

Gentium S.p.A.  
Form F-3/A  
December 19, 2006

As filed with the Securities and Exchange Commission on December 19, 2006  
Registration No. 333-139422

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

AMENDMENT NO. 1 TO 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, 13<sup>th</sup> Floor  
New York, New York 10011  
(12) 894-8940**

*(Name, address, including zip code, and telephone number, including area code, of agent for service)*

*Copy to:*

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

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

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

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

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

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

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

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

**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.**

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## EXPLANATORY NOTE

The purpose of this Amendment No. 1 is solely to file Exhibit 5.1 and Exhibit 23.1 to this registration statement as set forth below in Item 9 of Part II. No changes have been made to Part I or Items 8 and 10 of the registration statement. Accordingly, they have been omitted from this Amendment No. 1.

## PART II

### INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

#### Item 9. Exhibits.

| <b><u>Exhibit Number</u></b> | <b><u>Description of Documents</u></b>   |
|------------------------------|--|
| 1.1                          | Underwriting Agreement, dated June 16, 2005, between Gentium S.p.A. and Maxim Group LLC and I-Bankers Securities Inc., incorporated by reference to Exhibit 1.1 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on January 26, 2006. |
| 1.2                          | 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 Securities and Exchange Commission on June 9, 2005.         |
| 1.3                          | Form of Lock-Up Agreement, incorporated by reference to Exhibit 1.3 to Amendment No. 4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on May 31, 2005.   |
| 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. dated April 28, 2006, incorporated by reference to Exhibit 1(ii) to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the Securities and Exchange Commission on May 30, 2006.   |
| 4.2.1                        | Form of Series A senior convertible promissory note, incorporated by reference to Exhibit 4.2.1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.  |
| 4.2.2                        | Form of warrant, incorporated by reference to Exhibit 4.2.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.  |
| 4.2.3                        | Pledge Agreement between FinSirton S.p.A. (previously known as Finanziaria Sirton S.p.A.) and I-Bankers Securities Inc. as representative of the holders of the Series A senior convertible promissory notes dated October 15, 2004, incorporated by reference to Exhibit 4.2.3 to Amendment No. 1 to the Registration Statement on          |

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Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on January 26, 2006.

- 4.2.4 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 Securities and Exchange Commission on January 24, 2005.
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- 4.2.5 Form of subscription agreement for Series A senior convertible promissory note and warrant, incorporated by reference to Exhibit 4.2.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
- 4.2.6 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 Securities and Exchange Commission on May 31, 2005.
- 4.3 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 Securities and Exchange Commission on January 24, 2005.
- 4.4 Intentionally omitted.
- 4.5 Investors' Rights Agreement by and among Gentium S.p.A. and Sigma Tau Finanziaria S.p.A. made as of April 4, 2005, incorporated by reference to Exhibit 4.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
- 4.6 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.
- 4.7 Form of American Depositary Receipt (see Exhibit 4.6).
- 4.8.1 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto dated as of October 3, 2005, incorporated by reference to Exhibit 4.8.1 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on December 30, 2005.
- 4.8.2 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 Securities and Exchange Commission on December 30, 2005.
- 4.8.3 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 Securities and Exchange Commission on December 30, 2005.
- 4.8.4 Escrow Agreement between Gentium S.p.A. and The Bank of New York dated as of October 14, 2005, incorporated by reference to Exhibit 4.8.4 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on December 30, 2005.
- 4.9.1 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 Securities and Exchange Commission on July 6, 2006.
- 4.9.2

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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 Securities and Exchange Commission on July 6, 2006.

- 4.9.3 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 Securities and Exchange Commission on July 6, 2006.
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- 4.9.4 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 Securities and Exchange Commission on July 6, 2006.
- 5.1 Opinion of Gianni, Origoni, Grippo & Partners 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.
- 10.1 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 Securities and Exchange Commission on September 22, 2006.
- 10.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.3 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated November 20, 1996, incorporated by reference to Exhibit 10.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.4 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated May 27, 1999, incorporated by reference to Exhibit 10.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.5 Deed of Agreement of Assumption of Debts among Sirton Pharmaceuticals S.p.A., Gentium S.p.A. and Banca Nazionale del Lavoro S.p.A. dated February 14, 2003, regarding Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated November 20, 1996, and Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated May 27, 1999, incorporated by reference to Exhibit 10.5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.6 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 Securities and Exchange Commission on January 24, 2005.
- 10.7.1 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A. dated July 20, 2004, incorporated by reference to Exhibit 10.7 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.7.2 Deed of Pledge by Gentium S.p.A. in favor of Banca Nazionale del Lavoro S.p.A. dated May 16, 2006, incorporated by reference to Exhibit 4.7.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the Securities and Exchange Commission on May 30, 2006.
- 10.7.3 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

