

Gentium S.p.A.
Form F-3/A
January 10, 2011

As filed with the Securities and Exchange Commission on January 10, 2011
Registration No. 333-171443

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, 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

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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.

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.

EXPLANATORY NOTE

The purpose of this Amendment No. 1 is solely to amend the numbering of exhibits to Item 9 of Part II and to clarify that Mr. Salvatore Calabrese acts in the capacity of both Principal Financial Officer and Principal Accounting Officer for the Registrant. No changes have been made to Part I or Items 8 and 10 of Part II of the registration statement. Accordingly, they have been omitted from this Amendment No. 1.

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. |
| 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. |
| 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 | 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 December 28, 2010, 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 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* | 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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| Exhibit Number | Description of Documents |
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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. |
| 10.15* | 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. |
| 10.16 | 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. |
| 10.17 | 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. |
| 10.18 | 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. |
| 10.19 | 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. |
| 10.20 | 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. |
| 10.21 | 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 December 28, 2010. |
| 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.

** Previously filed herewith.

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. 333-171443) to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Villa Guardia (Como) Italy, on the 10th day of January, 2011.

GENTIUM S.p.A

By: /s/ Khalid Islam
 Dr. Khalid Islam,
 Chairman 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. 333-171443) 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) | January 10, 2011 |
| /s/ Salvatore Calabrese Salvatore Calabrese | Chief Financial Officer and Senior Vice President, Finance (principal financial officer and principal accounting officer) | January 10, 2011 |
| * Gigliola Bertoglio | Director | January 10, 2011 |
| * Marco Codella | Director | January 10, 2011 |
| * Dr. Glenn Cooper | Director | January 10, 2011 |
| * Dr. Laura Ferro | Director | January 10, 2011 |
| * Dr. Bobby W. Sandage, Jr. | Director | January 10, 2011 |

*By: /s/ Khalid Islam
 Attorney-in-Fact

INDEX TO EXHIBITS

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| 4.2 | Form of American Depositary Receipt (see Exhibit 4.1). |
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- 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.
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| Exhibit Number | Description of Documents |
|-------------------|--|
| 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. |
| 10.15* | 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. |
| 10.16 | 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. |
| 10.17 | 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. |
| 10.18 | 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. |
| 10.19 | 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. |
| 10.20 | 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. |
| 10.21 | 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 December 28, 2010. |
| 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.

** Previously filed herewith.

