[Exelixis Letterhead]

October 13, 2006

Via Edgar and Federal Express
Mr. James B. Rosenberg
Senior Assistant Chief Accountant
United States Securities and Exchange Commission
Division of Corporation Finance
100 First Street, N.E.
Washington, D.C. 20549

Re: Letter dated August 18, 2006 relating to Exelixis, Inc.'s Form 10-K for the fiscal year ended December 31, 2005 – File No. 000-30235

Dear Mr. Rosenberg:

Exelixis, Inc. ("Exelixis" or the "Company") is pleased to respond to the comment of the Staff of the Securities and Exchange Commission (the "Commission") regarding its Form 10-K for the fiscal year ended December 31, 2005 transmitted telephonically to Mr. Christoph Pereira on September 20, 2006. The Staff's comment followed the Company's letter, dated September 1, 2006, responding to the comments of the Staff set forth in a letter, dated August 18, 2006. We first set forth in bold face the comment as transmitted to us on September 20, 2006 and then provide our response.

Once the Staff has reviewed the response set forth below, the Company would welcome the opportunity to discuss any additional questions the Staff may have.

Comment: According to your discussion of the cancer collaboration agreement with BMS in your response to prior comment No. 1, Exelixis selects half of the validated targets. According to your discussion of the agreement with GSK, GSK has the right to select up to three of the 12 compounds Exelixis develops. For each of those agreements, you assert that there are no terms under which Exelixis can reacquire the targets or compounds selected by BMS or GSK, respectively. As it is still unclear whether you can obtain the results of research and development related to the other targets or compounds, please elaborate on why you believe SFAS 68 does not apply to these agreements. To the extent SFAS 68 does apply, please provide us with the disclosures under Paragraph 14(b) of SFAS 68 about the costs incurred under the agreements during each period presented.

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Response:

GlaxoSmithKline

The Company entered into the Product Development and Commercialization Agreement ("PDA") with GlaxoSmithKline ("GSK") to discover and develop novel therapeutics in the areas of vascular biology, inflammatory disease and oncology. GSK has the right to select up to three compounds from 12 compounds developed by the Company under the collaboration. The Company receives annual research and development funding over the research term. There are no terms under which the Company may reacquire the compounds selected by GSK (absent a termination or material breach by GSK).

Statement of Financial Accounting Standards No. 68, *Research and Development Arrangements* ("SFAS 68") is applicable to a research and development arrangement through which a party can obtain the results of the research and development *funded partially or entirely* by others. With respect to the compounds retained by Exelixis, the Company has concluded that SFAS 68 is also not applicable because the research and development funding provided by GSK to the Company does not fund, either partially or entirely, the research and development costs associated with the compounds retained by the Company.

Pursuant to the PDA, GSK has the right to select two compounds at the completion of Phase 2a clinical trial(s) for which the Company will receive a total of $90.0 million in research and development funding over a six-year period extending from October 2002 to October 2008. If GSK extends the collaboration, it can select up to three compounds for which the Company will receive a total of **[*]** in research and development funding over an eight-year period extending from 2002 to 2010. The Company has not historically tracked the total costs incurred in connection with the development of a compound because these data are not deemed relevant from a management perspective. However, the Company has tracked significant third-party costs, which include the clinical trial costs for the product candidates that are part of the GSK collaboration. Based on this information and an estimate of early research expenses, the Company has determined that the costs for each compound average approximately **[*]** from early research to the end of Phase 2a clinical trial(s). If GSK selects two compounds, the total research and development funding of $90.0 million will fall well short of the **[*]** required for the research and development of these two compounds through Phase 2a. Further, if GSK selects three compounds, the total research and development funding of **[*]** would also be insufficient to cover the **[*]** incurred in connection with the research and development of the three selected compounds. Taking into account the above-stated analysis, management has concluded that the amount of research and development funding received by the Company in connection with the GSK collaboration will not fully cover the costs incurred by the Company in the research and development of the two or three compounds to be selected by GSK and such funding does not fund, either partially or entirely, any of the compounds retained by the Company.

