., dated September 27, 2000, incorporated by reference to Exhibit 10.6 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
10.2	Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A. dated June 14, 2006 incorporated by reference to Exhibit 10.7.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
10.3	Loan Agreement for €230,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
10.4	Loan Agreement for €500,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
10.5	Loan Agreement for €225,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
10.6	Financing Contract between Banca Intesa Mediocredito S.p.A. and Gentium S.p.A. dated April 20, 2006, incorporated by reference to Exhibit 4.36.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
10.7	Loan Agreement, dated June 30, 2006, between San Paolo IMI S.p.A. and Gentium S.p.A., incorporated by reference to Exhibit 4.43 to the Annual Report on Form 20-F for the year ended December 31, 2006, previously filed with the SEC on April 30, 2007.
10.8.1	Master Services Agreement, dated March 14, 2007, between MDS Pharma Services (US), Inc. and Gentium S.p.A., incorporated by reference to Exhibit 1 to the report on Form 6-K, previously filed with the SEC on March 20, 2007.
10.8.2	Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (prospective arm), incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.
10.8.3	Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (historical arm), incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.

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- 10.9.1 License and Supply Agreement by and between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc. (assignee of Sigma Tau Industrie Farmaceutiche Riunite S.p.A.) dated December 7, 2001, incorporated by reference to Exhibit 10.15 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 10.9.2 Letter Agreement, dated October 12, 2007, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 99.4 to the report on Form 6-K, previously filed with the SEC on December 12, 2007.
- 10.9.3* Amendments to License and Supply Agreement and Letter Agreement, dated December 7, 2001 and October 12, 2007, respectively, effective January 7, 2010, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 2 to the Form 6-K, previously filed with the SEC on January 11, 2010.
- 10.10.1 Contract to Supply Active Ingredients between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 4.24.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 10.10.2 Amendment No. 1 to Contract to Supply Active Ingredients, effective as of December 7, 2007, by and between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A.

Exhibit Number	Description of Documents
10.11.1	Master Agreement, dated December 28, 2006, among Gentium S.p.A., Crinos S.p.A., SFI Stada Financial Investments Ltd. And SFS Stada Financial Services International Ltd., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
10.11.2	Distribution Agreement, dated December 28, 2006, between Gentium S.p.A. and Crinos S.p.A., incorporated by reference to Exhibit 6 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
10.13*	Technical Transfer Services Agreement, dated February 2, 2009, between Gentium S.p.A. and Patheon Italia S.p.A., incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
10.14.1	Technical Agreement, dated February 26, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
10.14.2*	Supply and Distribution Agreement, dated March 6, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
4.2.3*	Master Contract Clinical Research Agreement, dated September 29, 2009, between US Oncology Clinical Development and Gentium S.p.A., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on December 8, 2009.
10.15	Service Agreement between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.25.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
10.16	Service Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.26.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
10.17	Commercial Lease Contract between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. dated January 1, 2005, incorporated by reference to Exhibit 10.33 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.
10.18	

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Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2005, incorporated by reference to Exhibit 10.32 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.

10.19 Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2007, incorporated by reference to Exhibit 4.32.2 (improperly coded as Exhibit 4.43(2)) to the Annual Report on Form 20-F for the year ending December 31, 2006, previously filed with the SEC on April 30, 2007.

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

23.1 Consent of Reconta Ernst & Young S.p.A. dated May 27, 2011.

23.2 Consent of Gianni, Origoni, Grippo & Partners (included in Exhibit 5.1).

24.1 Power of Attorney (included on the signature page).

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

Item 10. Undertakings

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement.

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

Provided however, That: paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the registration statement is on Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) If the registrant is a foreign private issuer, to file a post-effective amendment to the registration statement to include any financial statements required by Item 8.A. of Form 20-F at the start of any delayed offering or throughout a continuous offering. Financial statements and information otherwise required by Section 10(a)(3) of the Act need not be furnished, provided, that the registrant includes in the prospectus, by means of a post-effective amendment, financial statements required pursuant to this paragraph (a)(4) and other information necessary to ensure that all other information in the prospectus is at least as current as the date of those financial statements. Notwithstanding the foregoing, with respect to registration statements on Form F-3, a post-effective amendment need not be filed to include financial statements and information required by Section 10(a)(3) of the Act or Rule 3-19 of this chapter if such financial statements and information are contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the Form F-3.

(5) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

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(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's Annual Report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form F-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Villa Guardia (Como) Italy, on the 27th day of May, 2011.

