December 21, 2007

Securities and Exchange Commission
Division of Corporate Finance
100 F Street, N.E.
Washington, D.C. 20549

Attention: Mr. Mark Brunhofer
Division of Corporate Finance

Re: Lexicon Pharmaceuticals, Inc.
Form 10-K for the fiscal year ended December 31, 2006
Form 10-Q for the quarterly period ended September 30, 2007
File No. 000-30111

Dear Mr. Brunhofer:

On behalf of Lexicon Pharmaceuticals, Inc., we have set forth below our responses to the comments received from Securities and Exchange Commission's staff in its November 16, 2007 letter regarding our annual report on Form 10-K for the fiscal year ended December 31, 2006 and our quarterly report on Form 10-Q for the quarterly period ended September 30, 2007. For your convenience, we have listed our responses in the same order as the comments were presented and have repeated each comment prior to the response.

Form 10-K for the Fiscal Year Ended December 31, 2006

Notes to Consolidated Financial Statements
Note 2: Summary of Significant Accounting Policies
Revenue Recognition, page F-8

1. You indicate that you recognize non-refundable upfront fees under drug discovery alliances on a straight-line basis over the estimated period of service, generally the contractual research term. Please revise your disclosure to indicate how you consider the contractual option granted in some of your contracts to extend the research term and separately reference the authoritative literature you rely upon to support your accounting. In addition, please explain to us why it is appropriate to consider only the research term of your agreements when it appears you are obligated or may be obligated to participate in continuing development of compounds. In this regard for example, it appears from your disclosure in your collaborations footnote beginning on page F-17 that you are jointly responsible for development under your N.V. Organon agreement.

Response: According to SAB 104, section 3(f), upfront fees are earned as the services are performed over the term of the arrangement or the expected period of performance and generally should be deferred and recognized systematically over the periods that the fees are earned. Additionally, the revenue recognition period should extend beyond the initial contractual period if the relationship with

the collaborator is expected to extend beyond the initial term and the collaborator continues to benefit from the payment of the upfront fee. In accordance with SAB 104, we defer non-refundable upfront fees under drug discovery alliances and generally recognize them over the contractual research term, as this period is our best estimate of the period over which the services will be rendered. We have determined that the level of effort we perform to meet our obligations is fairly constant throughout the estimated periods of service. As a result, we have determined that it is appropriate to recognize revenue from such agreements on a straight-line basis, as we believe this is reflective of how the services are provided.

In certain agreements, there are options under the collaborator's control to extend our period of service for additional fees, which fees are determined at the inception of the agreement. We believe that whether or not a collaborator will exercise an option to extend the service period is largely dependent on the results of the initial research period, and how such results affect the collaborator's perception of whether any additional benefit would be obtained from an extended period. Given the nature of our research arrangements, we do not believe that is determinable at the outset of an arrangement whether a collaborator will believe an extended service period will be beneficial and, therefore, elect to extend the contract. Further, our history does not support an assumption that collaborators will choose to extend the relevant service period, as there is no clear historical trend. As an example, in 2006, Bristol-Myers Squibb Company exercised its option to extend the service period under its agreement for an additional two years. Conversely, in 2007, Takeda Pharmaceutical Company Limited chose not to exercise a similar option to extend the service period under its agreement. For these reasons, we believe that we have considered the potential option periods when determining the estimated period of service under its revenue agreements. In future filings, we propose to revise our policy disclosure regarding upfront fees to discuss the determination of the estimated period of service as well as the reasons for recognizing revenue on a straight-line basis, as discussed above.

Additionally, we consider only the contractual research term of our target discovery efforts under these agreements as the period of service and not any additional time periods relating to the development of potential therapeutic products because we are not obligated under these agreements to participate in continuing such development.

Under the Organon agreement, we have an obligation to conduct target discovery efforts over a four-year contractual research term. From the results of such research, we and Organon may jointly select targets for further research and development. If such research and development is performed jointly, the parties will equally share costs and responsibility for such research activities, as well as revenues from any resulting products sold. At any time, either party may decline to participate in such further research or development efforts with respect to specific targets, in which case such party will receive royalty payments on sales of resulting products rather than sharing in revenue and costs. Accordingly, we are not obligated to provide research services relating to or otherwise participate in the development of therapeutic products pursuant to the Organon agreement.

Royalty payments are calculated as a percentage of product sales, and are agreed upon at the inception of the agreement. Further, we negotiated the upfront and research funding payments under the Organon agreement together, and considered such upfront payment when determining an appropriate price for the initial four-year target discovery program. We consider the upfront fee an access fee providing Organon the ability to access our technology and infrastructure with respect to the production and analysis of knockout mice that we had previously developed. For these reasons, we believe it is not appropriate to include in the estimated period of service under the Organon agreement any additional period beyond the four-year contractual research term of our target discovery efforts.