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Statement on Form F-3, Registration No. 333-135622, previously filed with the Securities and Exchange Commission on July 6, 2006.

- 10.8 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated March 2004, incorporated by reference to Exhibit 10.8 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
  - 10.9 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated May 2004, incorporated by reference to Exhibit 10.9 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
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- 10.10 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated June 2004, incorporated by reference to Exhibit 10.10 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.11 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated July 2004, incorporated by reference to Exhibit 10.11 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.12.1 Clinical Trial Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Dana-Farber/Partners Cancer Care, Inc. dated December 27, 1999, incorporated by reference to Exhibit 10.12.1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.12.2 Amendment No. 1 to Clinical Trial Agreement between Gentium S.p.A. and Dana-Farber/Partners Cancer Care, Inc. dated October 19, 2000, incorporated by reference to Exhibit 10.12.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.12.3 Amendment No. 2 to Clinical Trial Agreement between Gentium S.p.A. and Dana-Farber/Partners Cancer Care, Inc. dated January 28, 2004, incorporated by reference to Exhibit 10.12.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.13 Trial Agreement between the European Blood and Marrow Transplantation Group and Gentium S.p.A. dated February 26, 2004, incorporated by reference to Exhibit 10.13 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.14.1 Research Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Consorzio Mario Negri Sud dated June 14, 2000, incorporated by reference to Exhibit 10.14.1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.14.2 Letter from Gentium S.p.A. to Consorzio Mario Negri Sud dated February 23, 2004 extending Research Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Consorzio Mario Negri Sud dated June 14, 2000, incorporated by reference to Exhibit 10.14.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.15 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 Securities and Exchange Commission on January 24, 2005.
- 10.16 Umbrella Agreement among Sirton Pharmaceuticals S.p.A. (formerly known as Crinos Industria Farmacobiologica S.p.A.), Gentium S.p.A., Crinos S.p.A. and SFS Stada Financial Services Ltd dated May 17, 2002, incorporated by reference to Exhibit 10.16 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.17

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License Agreement between Crinos S.p.A. and Gentium S.p.A. dated July 15, 2004, incorporated by reference to Exhibit 10.17 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.

- 10.18 Purchase Agreement by and among Sirton Pharmaceuticals S.p.A., Gentium S.p.A. and Axcan Pharma Inc. dated October 9, 2002, incorporated by reference to Exhibit 10.18 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
  - 10.19 Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated October 9, 2002, regarding the Purchase Agreement with Axcan Pharma Inc., incorporated by reference to Exhibit 10.19 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
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- 10.20 License and Supply Agreement between Gentium S.p.A. and Abbott S.p.A. dated June 11, 2002, incorporated by reference to Exhibit 10.20 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.21 Supply Agreement between Gentium S.p.A. and La.bu.nat. S.r.l. dated January 12, 2004, incorporated by reference to Exhibit 10.21 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.22 Supply Agreement between Gentium S.p.A. and La.bu.nat. S.r.l. dated January 12, 2004, incorporated by reference to Exhibit 10.22 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.23 Supply Agreement between Gentium S.p.A. and Samil Pharm. Co. Ltd. dated November 11, 2003, incorporated by reference to Exhibit 10.23 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.24.1 Active Pharmaceutical Ingredient Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.24 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.24.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.25.1 Agreement for the Supply of Services between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.25 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.25.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.26.1 Agreement for the Supply of Services between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.26 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.26.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.27 Service Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.27 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.28 Lease Agreement between Sirton Pharmaceuticals S.p.A. (formerly known as Crinos Industria Farmacobiologica S.p.A.) and Gentium S.p.A. (formerly known as Pharma Research S.r.L.) dated January 2, 2001, incorporated by reference to Exhibit 10.28 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.29

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8% Promissory Note in the amount of €106,000 issued by Gentium S.p.A. to Alexandra Global Master Fund Ltd. dated March 29, 2005, incorporated by reference to Exhibit 10.29 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.