GENTIUM, S.p.A

By: /s/ Khalid Islam

Dr. Khalid Islam,
Chairman and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Khalid Islam, Chairman and Chief Executive Officer, and Salvatore Calabrese, Chief Financial Officer and Senior Vice President, Finance, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title(s)	Date
/s/ Khalid Islam Dr. Khalid Islam	Chairman, Chief Executive Officer and Director (principal executive officer)	May 27, 2011
/s/ Salvatore Calabrese Salvatore Calabrese	Chief Financial Officer and Senior Vice President, Finance (principal financial officer and principal accounting officer)	May 27, 2011
/s/ Gigliola Bertoglio Gigliola Bertoglio	Director	May 27, 2011
/s/ Marco Codella Marco Codella	Director	May 27, 2011
/s/ Glenn Cooper Dr. Glenn Cooper	Director	May 27, 2011
/s/ Laura Ferro Dr. Laura Ferro	Director	May 27, 2011
/s/ Bobby W. Sandage, Jr. Dr. Bobby W. Sandage, Jr.	Director	May 27, 2011

INDEX TO EXHIBITS

Exhibit

Number Description of Documents

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- 3(ii) Amended and Restated Bylaws of Gentium S.p.A., as amended on May 9, 2011.
- 4.1 Form of Deposit Agreement among Gentium S.p.A., The Bank of New York and the owners and beneficial owners from time to time of American Depositary Receipts (including as an exhibit the form of American Depositary Receipt), incorporated by reference to Exhibit 4.6 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on June 9, 2005.
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- 4.3 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto dated as of May 31, 2006, incorporated by reference to Exhibit 4.9.1 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 4.4 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto, dated as of February 6, 2007, incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on February 7, 2007.
- 4.5 Form of warrant (regarding Series A financing), incorporated by reference to Exhibit 4.2.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 4.6 Form of Representatives' Purchase Option between Gentium S.p.A. and Maxim Group LLC and I-Bankers Securities Inc., incorporated by reference to Exhibit 1.2 to Amendment No. 5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on June 9, 2005.
- 4.7 Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated October 14, 2005, incorporated by reference to Exhibit 4.8.2 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.

- 4.8 Form of American Depositary Shares Purchase Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.2 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
 - 4.9 Form of Ordinary Share Warrant by Gentium S.p.A. dated June 6, 2006, incorporated by reference to Exhibit 4.9.3 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
 - 4.10 Form of Investors' Rights Agreement between Gentium S.p.A. and holders of the Series A senior convertible promissory notes and warrants dated October 15, 2004, incorporated by reference to Exhibit 4.2.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
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- 4.11 Amendment No. 1 to Gentium S.p.A. Series A Senior Convertible Promissory Notes, Warrants, Subscription Agreements and Investor Rights Agreements among Gentium S.p.A. and the other parties thereto dated May 27, 2005, incorporated by reference to Exhibit 4.2.6 to Amendment No. 4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 31, 2005.
- 4.12 Investors' Rights Agreement by and among Gentium S.p.A., Alexandra Global Master Fund Ltd. And Generation Capital Associates made as of January 10, 2005, incorporated by reference to Exhibit 4.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 4.13 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of October 14, 2005, incorporated by reference to Exhibit 4.8.3 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the SEC on December 30, 2005.
- 4.14 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of June 6, 2006, incorporated by reference to Exhibit 4.9.4 to the Registration Statement on Form F-3, Registration No. 333-135622, previously filed with the SEC on July 6, 2006.
- 4.15 Registration Rights Agreement among Gentium S.p.A. and the other parties thereto made and entered into as of February 9, 2007, incorporated by reference to Exhibit 4.10.3 to the Registration Statement on Form F-3, Registration No. 333-141198, previously filed with the SEC on March 9, 2007.
- 4.16.1 Amended and Restated 2004 Equity Incentive Plan, incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-8, Registration No. 333-137534, previously filed with the SEC on September 22, 2006.
- 4.16.2 Amendment No. 1 to Amended and Restated 2004 Equity Incentive Plan, made as of March 26, 2007, incorporated by reference to Exhibit 4.1.2 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.
- 4.17 Amended and Restated Nonstatutory Share Option Plan and Agreement dated March 23, 2006, incorporated by reference to Exhibit 4.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.

4.18

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

4.19 2007 Stock Option Plan, dated March 26, 2007, incorporated by reference to Exhibit 4.42 to the Annual Report on Form 20-F for the year ended December 31, 2007, previously filed with the SEC on April 30, 2007.

5.1 Opinion of Gianni. Origoni, Grippo & Partners, dated May 27, 2011, as to the legality of the ordinary shares underlying the American Depositary Shares being offered by the prospectus forming a part of this Registration Statement, filed herewith.

