September 22, 2008

VIA EDGAR

Jim B. Rosenberg, Senior Assistant Chief Accountant
Securities and Exchange Commission
Division of Corporation Finance
100 F. Street, N.E.
Washington, D.C. 20549

RE: Exelixis, Inc.
Form 10-K for the Fiscal Year Ended December 28, 2007
Filed February 25, 2008
File Number: 000-30235

Dear Mr. Rosenberg,

Exelixis, Inc. (the "Company") is pleased to respond to the Staff's comment letter, dated August 29, 2008 regarding the Company's Annual Report on Form 10-K for the fiscal year ended December 28, 2007 (the "2007 Form 10-K"). The following information is provided in response to the Staff's comments, which comments are included below in bold italics. Please note that the heading and number of the response set forth below correspond to the heading and number of the comment contained in the Staff's letter.

Management's Discussion and Analysis of Financial Condition and Results of Operations

Results of Operations

Research and Development Expenses, page 50

1. ***We believe that your disclosures about historical research and development expenses and estimated future expenses related to your major research and development projects could be enhanced for investors. Please refer to the Division of Corporation Finance "Current Issues and Rulemaking Projects Quarterly Update" under section VIII – Industry Specific Issues – Accounting and Disclosure by Companies Engaged in Research and Development Activities. You can find it at the following website address: http://www.sec.give/divisions/corpfin/cfcrq032001.htm. Please revise your MD&A to disclose the following information for each of your major research and development projects.***

   a. ***The current status of the project;***

   b. ***The costs incurred during each period presented and to date on each project;***

   c. ***The nature, timing and estimated costs of the efforts necessary to complete each project;***

   d. ***The anticipated completion dates of each project;***

   e. ***The risks and uncertainties associated with completing development on schedule, and the consequences to operations, financial position and liquidity if each project is not completed timely; and finally***

f. The period in which material net cash inflows from significant projects are expected to commence for each project.

Regarding b., if you do not maintain and research and development costs by project, disclose that fact and explain why management does not maintain and evaluate research and development costs by project. Provide other quantitative or qualitative disclosure that indicates the amount of the company's resources being used on the project.

Regarding c. and d., disclose the amount or range of estimated costs and timing to complete the phase in process and each future phase. To the extent that information is not estimable, disclose those facts and circumstances indicating the uncertainties that preclude you from making a reasonable estimate.

To address the Staff's comment, we have broken down our response to correspond to the clauses above.

Comment 1(a). The Company respectfully advises the Staff that detailed information regarding the current status of each of the Company's drug candidates is disclosed beginning on page 8 of the 2007 Form 10-K. In addition, summary information regarding the stage of development for the Company's drug candidates in clinical development is included on page 4 and on page 42 of the 2007 Form 10-K. We believe that our existing disclosure provides investors with meaningful detail to enable them to assess the status of each of our drug candidates in development and to make an informed investment decision. We expect to include a comparable level of detail in our future Annual Reports on Form 10-K. We also disclose summary information in each of our Quarterly Reports on Form 10-Q and expect to continue doing so in the future.

Comment 1(b). The Company does not track total research and development expenses separately for each program. For fiscal years prior to 2006, the Company did not track any component of these expenses by program. However, beginning in fiscal 2006, the Company began tracking third party expenditures directly relating to each program as a way of monitoring external costs. In managing our research and development activities, third party expenditures are considered only in the context of the qualitative factors described below. Our third party research and development expenditures relate principally to our clinical trial and related development activities, such as preclinical studies and contract manufacturing, and represent only a portion of the costs related to each program. Aggregate third party expenditures relating directly to specific programs represented approximately one-third of our research and development expenses in the 2007 fiscal year. Third party expenditures for programs initiated prior to the beginning of fiscal 2006 have not been tracked from project inception, and therefore such expenditures from inception for most of our programs are not available. The Company does not accumulate on a program-specific basis internal research and development expenses, such as (i) salaries and personnel expenses, (ii) facilities overhead expenses and (iii) external costs not directly attributable to a specific project. We do not believe that accumulating internal research and development expenses on a program by program basis provides a meaningful measure of performance, as internal resources are dynamically allocated among our programs as needs dictate. In light of the foregoing, we believe that disclosure of only third party expenditures by program would not be meaningful to investors, and, in fact, could be misleading.

The Company generally reviews its research and development expenses by focusing on three broad categories: drug discovery; development; and other. Our drug discovery group utilizes a variety of high-throughput technologies to enable the rapid discovery, optimization and extensive characterization of lead compounds such that we are able to select development candidates with the best potential for further evaluation and advancement into clinical development. Drug discovery expenses relate primarily to personnel expense, lab supplies and general corporate costs. Our development group leads the development and implementation of our clinical and regulatory strategies and prioritizes disease indications in which our compounds may be studied in clinical trials. Development expenses relate primarily to clinical trial, personnel and general corporate costs. Other primarily includes stock compensation expense relating to personnel in our drug discovery and development groups.