- 10.30 General Consulting Agreement between Gentium S.p.A. and Bradstreet Clinical Research & Associates, Inc., dated March 19, 2004, incorporated by reference to Exhibit 10.30 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
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- 10.31 Consulting Agreement between Gentium S.p.A. and KKS-UKT, GmbH, dated April 20, 2004, incorporated by reference to Exhibit 10.31 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
- 10.32 Commercial Lease Agreement 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 Securities and Exchange Commission on May 10, 2005.
- 10.33 Commercial Lease Agreement 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 Securities and Exchange Commission on May 10, 2005.
- 10.34 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 Securities and Exchange Commission on May 10, 2005.
- 10.35 Services Agreement between MDS Pharma Services s.r.l. and Gentium S.p.A. dated October 24, 2005, incorporated by reference to Exhibit 4.35 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the Securities and Exchange Commission on May 30, 2006.
- 10.36 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 Securities and Exchange Commission on May 30, 2006.
- 23.1 Consent of Reconta Ernst & Young S.p.A. dated December 19, 2006.
- 23.2 Consent of Gianni, Origoni, Grippo & Partners (included in Exhibit 5.1).
- 24.1 Power of Attorney (included on the signature page).

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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 Amendment No. 1 to the Registration Statement on Form F-3 (File No. 333-139422) to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Villa Guardia (Como) Italy, on the 19th day of December, 2006.

GENTIUM, S.p.A

By: /s/ Laura Ferro  
 Dr. Laura Ferro,  
 President and Chief Executive Officer  
 (Principal Executive Officer)

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 1 to the Registration Statement on Form F-3 (File No. 333-139422) has been signed by the following persons in the capacities and on the dates indicated:

| <u>Signature</u>                   | <u>Title(s)</u>  | <u>Date</u>          |
|------------------------------------|--|----------------------|
| *<br>_____<br>Dr. Laura Ferro      | President, Chief Executive Officer<br>and Director (principal executive<br>officer)                                    | December 19,<br>2006 |
| *<br>_____<br>Gary Gemignani       | Executive Vice-President, Chief<br>Financial Officer and Authorized<br>Representative (principal financial<br>officer) | December 19,<br>2006 |
| *<br>_____<br>Salvatore Calabrese  | Vice-President, Finance and<br>Secretary (controller)  | December 19,<br>2006 |
| *<br>_____<br>Dr. Kenneth Anderson | Director   | December 19,<br>2006 |
| *<br>_____<br>Gigliola Bertoglio   | Director   | December 19,<br>2006 |
| *<br>_____<br>Luca Breveglieri     | Director   | December 19,<br>2006 |
| *<br>_____<br>Marco Codella        | Director   | December 19,<br>2006 |
| *<br>_____<br>David E. Kroin       | Director   | December 19,<br>2006 |
|                                    | Director   |                      |

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December 19,  
2006

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Dr. Lee M. Nadler

\* By: /s/ Laura Ferro  
Laura Ferro, M.D.  
Attorney-in-Fact

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INDEX TO EXHIBITS

| <b><u>Exhibit Number</u></b> | <b><u>Description of Documents</u></b>   |
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| 1.1                          | Underwriting Agreement, dated June 16, 2005, between Gentium S.p.A. and Maxim Group LLC and I-Bankers Securities Inc., incorporated by reference to Exhibit 1.1 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on January 26, 2006.   |
| 1.2                          | 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 Securities and Exchange Commission on June 9, 2005.   |
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| 4.2.2                        | Form of warrant, incorporated by reference to Exhibit 4.2.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.  |
| 4.2.3                        | Pledge Agreement between FinSirton S.p.A. (previously known as Finanziaria Sirton S.p.A.) and I-Bankers Securities Inc. as representative of the holders of the Series A senior convertible promissory notes dated October 15, 2004, incorporated by reference to Exhibit 4.2.3 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on January 26, 2006. |
| 4.2.4                        | 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 Securities and Exchange Commission on January 24, 2005.   |
| 4.2.5                        | Form of subscription agreement for Series A senior convertible promissory note and warrant, incorporated by reference to Exhibit 4.2.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed   |



with the Securities and Exchange Commission on April 7, 2005.

