September 1, 2006

Via Edgar and Federal Express

Mr. Jim 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 comments of the Staff of the Securities and Exchange Commission (the "Commission") regarding our Form 10-K for the fiscal year ended December 31, 2005. We first set forth in bold face the comment as submitted to us in your letter dated August 18, 2006 and then provide our response.

We understand that you will be reviewing our comments and may have additional comments. We welcome any questions you may have concerning our responses and thank you for your attention to our filing. Please feel free to call us at the telephone numbers listed at the end of this letter.

Form 10-K for the Fiscal Year Ended December 31, 2005

Item 8. Financial Statements and Supplementary Data, page 57

Notes to Consolidated Financial Statements, page 65

Note 3 Research and Collaboration Agreements, page 74

Comment: For those agreements within the scope of SFAS 68, please provide us the disclosures required by paragraph 14(b) of SFAS 68 about the costs incurred under the agreements during each period presented.

Response: SFAS 68 applies to "…research and development arrangements through which [an enterprise] can obtain the results of research and development funded partially or entirely by others." The Company is not entitled to obtain the results of the research and development activities funded by its collaborators and licensees. Accordingly, the Company does not believe these agreements are within the scope of SFAS 68 and, therefore, the Company has historically not disclosed the costs related to its research and collaboration agreements separately.

We believe SFAS 68 is primarily intended to address the temporary transfer of intellectual property to a third party (SFAS 68 Appendix A). SFAS 68 presumes that such a third party is

a financial buyer or special purpose entity, which can provide off-balance sheet funding of the research and development (SFAS 68 paragraph 16 d., e. and f.) with contractual provisions that provide for the licensor to reacquire the results of the research and development (SFAS 68 paragraph 20) at a subsequent date for a monetary sum such as a fixed payment, royalty payments or some other form of compensation (SFAS 68 paragraphs 22 and 23).

All of the Company's collaboration agreements that provide for research and development funding are licensing agreements that are structured as permanent transfers of the intellectual property to large pharmaceutical companies that possess the capabilities to complete, and may complete, development as well as the manufacture and commercialization of these product candidates. None of our collaboration agreements that provide for research and development funding contains provisions that enable us, at our option, to reacquire the results of the research and development (such as purchase options or repurchase rights) nor do such agreements require the Company to pay for, or reacquire the results of, its research and development efforts. We therefore concluded that SFAS 68 does not apply.

In the event of certain terminations or material breaches by the collaborator, the intellectual property that the Company licensed to the collaborator would revert to the Company with either no or de minimis monetary obligations. The Company believes that a termination or material breach of these agreements by the collaborator is unlikely and, more importantly, such conditions are not within the Company's control. We believe that arrangements under which an enterprise "can" obtain the results of research and development, in the context of SFAS 68, means arrangements under which the enterprise intends to and is likely to obtain such results or has the unilateral right to obtain such results — not merely arrangements under which the enterprise "could or might" obtain the results.

Because none of the collaboration agreements that provide for research and development funding contains provisions enabling or allowing the Company to pay a collaborator to reacquire the results of its research and development activities or product candidates, the Company has concluded that its collaboration agreements are not within the scope of SFAS 68. In fact, the Company may actually be entitled to receive royalties on sales by the licensees of any resulting products, without the Company having to "repurchase" or "reacquire" any licensed rights to the results of research and development funded partially or entirely by the collaborators. The Company will review its financial footnote disclosure beginning with its Form 10-Q for the quarterly period ended September 30, 2006 to clarify that the Company has no rights to reacquire the results of its research and development funded partially or entirely by the Company's collaborators.

We supplementally advise the Staff that our business strategy is focused on developing new drug candidates for commercialization rather than performing contract research for others. Management does not view costs related to its collaboration agreements as a key performance indicator and historically did not track such information separately to manage the business. The Company only tracked the time incurred by each of its scientists on a full-time equivalent basis and such measure served as the basis for fulfilling its contractual obligations. The Company did not have the systems and processes in place to capture costs in a manner that would be consistent with U.S. GAAP on a program basis. As a result, no disclosure of costs related to the Company's collaboration agreements has been made in our Form 10-K Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Set forth below is a summary of the applicable terms of the Company's research and collaboration agreements that support the Company's conclusion that the agreements included in Note 3 of its consolidated financial statements are not within the scope of SFAS 68. We have also identified in the summary those collaborations described in Note 3 that do not have a research and development component and as such do not fall within the scope of SFAS 68.

Wyeth Pharmaceuticals:

The Company entered into a license agreement with Wyeth under which the Company granted Wyeth an exclusive, worldwide license to certain intellectual property. The Company is not entitled to receive any research and development funding under the agreement and does not have any purchase options or repurchase rights with respect to the intellectual property (absent a termination or material breach by Wyeth).