249 East Grand Ave. P.O. Box 511 South San Francisco, CA 94803-0511 main 650.837.7000 fax 650.837.8300 www.exelixis.com

In addition to reviewing the three categories of research and development expenses described in the preceding paragraph, the Company principally considers qualitative factors in making decisions regarding our research and development programs. Such factors include enrollment in clinical trials for our drug candidates, the results of and data from clinical trials, the potential indications for our drug candidates, the clinical and commercial potential for our drug candidates and competitive dynamics. We also make our research and development decisions in the context of our overall business strategy, which includes the pursuit of commercial collaborations with major pharmaceutical and biotechnology companies for the development of our drug candidates.

In response to clause (b) of the Staff's comment, we propose to include additional disclosure under the heading "—Research and Development Expenses" before "Certain Factors That May Affect Our Business) in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our future annual reports on Form 10-K and quarterly reports on Form 10-Q (commencing with our Quarterly Report on Form 10-Q for the quarter ending September 28, 2008 (the "Q3 2008 Form 10-Q")) describing the three broad categories of our research and development expenses and presenting the expenses attributed to each of these categories during the period covered by the report as well as for the comparable period in the prior year (the prior two fiscal years in the case of our Form 10-Ks). In addition, we propose to include a ranking of those programs that we believe represented the greatest portion of our research and development expenses, based on estimates of our research and development efforts and expenses, during the most recent period covered by the report. Since these estimates would be derived, in part, from non-financial management tools, we would not include quantitative disclosure of the estimates themselves. The proposed disclosure would be substantially as set forth on Exhibit A hereto.

Comment 1(c), (d) and (f). As with most biotechnology companies with drug candidates in development, the path to marketing approval by the Food and Drug Administration and comparable foreign agencies for each such candidate is long and uncertain. The regulatory process, both domestically and abroad, can be a multi-year process with no certainty when and if a drug candidate will be approved for commercial use. The development path for a particular drug candidate typically includes a variety of clinical trials. While we have a general estimate of the timeframe for our clinical trials, the actual anticipated completion dates for each of our drug candidates are uncertain due to a wide variety of risks, including those described in the risk factors referenced in our response to Comment 1(e) below. The length of time for a clinical trial may vary substantially according to factors relating to the particular clinical trial, such as the type and intended use of the drug candidate, the clinical trial design and the ability to enroll suitable patients. In addition, it may be necessary to undertake additional unanticipated clinical trials during the development path.

These same factors prevent the Company from reasonably estimating the total costs to complete the development of any of our drug candidates. Similarly, we do not have a reasonable basis to predict when or if material net cash inflows from the commercialization and sale of our drug candidates will occur. To date, we have not commercialized any of our drug candidates and in fact may never do so.

In response to clauses (c), (d) and (f) of the Staff's comment, disclosure regarding in the uncertainty of timing and costs regarding our drug candidates is included on Exhibit A hereto. Since the disclosure regarding timing and total costs reflected in the second and third full paragraphs on page 51 of the 2007 Form 10-K (i.e., in the period over period discussion of research and development expenses) would be incorporated into the new disclosure set forth on Exhibit A, we would delete those paragraphs in future filings.

249 East Grand Ave. P.O. Box 511 South San Francisco, CA 94803-0511 main 650.837.7000 fax 650.837.8300 www.exelixis.com

Comment 1(e). As noted above, the Company does not believe it is possible to reliably determine completion dates for the development of each of the Company's drug candidates. The Company believes that the risks and uncertainties with respect to development and the consequences to the Company's operations, financial position and liquidity are generally the same for each of the Company's drug candidates. The Company believes that these risks and uncertainties are disclosed in the Company's 2007 Form 10-K under:

- "Item 1A. Risk Factors—Risks Related to Our Need for Additional Financing and Our Financial Results—If additional capital is not available to us, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts and we may breach our financial covenants;"
- "Item 1A. Risk Factors—Risks Related to Development of Product Candidates—Clinical testing of our product candidates is a lengthy, costly, complex and uncertain process and may fail to demonstrate safety and efficacy;"
- "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Certain Factors That May Affect Our Business —Company-specific Factors;" and
- "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Cash Requirements."

In response to clause (e) of the Staff's comment, we have included a cross-reference to "Risk Factors" in the proposed disclosure set forth on Exhibit A.