- 4.2.6 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 Securities and Exchange Commission on May 31, 2005.
  - 4.3 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 Securities and Exchange Commission on January 24, 2005.
  - 4.4 Intentionally omitted.
  - 4.5 Investors' Rights Agreement by and among Gentium S.p.A. and Sigma Tau Finanziaria S.p.A. made as of April 4, 2005, incorporated by reference to Exhibit 4.5 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
  - 4.6 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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- 4.7 Form of American Depositary Receipt (see Exhibit 4.6).
  - 4.8.1 Securities Subscription Agreement among Gentium S.p.A. and the other parties thereto dated as of October 3, 2005, incorporated by reference to Exhibit 4.8.1 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on December 30, 2005.
  - 4.8.2 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 Securities and Exchange Commission on December 30, 2005.
  - 4.8.3 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 Securities and Exchange Commission on December 30, 2005.
  - 4.8.4 Escrow Agreement between Gentium S.p.A. and The Bank of New York dated as of October 14, 2005, incorporated by reference to Exhibit 4.8.4 to the Registration Statement on Form F-1, Registration No. 333-130796, previously filed with the Securities and Exchange Commission on December 30, 2005.
  - 4.9.1 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 Securities and Exchange Commission on July 6, 2006.
  - 4.9.2 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 Securities and Exchange Commission on July 6, 2006.
  - 4.9.3 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 Securities and Exchange Commission on July 6, 2006.
  - 4.9.4 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 Securities and Exchange Commission on July 6, 2006.
  - 5.1 Opinion of Gianni, Origoni, Grippo & Partners 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.
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- 10.1 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 Securities and Exchange Commission on September 22, 2006.
- 10.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.3 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated November 20, 1996, incorporated by reference to Exhibit 10.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.4 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated May 27, 1999, incorporated by reference to Exhibit 10.4 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.5 Deed of Agreement of Assumption of Debts among Sirton Pharmaceuticals S.p.A., Gentium S.p.A. and Banca Nazionale del Lavoro S.p.A. dated February 14, 2003, regarding Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated November 20, 1996, and Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., dated May 27, 1999, incorporated by reference to Exhibit 10.5 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.6 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 Securities and Exchange Commission on January 24, 2005.
- 10.7.1 Loan Agreement between Banca Nazionale del Lavoro S.p.A. and Gentium S.p.A. dated July 20, 2004, incorporated by reference to Exhibit 10.7 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.7.2 Deed of Pledge by Gentium S.p.A. in favor of Banca Nazionale del Lavoro S.p.A. dated May 16, 2006, incorporated by reference to Exhibit 4.7.2 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the Securities and Exchange Commission on May 30, 2006.
- 10.7.3 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 Securities and Exchange Commission on July 6, 2006.
- 10.8 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated March 2004, incorporated by reference to Exhibit 10.8 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.9

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Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated May 2004, incorporated by reference to Exhibit 10.9 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.

- 10.10 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated June 2004, incorporated by reference to Exhibit 10.10 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
  - 10.11 Loan Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated July 2004, incorporated by reference to Exhibit 10.11 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
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- 10.12.1 Clinical Trial Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Dana-Faber/Partners Cancer Care, Inc. dated December 27, 1999, incorporated by reference to Exhibit 10.12.1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.12.2 Amendment No. 1 to Clinical Trial Agreement between Gentium S.p.A. and Dana-Farber/Partners Cancer Care, Inc. dated October 19, 2000, incorporated by reference to Exhibit 10.12.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.12.3 Amendment No. 2 to Clinical Trial Agreement between Gentium S.p.A. and Dana-Farber/Partners Cancer Care, Inc. dated January 28, 2004, incorporated by reference to Exhibit 10.12.3 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.13 Trial Agreement between the European Blood and Marrow Transplantation Group and Gentium S.p.A. dated February 26, 2004, incorporated by reference to Exhibit 10.13 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.14.1 Research Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Consorzio Mario Negri Sud dated June 14, 2000, incorporated by reference to Exhibit 10.14.1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.14.2 Letter from Gentium S.p.A. to Consorzio Mario Negri Sud dated February 23, 2004 extending Research Agreement between Gentium S.p.A., successor in interest to Crinos Industria Farmacobiologica S.p.A., and Consorzio Mario Negri Sud dated June 14, 2000, incorporated by reference to Exhibit 10.14.2 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.15 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 Securities and Exchange Commission on January 24, 2005.
- 10.16 Umbrella Agreement among Sirton Pharmaceuticals S.p.A. (formerly known as Crinos Industria Farmacobiologica S.p.A.), Gentium S.p.A., Crinos S.p.A. and SFS Stada Financial Services Ltd dated May 17, 2002, incorporated by reference to Exhibit 10.16 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.17 License Agreement between Crinos S.p.A. and Gentium S.p.A. dated July 15, 2004, incorporated by reference to Exhibit 10.17 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.18 Purchase Agreement by and among Sirton Pharmaceuticals S.p.A., Gentium S.p.A. and Axcan Pharma Inc. dated October 9, 2002, incorporated by reference to Exhibit 10.18 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.19