The Company has concluded that the GSK agreement is not within the scope of SFAS 68 because there are no terms under which the Company may reacquire the compounds selected by GSK. Furthermore, with respect to the compounds retained by Exelixis, the Company has also concluded that SFAS 68 is not applicable because the research and development funding provided by GSK under the collaboration does not fund, either partially or entirely, any of the research and development costs associated with the compounds retained by Exelixis.

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Bristol-Myers Squibb - Cancer Collaboration Agreement:

The Company entered into a Cancer Collaboration Agreement with Bristol-Myers Squibb ("BMS") pursuant to which the Company delivers validated cancer targets to BMS and the parties share responsibilities for work associated with the further validation of such targets. Once the targets have been validated, each party selects its half of the targets. BMS is required to provide annual research funding over the research term, and there are no terms under which the Company can reacquire the targets selected by BMS (absent a termination or material breach by BMS).

SFAS 68 states, "The provisions of this Statement need not be applied to immaterial items." The Company has evaluated whether disclosures of the costs incurred under the BMS agreement would be material to the users of the financial statements. This analysis included consideration of Staff Accounting Bulletin No. 99, *Materiality* ("SAB 99"). Materiality is defined as the magnitude of an omission or misstatement that, individually or in the aggregate, in light of the surrounding circumstances, makes it probable that the judgment of a reasonable person relying on the financial statements would have been changed or influenced by such omission or misstatement.

As an initial step, the Company analyzed whether the BMS expenses are quantitatively material, measured as a percentage of the Company's total research and development expenses. We estimate that our total 2006 expenses related to the BMS Cancer Collaboration will be approximately **[*]** and that we also incurred expenses of a similar magnitude for each of the years ended December 31, 2003, 2004 and 2005, respectively. The Company incurred total research and development expenses of $127.6 million, $137.7 million and $141.1 million in 2003, 2004 and 2005, respectively, and management expects to incur total research and development expenses of approximately **[*]** in 2006. As a result, the Company's research expenses attributable to the BMS Cancer Collaboration as a percentage of its total research and development expenses were in a range of approximately [*] in 2003, 2004 and 2005, respectively, and are estimated to be **[*]** of its total research and development expenses in 2006. Because the Company's BMS research expenses are **[*]** of the Company's total research and development expenses in each of the relevant periods, the Company has concluded that the BMS research expenses are quantitatively immaterial in comparison to the Company's total research and development expenses.

The Company has also undertaken a review of all relevant facts of the BMS Cancer Collaboration in order to determine whether the BMS expenses are material from a qualitative perspective. As described in Item 2 of our Quarterly Report on Form 10-Q for the quarter ended June 30, 2006, the Company's predominate business strategy is focused on developing new drug candidates for commercialization, rather than performing contract research for third parties. The overwhelming majority of this disclosure of our business strategy is focused on the compounds we have in clinical and pre-clinical development. Furthermore, a substantial majority of the questions we receive from investors relate to the status of our product development. Therefore, the Company does not view (and based on our investors' questions, it believes that investors do not view) costs related to the BMS

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Cancer Collaboration as a key performance indicator for investors because such costs are not relevant in light of the Company's predominate business model. We believe that it is improbable that the judgment of a reasonable investor relying upon the Company's financial reports would be changed or influenced by the inclusion of the BMS research expenses in the Company's footnote disclosure.

The Company has concluded that the BMS agreement is not within the scope of SFAS 68 because there are no terms under which the Company may reacquire the compounds selected by BMS. Furthermore, with respect to the compounds retained by Exelixis, we have concluded that the BMS research costs are quantitatively and qualitatively immaterial and therefore no disclosure is required.

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Should you have any questions regarding our comments or require any additional information, please contact Christoph Pereira at (650) 837-7950 or me at (650) 837-7565.

Very truly yours,

/s/ Frank Karbe

Frank Karbe
Senior Vice President and
Chief Financial Officer

cc: Oscar Young, Securities and Exchange Commission
Keira Ino, Securities and Exchange Commission
Christoph Pereira, Vice President, Legal Affairs and Secretary
Debbie Burke, Controller
Daniel Coleman, Ernst & Young LLP
Suzanne Sawochka Hooper, Cooley Godward Kronish L.L.P.

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