Bristol-Myers Squibb:

Research and Technology Transfer Agreement

The Company entered into a research and technology transfer agreement with Bristol-Myers Squibb Company ("BMS") to identify the mechanism of action of compounds delivered to the Company by BMS. The Company received annual research funding to perform specified experiments on chemical compounds provided by BMS. The compounds supplied by BMS remain the property of BMS. The Company does not have any purchase options or repurchase rights that enable it to reacquire the results of the research and development (absent a termination or material breach by BMS). The research term of the agreement expired in 2004. In addition, the agreement also included a technology sharing program under which BMS and the Company shared certain core technologies in genomics and lead optimization, but no research funding was provided for the technology sharing program and the Company does not have any purchase options or repurchase rights with respect to the shared technologies.

Cancer Collaboration Agreement

The Company entered into a Cancer Collaboration Agreement with 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).

LXR Agreement

In December 2005, the Company entered into a license agreement with BMS under which the Company granted BMS a license to certain intellectual property. The Company receives annual research and development funding over the research term. The BMS licensing agreement is structured as a permanent transfer of the intellectual property and the Company does not have purchase options or repurchase rights that enable it to reacquire the results of the research and development (absent a termination or material breach by BMS).

Genentech:

The Company entered into a license agreement with Genentech pursuant to which the Company granted Genentech a license to certain intellectual property. Genentech is required to provide research and development funding over the research term. The Company can elect to profit share in therapeutic areas that are not the primary focus of the collaboration but such election is not conditioned on any payments by the Company. There are no terms under which the Company can reacquire from Genentech the license or products developed under the collaboration (absent a termination or material breach by Genentech).

Helsinn Healthcare:

The Company entered into a license agreement with Helsinn under which the Company granted Helsinn a license to certain intellectual property. The Company is not entitled to receive any research and development funding and received only minor cost reimbursement for certain trial management expenses incurred during a 6-month transition period commencing on the date of execution of the agreement and ending on the date of transfer of the Investigational New Drug Application for XL119 from the Company to Helsinn.

Bayer:

The Company entered into a research collaboration agreement with Bayer to identify and develop novel screening targets for pesticides in the area of crop protection. This agreement was superseded by a subsequent research collaboration agreement pursuant to which the Company and Bayer formed a joint venture, Genoptera LLC. Bayer held a 60% ownership interest and the Company held a 40% ownership interest in Genoptera. Bayer provided capital funding to Genoptera and the Company provided research services focused on developing insecticides and nematicides in the area of crop protection. The Company received annual research funding over the research term. There are no terms under which the Company can reacquire the developed insecticides and nematicides from Bayer (absent a termination or material breach by Bayer).

The Genoptera joint venture agreement was subsequently amended, which resulted in the termination of the research term as well as Bayer's purchase of the Company's 40% interest in Genoptera. Under the terms of the amended agreement, Bayer obtained exclusive rights in the field of agriculture to all assays, compounds and products developed under the collaboration and the Company obtained the rights in all other fields. The collaboration was terminated in 2005. There are no terms under which the Company can reacquire Bayer's targets or related materials (absent a termination or material breach by Bayer).

GlaxoSmithKline:

The Company entered into the Product Development and Commercialization Agreement 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 can reacquire the compounds selected by GSK (absent a termination or material breach by GSK).

Combinatorial Chemistry Collaborations:

The Company entered into a number of combinatorial chemistry collaborations under which the Company generated agreed-upon compounds. Under these agreements, the Company was not entitled to receive any research and development funding nor are there any terms under which the Company can reacquire the results of the collaborations. All but one of the Company's compound collaborations were terminated in 2004.

Protein Design Labs:

The Company entered into a collaboration agreement with Protein Design Labs ("PDL") to create and develop drug candidates for which the Company received annual research funding. There are no terms under which the Company could acquire the drug candidates developed under this agreement from PDL (absent a termination or material breach by PDL). The research term of the collaboration expired in 2003.

Note 4 Symphony Evolution, page 79

Comment: Please explain how you had determined that SEI was a variable interest entity and that the company was the primary beneficiary. As you disclosed that you determined this in accordance with FIN 46R, please cite the specific paragraphs within FIN 46R supporting this determination.

Response:

Is Symphony Evolution, Inc. ("SEI") a variable interest entity?

A variable interest entity refers to an entity that is subject to consolidation in accordance with FIN 46R. Paragraph 5 of FIN 46R states that an entity shall be subject to consolidation if one of the conditions of paragraph 5 a., b. or c. exists. SEI satisfies conditions b.(1) and b.(3) of paragraph 5.