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Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated October 9, 2002, regarding the Purchase Agreement with Axcan Pharma Inc., incorporated by reference to Exhibit 10.19 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.

- 10.20 License and Supply Agreement between Gentium S.p.A. and Abbott S.p.A. dated June 11, 2002, incorporated by reference to Exhibit 10.20 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
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- 10.21 Supply Agreement between Gentium S.p.A. and La.bu.nat. S.r.l. dated January 12, 2004, incorporated by reference to Exhibit 10.21 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.22 Supply Agreement between Gentium S.p.A. and La.bu.nat. S.r.l. dated January 12, 2004, incorporated by reference to Exhibit 10.22 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.23 Supply Agreement between Gentium S.p.A. and Samil Pharm. Co. Ltd. dated November 11, 2003, incorporated by reference to Exhibit 10.23 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.24.1 Active Pharmaceutical Ingredient Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.24 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.24.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.25.1 Agreement for the Supply of Services between FinSirton S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.25 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.25.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.26.1 Agreement for the Supply of Services between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.26 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.26.2 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 Securities and Exchange Commission on May 30, 2006.
- 10.27 Service Agreement between Sirton Pharmaceuticals S.p.A. and Gentium S.p.A. dated January 2, 2004, incorporated by reference to Exhibit 10.27 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.28 Lease Agreement between Sirton Pharmaceuticals S.p.A. (formerly known as Crinos Industria Farmacobiologica S.p.A.) and Gentium S.p.A. (formerly known as Pharma Research S.r.L.) dated January 2, 2001, incorporated by reference to Exhibit 10.28 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on January 24, 2005.
- 10.29 8% Promissory Note in the amount of €106,000 issued by Gentium S.p.A. to Alexandra Global Master Fund Ltd. dated March 29, 2005, incorporated by reference to Exhibit 10.29 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.

- 10.30 General Consulting Agreement between Gentium S.p.A. and Bradstreet Clinical Research & Associates, Inc., dated March 19, 2004, incorporated by reference to Exhibit 10.30 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
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- 10.31 Consulting Agreement between Gentium S.p.A. and KKS-UKT, GmbH, dated April 20, 2004, incorporated by reference to Exhibit 10.31 to Amendment No. 1 to the Registration Statement on Form F-1, Registration No. 333-122233, previously filed with the Securities and Exchange Commission on April 7, 2005.
- 10.32 Commercial Lease Agreement 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 Securities and Exchange Commission on May 10, 2005.
- 10.33 Commercial Lease Agreement 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 Securities and Exchange Commission on May 10, 2005.
- 10.34 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 Securities and Exchange Commission on May 10, 2005.
- 10.35 Services Agreement between MDS Pharma Services s.r.l. and Gentium S.p.A. dated October 24, 2005, incorporated by reference to Exhibit 4.35 to the Annual Report on Form 20-F for the year ended December 31, 2005, previously filed with the Securities and Exchange Commission on May 30, 2006.
- 10.36 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 Securities and Exchange Commission on May 30, 2006.
- 23.1 Consent of Reconta Ernst & Young S.p.A. dated December 19, 2006.
- 23.2 Consent of Gianni, Origoni, Grippo & Partners (included in Exhibit 5.1).
- 24.1 Power of Attorney (included on the signature page).

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