2. You disclose that you allocate revenue from multiple element contracts to each element based on the relative fair value of the elements determined using objective evidence. You also disclose that you recognize the revenue for an element upon completion when it is tied to a separate earnings process and on a straight-line basis over the life of the term of the agreement when it is not specifically tied to a separate earnings process. Please address the following comments:

   a. Please revise your policy disclosure to clarify how you assess deliverables under paragraph 9 of EITF 00-21. In this regard, please ensure that you address standalone value for your deliverables.

Response: In future filings, we propose to revise our policy disclosure regarding revenue from multiple element contracts as follows:

> The Company analyzes its multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting in accordance with EITF No. 00-21, “Revenue Arrangements with Multiple Deliverables.” An element of a contract can be accounted for separately if the delivered elements have standalone value to the collaborator and the fair value of any undelivered elements is determinable through objective and reliable evidence. If an element is considered to have standalone value but the fair value of any of the undelivered items cannot be determined, all elements of the arrangement are recognized as revenue over the period of performance for such undelivered items or services.

   b. Please revise your collaborations disclosure in Note 13 to identify the deliverables under each agreement and clearly indicate whether you have separated these deliverables into separate units of account as required by paragraph 18 of EITF 00-21.

Response: Our drug discovery alliances, which are the primary agreements which include multiple elements, include the following:

(1) *Access to technology and infrastructure.* Consideration for this access is received in the form of non-refundable upfront payments. The access to

technology is generally provided over the contractual research term of our drug target discovery efforts, but may be continued if such research term is extended by a collaborator, based on the considerations discussed in our response to Comment 1 above. The collaborator's access to technology may not be used outside of its relationship with us.

(2) *Research.* This generally includes production and/or specified phenotypic analysis of knockout mice. Consideration for this research is received in the form of research funding throughout the contractual research term of our target discovery efforts.

(3) *Additional performance measures.* The Company may receive nonrefundable milestone payments for achieving certain objectives and accomplishing predetermined goals.

(4) *Royalty payments.* The Company will earn royalties on sales of therapeutic products commercialized by the collaborator. These royalty payments are generally based on a predetermined percentage of product sales.

We have concluded that our drug discovery alliances that include the above elements do not have separate deliverables with standalone value at inception, and that the entire agreement should be accounted for as a single unit of accounting. Revenue is recognized over the estimated period of service, which is generally concurrent with the contractual research term of our target discovery efforts, as discussed in our response to Comment 1 above. Under our agreements, there is no guarantee of any additional payments beyond the contractual research term, as milestone and royalty payments will only be received if certain goals and commercialization of products are achieved. Milestone payments are for substantive work and are at risk with no assurances of being achieved.

Additionally, no additional performance by us is required once milestones are achieved. Similarly, the receipt of royalties does not require any performance by us after product sales have commenced. As such, we have concluded that it is appropriate to recognize revenue from such milestone payments and royalties upon achievement of the milestone or receipt of royalty payments, respectively.

In future filings, we propose to revise our revenue recognition policy disclosures in Note 2 to include the above and our collaborations disclosure in Note 13 to identify the deliverables under each agreement and discuss the units of accounting as shown in Appendix A.

Form 10-Q for the Quarterly Period Ended September 30, 2007

Notes to Consolidated Financial Statements
Note 7: Arrangements with Symphony Icon, Inc., page 9

3. You disclose that you consolidate Symphony Icon because it is a variable interest entity and you are the primary beneficiary. Please address the following comments:

a. Please revise your disclosure to clarify how Symphony Icon, Inc. is a variable interest entity and how you are the primary beneficiary when it appears that Symphony Icon Holdings LLC contributed all the working capital to Symphony Icon, Inc. Separately demonstrate to us why you consolidate Symphony Icon and reference for us the authoritative literature you rely upon to support your accounting.

Response: We performed the following analysis to determine that Symphony Icon, Inc. is a variable interest entity and that we are the primary beneficiary and therefore should consolidate Symphony Icon:

Is Symphony Icon a variable interest entity?

A variable interest entity refers to an entity that is subject to consolidation in accordance with FASB Interpretation No. 46 (revised 2003), "Consolidation of Variable Interest Entities" ("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.

