

Gentium S.p.A.  
Form 424B3  
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GENTIUM S.P.A.

PROSPECTUS SUPPLEMENT NO. 3  
DATED MARCH 16, 2009

TO PROSPECTUS DATED  
JULY 13, 2006

This Prospectus Supplement No. 3 supplements information contained in our prospectus dated July 13, 2006, as amended and supplemented from time to time (the "Original Prospectus"). The information in this Supplement No. 3 supplements, modifies and supersedes some of the information contained in the Original Prospectus.

The purpose of this Prospectus Supplement No. 3 is to (i) inform you that the selling security holder identified as "Mallette Capital Master Fund LTD" has assigned its warrant to subscribe up to 33,548 ordinary shares of Gentium S.p.A. to Warrant Strategies Fund, LLC, (ii) inform you that the selling security holder identified as "Hyde Street Holdings LLC" has assigned its warrant to subscribe up to 77,741 ordinary shares of Gentium S.p.A. to Warrant Strategies Fund, LLC, (iii) correct the number of registered ADSs for resale for the security holder identified as "Iroquois Master Fund LTD," and (iv) to inform you that the selling security holders identified as "Visium Balanced Fund, LP," "Visium Balanced Offshore Fund, Ltd.," "Visium Long Bias Fund, LP," and "Visium Long Bias Offshore Fund, Ltd." have transferred their American Depositary Shares ("ADSs") to Visium Master Fund Ltd. These changes are set forth in the selling security holder table below, which amends the selling security holder table contained in the Original Prospectus. The selling security holder table contained in the Original Prospectus is being amended to permit the resale of such ordinary shares under the Registration Statement and pursuant to the Original Prospectus. No additional securities are being registered hereby.

You should read this Prospectus Supplement No. 3 in conjunction with the Original Prospectus, Prospectus Supplement No. 1 dated October 19, 2007 and Prospectus Supplement No. 2 dated July 22, 2008. This Prospectus Supplement No. 3 is not complete without, and may not be delivered or utilized except in connection with, the Original Prospectus including any amendments or supplements thereto.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

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## SELLING SECURITY HOLDERS

Our ADSs to which this prospectus relates are being registered for resale by the selling security holders.

The selling security holders may resell all, a portion or none of such ADSs from time to time. The table below sets forth with respect to each selling security holder, based upon information available to us as of the date of this prospectus, the number and percentage of ADSs (or, in the case of security holders who currently hold ordinary shares or securities exercisable into ordinary shares, the number and percentage of ordinary shares) beneficially owned before this offering, the number of ADSs registered for resale by this prospectus and the number and percent of ADSs that will be beneficially owned immediately after this offering assuming the sale of all of the registered ADSs.

Beneficial ownership and percentage ownership are determined in accordance with the rules of the SEC. ADSs or ordinary shares underlying our convertible securities that are exercisable within 60 days from the date of this prospectus are deemed outstanding for computing the amount and percentage owned by the person or group holding such convertible securities, but are not deemed outstanding for computing the percentage owned by any other person or group.

| Holder                               | ADSs Beneficially Owned Before The Offering |         | ADSs Offered   | ADSs Beneficially Owned After The Offering |         |
|--------------------------------------|---|---------|----------------|--|---------|
|                                      | ADSs  | Percent |                | ADSs                                       | Percent |
| Iroquois Master Fund LTD (1)         | 24,000                                      | *       | 34,548         | 0  | 0       |
| Mallette Capital Master Fund LTD (2) | 162,741                                     | 1.1     | 162,741        | 0  | 0       |
| Warrant Strategies Fund, LLC (3)     | 0   | *       | 110,289        | 0  | 0       |
| Visium Balanced Master Fund, Ltd (4) | 218,931                                     | 1.5     | 218,931        | 0  | 0       |
| Visium Balanced Fund, LP             | 0   | *       | 11,284 (5)     | 0  | 0       |
| Visium Balanced Offshore Fund, Ltd.  | 0   | *       | 17,585 (5)     | 0  | 0       |
| Visium Long Bias Fund, LP            | 0   | *       | 3,479 (5)      | 0  | 0       |
| Visium Long Bias Offshore Fund, Ltd. | 0   | *       | 11,438 (5)     | 0  | 0       |
| <b>Total ADSs Offered:</b>           |   |         | <b>570,295</b> |  |         |

\* Less than 1%

(1) Address is 641 Lexington Avenue, 26th Floor, New York, New York 10022. ADSs offered include 10,548 ADSs issuable upon exercise of warrants, 5748 of which were transferred from Valesco Healthcare Master Fund, L.P. on June 10, 2008. Joshua Silverman has voting and investment control over the ADSs held by Iroquois Master Fund Ltd. Mr. Silverman disclaims beneficial ownership over such securities.

(2) Address is 800 Third Avenue, 9th Floor, New York, New York 10022. Quinterol Mallette, MD is the chief executive officer of Mallette Capital Master Fund LTD. By reason of such relationship, Dr. Mallette may be deemed to share voting and/or dispositive control over the ADSs beneficially owned and offered by Mallette Capital Master Fund LTD and therefore may be deemed to beneficially own such securities.

(3) Address is 350 Madison Avenue, 11th Floor, New York, New York 10017. ADSs offered include 110,289 ADSs issuable upon exercise of warrants, 33,548 of which were transferred from Mallette Capital Master Fund LTD on April 20, 2007, and 77,741 of which were transferred from Hyde Street Holdings LLC on February 9, 2009. Sean Molloy has voting and investment control over the ADSs held by Warrant Strategies Fund, LLC. Sean Molloy disclaims beneficial ownership over such securities.

(4) Address is 950 Third Avenue, 29th Floor, New York, New York 10022.

(5) Address is 950 Third Avenue, 29th Floor, New York, New York 10022. ADSs offered consist of ADSs issuable upon exercise of warrants

The selling security holders have not within the past three years had any position, office or other material relationship with our company.

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The information provided above with respect to the selling security holders has been obtained from such selling security holders. Because the selling security holders may sell all or some portion of the ADSs or ordinary shares beneficially owned by them, only an estimate (assuming the selling security holders sell all of the ADSs or ordinary shares offered in this prospectus) can be given as to the number of ADSs or ordinary shares that will be beneficially owned by the selling security holders after this offering, and as to the percentage of all outstanding ADSs or ordinary shares constituted by such ADSs or ordinary shares. In addition, the selling security holders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time or from time to time since the dates on which they provided the information regarding the ADSs or ordinary shares beneficially owned by them, all or a portion of the ADSs or ordinary shares beneficially owned by them in transactions exempt from the registration requirements of the Securities Act.