Notes to Consolidated Financial Statements

Note 2. Dispositions, page 75

2. ***Please tell us your consideration of SAB Topic 5E in your decision to recognize a gain from the sale of the plant trait business and the sale of 80.1% of Artemis. Specifically address whether the risks of business have been transferred. Also please tell us why these sales were not treated as discontinued operations and your consideration of paragraphs 41 through 44 of SFAS 144.***

To address the Staff's comment, we have broken down our response to correspond to each of the components of the comment.

SAB Topic 5E. Staff Accounting Bulletin Topic 5E, "Accounting For Divestiture Of A Subsidiary Or Other Business Operation", provides guidance on the accounting for the transfer of certain operations given certain assumed facts and circumstances. The facts assumed in Topic 5E include a purchaser with questionable creditworthiness, a significant amount of consideration in the form of promissory notes, the retention of the seller of a contingent liability related to the performance on existing contracts, and a guarantee by the seller of debt of the transferred operations.

The Company does not believe that the facts included in the SAB Topic 5E example are analogous to the sale of our plant trait business. The plant traits business was sold to The Dow Chemical Company ("Dow") in consideration for a cash payment of $22.5 million, of which $18 million was received upon execution. The additional $4.5 million is a contractual obligation due on the one year anniversary of the execution of the transaction and is not dependent upon the operating results of the assets sold. In our view, Dow does not have questionable creditworthiness. In addition, the consideration is not subject to return or dependent upon future operating results of the assets sold and is therefore not subject to uncertainty. Based on these facts, we believe that the risks and other incidents of ownership associated with these assets have been transferred with sufficient certainty that SAB Topic 5E is not applicable.

249 East Grand Ave. P.O. Box 511 South San Francisco, CA 94803-0511 main 650.837.7000 fax 650.837.8300 www.exelixis.com

We also do not believe that the facts included in the SAB Topic 5E example are analogous to the sale of 80.1% of Artemis Pharmaceuticals GmbH. This transaction was between the Company and Taconic Farms, Inc. in consideration for an up-front cash payment of $19.8 million. The cash received is not subject to a right of return and is not dependent upon future operating results of the entity sold. We therefore believe that the risks and other incidents of ownership associated with the 80.1% of the business have been transferred with sufficient certainty that SAB Topic 5E is not applicable.

SFAS 144. Paragraph 42 of FASB Statement No. 144 "Accounting for the Impairment or Disposal of Long-Lived Assets" states that "the results of operations of a component of an entity that has been disposed of …. shall be reported in discontinued operations in accordance with paragraph 43 if both of the following conditions are met: (a) the operations and cash flows of the component have been (or will be) eliminated from the ongoing operations of the entity as a result of the disposal transaction and (b) the entity will not have any significant continuing involvement in the operations of the component after the disposal transaction." EITF Issue 03-13, "Applying the Conditions in Paragraph 42 of FASB Statement No. 144 in Determining Whether to Report Discontinued Operations," (Issue 03-13) provides additional guidance in determining whether the continuing involvement is deemed to be significant.

The Company does not believe that the disposal of the plant trait business qualifies as discontinued operations under SFAS 144 paragraph 42, as we are responsible for paying, supervising and managing all of the employees of the disposed component for up to five years in accordance with the Contract Research Agreement (the "CRA"). We entered into the CRA with Dow in connection with the sale of the plant trait business, and Dow has agreed to pay up to $24.7 million in research and development funding to the Company over the term of the CRA to fully cover employee costs, facilities expenses and capital expenditures. In evaluating this disposal under Issue 03-13, we concluded that substantially all of the cash flows of the plant traits business will continue to be borne by Exelixis during the term of the CRA. Since the cash flows are clearly more than the 20% threshold established by Issue 03-13, we concluded that presentation as discontinued operations is not appropriate.

We do not believe that the disposal of 80.1% of Artemis qualifies as discontinued operations under SFAS 144 paragraph 42 and EITF 03-13, Applying the Conditions in Paragraph 42 of FASB Statement No. 144 in Determining Whether to Report Discontinued Operations, as we have retained significant continuing involvement with the operations of Artemis. We have determined that our rights as a continuing 19.9% shareholder, together with our representation on Artemis' Shareholder Committee, allow us to have significant influence over Artemis going forward. For instance, as a member of the Shareholder Committee, our representative must approve most major business or strategic decisions. Our member on the Shareholder Committee also participates in decisions related to establishing the budget and the retention and compensation of the managing directors. We supplementally advise the Staff that we apply the equity method of accounting for our retained 19.9% investment in Artemis. Based on our significant continued involvement, we have determined that discontinued operations presentation is not appropriate.