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

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

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

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- 10.4 Loan Agreement for €500,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
- 10.5 Loan Agreement for €225,000 with Banca Intesa S.p.A., dated December 20, 2006, incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on February 2, 2007.
- 10.6 Financing Contract between Banca Intesa Mediocredito S.p.A. and Gentium S.p.A. dated April 20, 2006, incorporated by reference to Exhibit 4.36.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 10.7 Loan Agreement, dated June 30, 2006, between San Paolo IMI S.p.A. and Gentium S.p.A., incorporated by reference to Exhibit 4.43 to the Annual Report on Form 20-F for the year ended December 31, 2006, previously filed with the SEC on April 30, 2007.
- 10.8.1 Master Services Agreement, dated March 14, 2007, between MDS Pharma Services (US), Inc. and Gentium S.p.A., incorporated by reference to Exhibit 1 to the report on Form 6-K, previously filed with the SEC on March 20, 2007.
- 10.8.2 Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (prospective arm), incorporated by reference to Exhibit 3 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.
- 10.8.3 Statement of Work, effective August 8, 2007, between Gentium S.p.A. and MDS Pharma Services, Inc. (historical arm), incorporated by reference to Exhibit 4 to the report on Form 6-K, previously filed with the SEC on August 22, 2007.
- 10.9.1 License and Supply Agreement by and between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc. (assignee of Sigma Tau Industrie Farmaceutiche Riunite S.p.A.) dated December 7, 2001, incorporated by reference to Exhibit 10.15 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on January 24, 2005.
- 10.9.2 Letter Agreement, dated October 12, 2007, between Gentium S.p.A. and Sigma-Tau Pharmaceuticals, Inc., incorporated by reference to Exhibit 99.4 to the report on Form 6-K, previously filed with the SEC on December 12, 2007.
- 10.9.3*

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

- 10.10.1 Contract to Supply Active Ingredients between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 4.24.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
 - 10.10.2 Amendment No. 1 to Contract to Supply Active Ingredients, effective as of December 7, 2007, by and between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A.
 - 10.11.1 Master Agreement, dated December 28, 2006, among Gentium S.p.A., Crinos S.p.A., SFI Stada Financial Investments Ltd. And SFS Stada Financial Services International Ltd., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
 - 10.11.2 Distribution Agreement, dated December 28, 2006, between Gentium S.p.A. and Crinos S.p.A., incorporated by reference to Exhibit 6 to the report on Form 6-K, previously filed with the SEC on January 3, 2007.
 - 10.13* Technical Transfer Services Agreement, dated February 2, 2009, between Gentium S.p.A. and Patheon Italia S.p.A., incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
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- 10.14.1 Technical Agreement, dated February 26, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 10.14.2* Supply and Distribution Agreement, dated March 6, 2009, between Gentium S.p.A. and IDIS Limited, incorporated by reference to Exhibit 4.21 to the Annual Report on Form 20-F for the year ended December 31, 2008, previously filed with the SEC on March 31, 2009.
- 4.2.3* Master Contract Clinical Research Agreement, dated September 29, 2009, between US Oncology Clinical Development and Gentium S.p.A., incorporated by reference to Exhibit 2 to the report on Form 6-K, previously filed with the SEC on December 8, 2009.
- 10.15 Service Agreement between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.25.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 10.16 Service Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2006, incorporated by reference to Exhibit 10.26.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the SEC on May 30, 2006.
- 10.17 Commercial Lease Contract between Gentium S.p.A. and Sirton Pharmaceuticals S.p.A. dated January 1, 2005, incorporated by reference to Exhibit 10.33 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.
- 10.18 Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2005, incorporated by reference to Exhibit 10.32 to Amendment No. 2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the SEC on May 10, 2005.
- 10.19 Commercial Lease Contract between Gentium S.p.A. and FinSirton S.p.A. dated January 1, 2007, incorporated by reference to Exhibit 4.32.2 (improperly coded as Exhibit 4.43(2)) to the Annual Report on Form 20-F for the year ending December 31, 2006, previously filed with the SEC on April 30, 2007.
- 10.20 Form of indemnification agreement between Gentium S.p.A. and each officer and director, incorporated by reference to Exhibit 10.34 to Amendment No. 2 to the Registration Statement on Form F-1, Registration

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No. 333-122233, previously filed with the SEC on May 10, 2005.

23.1 Consent of Reconta Ernst & Young S.p.A. dated May 27, 2011.

23.2 Consent of Gianni, Origoni, Grippo & Partners (included in Exhibit 5.1).

24.1 Power of Attorney (included on the signature page).