Pursuant to paragraph 5 b.(1), an entity will be subject to consolidation if the holders of the equity investment at risk, as a group, lack the direct or indirect ability through voting rights or similar rights to make decisions about the activities of the entity that have a significant effect on the success of the entity. SEI is a variable interest entity because

Symphony Holdings LLC (“Holdings”), the equity owner of SEI, has limited ability to make decisions about the activities of SEI that have a significant effect on its success. Pursuant to an Amended and Restated Research and Development Agreement, dated June 9, 2005, among the Company, SEI and Holdings (the “R&D Agreement”), the Company is primarily responsible for the development of the research and development programs that have been licensed to SEI. These programs constitute the entire business of SEI. The R&D Agreement provides that SEI and the Company will develop the programs in accordance with a specified development plan and related development budget. The Company’s development activities are supervised by SEI’s Development Committee, which is comprised of an equal number of representatives from the Company and SEI. The Development Committee reports to SEI’s Board of Directors, which is comprised of five members. The Company has one seat on SEI’s Board of Directors and has the right to approve two of the four directors that Holdings is entitled to nominate. Accordingly, Holdings does not have controlling rights with respect to decisions about SEI’s activities.

Further, pursuant to paragraph 5 b.(3), an entity will be subject to consolidation if the holders of the equity investment at risk, as a group, lack the right to receive the expected residual returns of the entity. Holdings does not have the right to receive SEI’s expected residual returns, as defined by paragraph 5 b.(3), because Holdings’ arrangements with SEI and the Company permit the Company to acquire 100% of the equity of SEI at a fixed exercise price. If exercised, this option caps Holdings’ potential returns on its investment in SEI. Holdings would obtain SEI’s expected residual returns only if the Company does not exercise its option to acquire 100% of the equity of SEI from Holdings.

Who are the variable interest holders of SEI?

Variable interests in a variable interest entity are defined in paragraph 2 c. of FIN 46R as contractual, ownership or other pecuniary interests in an entity that change with changes in the fair value of the entity’s net assets exclusive of variable interests. The variable interest holders of SEI are:

i. Holdings because, in return for receiving 100% of the equity of SEI, it provided all of SEI’s funding and such funds are at risk and sufficient to fund SEI’s operations; and

ii. The Company because it contributed the intellectual property to SEI in return for an exclusive option from Holdings to purchase all of SEI’s equity at a predetermined price.

Are the variable interest holders related parties?

Under paragraph 16 d. of FIN 46R, related parties include those parties that have a relationship where one party cannot sell, transfer or encumber its interest in the variable interest entity without the prior approval of the other party.

The agreements between the Company and Holdings prohibit Holdings from selling, transferring or encumbering its interest in SEI without the Company’s prior approval during

the period in which the Company has the option described above. The Company's pre-approval rights limit Holdings' ability to manage the economic risks or to realize the economic rewards from its interest in SEI through the sale, transfer or encumbrance of such interest during the restricted period. Holdings' inability to transfer its interest in SEI without the Company's prior approval creates a related party relationship between Holdings and the Company.

Who is the primary beneficiary?

The requirements of paragraph 17 of FIN 46R provide that if two or more related parties hold variable interests in the same variable interest entity and the aggregate variable interest held by those parties would, if held by a single party, identify that party as the primary beneficiary, then the party within the related party group that is most closely associated with the variable interest entity is the primary beneficiary. The determination of which party within the related party group is most closely associated with the variable interest entity requires judgment and is based on an analysis of the relevant facts in accordance with paragraph 17 of FIN 46R.

We concluded that Exelixis is the entity most closely associated with the activities of SEI, the variable interest entity. We considered the criteria in paragraph 17 of FIN 46R and believe the significance of SEI's activities to Exelixis (*i.e.*, criterion 17 b.) and SEI's design (*i.e.*, criterion 17 d.) are strong indicators that Exelixis is the primary beneficiary. The following factors were considered:

i. The technology contributed to SEI was originally developed by Exelixis;

ii. Exelixis will continue to serve as the Investigational New Drug Application sponsor during the development term;

iii. Exelixis' employees will continue to perform substantially all of the development work;

iv. Exelixis intends to exercise its purchase option to reacquire the technology rights upon the successful clinical development of the product candidates licensed to SEI;

v. Exelixis significantly influenced SEI's design as well as its primary operations and activities;

vi. Exelixis has the ability through its representation on the board of directors of SEI and SEI's development committee to make decisions that have a significant effect on the success of SEI's activities; and

vii. The operations and activities of Exelixis are substantially similar to the operations and activities of SEI.

Based on our analysis of the above-referenced factors, we concluded that SEI is a variable interest entity for which the Company is the primary beneficiary.

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In connection with our response to the Staff's comments, Exelixis acknowledges the following:

- Exelixis is responsible for the adequacy and accuracy of the disclosure in its filings.
- The Staff comments or changes to disclosure in response to Staff comments do not foreclose the Commission from taking any action with respect to the filing.
- Exelixis may not assert Staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

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 LLP