249 East Grand Ave. P.O. Box 511 South San Francisco, CA 94803-0511 main 650.837.7000 fax 650.837.8300 www.exelixis.com

Note 3. Research and Collaboration Agreements, page 76

3. ***For all of your research and collaboration agreements, please clarify in your disclosure whether the company is entitled to obtain the results of the research and development funded partially or entirely by the collaborators.***

In response to the Staff's comment, commencing with our Annual Report on Form 10-K for the Fiscal Year Ending January 2, 2009, we will enhance the disclosure in our "Research and Collaboration Agreements" footnote to clarify with respect to the relevant research and collaboration agreements whether we are entitled to obtain the results of the research and development funded partially or entirely by the collaborators.

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

- The Company is responsible for the adequacy and accuracy of the disclosure in the filing;
- 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; and
- The Company 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 additional questions or comments regarding the foregoing, please contact the undersigned at (650) 837-7565 or James B. Bucher, Vice President, Corporate Legal Affairs & Secretary at (650) 837-7251.

Sincerely,

/s/ Frank Karbe
Frank Karbe
Executive Vice President and
Chief Financial Officer

cc: Vanessa Robertson, Staff Accountant
Lisa Vanjoske, Assistant Chief Accountant
James B. Bucher, Vice President, Corporate Legal Affairs & Secretary
Leone Patterson, Vice President, Finance
Debbie Burke, Senior Director, Finance & Controller
Daniel Coleman, Ernst & Young LLP
Suzanne Sawochka Hooper, Cooley Godward Kronish LLP

249 East Grand Ave. P.O. Box 511 South San Francisco, CA 94803-0511 main 650.837.7000 fax 650.837.8300 www.exelixis.com

EXHIBIT A

Research and Development Expenses

Research and development expenses consist primarily of personnel expenses, stock-based compensation, clinical trials, consulting, laboratory supplies and general corporate costs. We group our research and development expenses into three categories: drug discovery, development and other. Our drug discovery group utilizes a variety of high-throughput technologies to enable the rapid discovery, optimization and extensive characterization of lead compounds such that we are able to select development candidates with the best potential for further evaluation and advancement into clinical development. Drug discovery expenses relate primarily to personnel expense, lab supplies and general corporate costs. Our development group leads the development and implementation of our clinical and regulatory strategies and prioritizes disease indications in which our compounds may be studied in clinical trials. Development expenses relate primarily to clinical trial, personnel and general corporate costs. Other primarily includes stock compensation expense.

In addition to reviewing the three categories of research and development expenses described above, we principally consider qualitative factors in making decisions regarding our research and development programs. Such factors include enrollment in clinical trials for our drug candidates, the results of and data from clinical trials, the potential indications for our drug candidates, the clinical and commercial potential for our drug candidates and competitive dynamics. We also make our research and development decisions in the context of our overall business strategy, which includes the pursuit of commercial collaborations with major pharmaceutical and biotechnology companies for the development of our drug candidates.

The expenditures summarized in the following table reflect total research and development expenses by category, including allocations for general and administrative expenses.

	Three months Ended June 30,		Six months Ended June 30,	
Categories	2008	2007	2008	2007
Drug discovery	$26.2	$26.6	$ 52.7	$ 51.0
Development	38.7	23.5	74.2	43.8
Other	4.0	6.2	7.9	11.7
Total research and development expense	$68.9	$56.3	$134.8	$106.5

For the six month period ended June 30, 2008, the programs representing the greatest portion of our research and development expenses (in approximate order of magnitude), based on estimates of the allocation of our research and development efforts and expenses among specific programs, were XL647, X184, XL765, XL147 and XL019. The expenses for these programs are included in the development category of our research and development expenses.

We currently do not have reliable estimates regarding the timing of our clinical trials. We estimate that typical phase 1 clinical trials last approximately one year, phase 2 clinical trials last approximately one to two years and phase 3 clinical trials last approximately two to four years. However, the length of time may vary substantially according to factors relating to the particular clinical trial, such as the type and intended use of the drug candidate, the clinical trial design and the ability to enroll suitable patients.

We also currently do not have reliable estimates of total costs for a particular drug candidate to reach the market, as there is great variability in the costs necessary to develop a drug candidate. Our potential therapeutic products are subject to a lengthy and uncertain regulatory process that may involve unanticipated additional clinical trials and may not result in receipt of the necessary regulatory approvals. Failure to receive the necessary regulatory approvals would prevent us from commercializing the drug candidates affected. In addition, clinical trials of our potential products may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval. Our development costs for a particular drug candidate may also be impacted by scope and timing of enrollment in clinical trials for the drug candidate, future decisions to study new indications for the drug candidate and whether in the future

we decide to pursue development of the drug candidate with a partner or independently. Similarly, we do not have a reasonable basis to predict when or if material net cash inflows from the commercialization and sale of our drug candidates will occur. To date, we have not commercialized any of our drug candidates and in fact may never do so. For a discussion of the risks and uncertainties associated with the timing and costs of completing the development of the Company's drug candidates, see "Part II. Item 1A. Risk Factors."