We believe that Symphony Icon satisfies the condition described in paragraph 5(b)(1) as a result of the equity investor in Symphony Icon, Symphony Icon Holdings LLC ("Holdings"), lacking the direct or indirect ability, through voting rights or similar rights, to make decisions about Symphony Icon's activities that have a significant effect on its success. Pursuant to an amended and restated research and development agreement, dated June 15, 2007, among us, Symphony Icon and Holdings, we are primarily responsible for the development of the research and development programs that have been licensed to Symphony Icon, which programs constitute the entire business of Symphony Icon. The research and development agreement provides that the programs will be developed in accordance with a development plan and related development budget that have been approved by both us and Symphony Icon. Our development activities with respect to the programs are supervised by Symphony Icon's development committee, which is comprised of an equal number of representatives from us and Symphony Icon. The development committee reports to Symphony Icon's board of directors, which is comprised of five members, including one member designated by us and two independent members selected by us and Holdings. Accordingly, we do not believe that Holdings has controlling rights with respect to decisions about Symphony Icon's activities, as specified in paragraph 5(b)(1).

We further believe that Symphony Icon satisfies the condition described in paragraph 5(b)(3), which specifies that 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 Symphony Icon's expected residual returns, as defined by FIN 46R, because Holdings' arrangements with Symphony Icon and us permit us to acquire 100% of the equity of Symphony Icon at predetermined amounts pursuant to an exclusive purchase option under a purchase option agreement, dated June 15, 2007 among us, Symphony Icon and Holdings. If exercised, this option would limit Holdings' potential returns on its investment in Symphony

Icon. Holdings would obtain Symphony Icon's expected residual returns only if we do not exercise our option to acquire 100% of the equity of Symphony Icon from Holdings.

Do we have a variable interest in Symphony Icon?

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. We believe that we are a variable interest holder in Symphony Icon as a result of our issuance of shares of our common stock to Holdings in exchange for the purchase option. We further believe that Holdings is an additional variable interest holder in Symphony Icon as a result of its contribution to Symphony Icon's funding, which funds remain at risk, in exchange for 100% of the equity of Symphony Icon.

Are the variable interest holders related parties?

Under paragraph 16(d) of FIN 46R, related parties include those parties having 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 series of related agreements between us and Holdings prohibit Holdings from selling, transferring or encumbering its interest in Symphony Icon without our prior approval during the period in which we have the purchase option, or four years from the date of those agreements. We believe that Holdings' inability to transfer its interest in Symphony Icon without our prior approval creates a related party relationship between Holdings and us.

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 primary factor we considered in our determination that we are the primary beneficiary of Symphony Icon was the relationship of us and Holdings to the activities of Symphony Icon and the significance of those activities (paragraph 17(b)). We believe that Symphony Icon's activities are more significant to us than to Holdings because (1) the programs contributed to Symphony Icon were originally developed by us, (2) we intend to exercise the purchase option if Symphony Icon successfully completes the clinical development of the programs, and (3) our employees continue to perform, or direct the performance by third parties of, substantially all of the development activities with respect to the programs.

Another factor we considered was the existence of a principal-agency relationship between us and Holdings (paragraph 17(a)). For purposes of FIN 46R, we believe that we should be considered a principal, and Holdings should

be considered a de facto agent, as a result of the restrictions on Holdings' ability to sell, transfer or encumber its interests in Symphony Icon without our prior approval.

Based on the above analysis, we believe we are the primary beneficiary of Symphony Icon, and are therefore required to consolidate Symphony Icon as part of our consolidated financial statements.

In future filings, we propose to replace the last paragraph in Note 7 (and similar disclosure appearing elsewhere in our filings) with the following paragraph:

> In accordance with FIN 46R, Lexicon has determined that Symphony Icon is a variable interest entity for which it is the primary beneficiary. This determination was based on Holdings' lack of controlling rights with respect to Symphony Icon's activities and the limitation on the amount of expected residual returns Holdings may expect from Symphony Icon if Lexicon exercises its Purchase Option. Additionally, Lexicon has determined that it is the primary beneficiary of Symphony Icon as a result of certain factors including its ability to acquire the equity of Symphony Icon pursuant to the Purchase Option, its primary responsibility for the development of the Programs and its contribution of the Programs.

b. Please explain to us how the separate presentation of short-term investments held by Symphony Icon on your balance sheet complies with consolidation accounting and reference for us the authoritative literature you rely upon to support your accounting.

Response: We have separately presented short-term investments held by Symphony Icon primarily as a result of our belief that the inclusion of such investments with cash and cash equivalents could be misleading to investors, as such investments are not available to us to fulfill our general funding requirements outside of the Symphony relationship. As of September 30, 2007, the short-term investments held by Symphony Icon of $39.6 million include $25,000 of cash with the remainder in cash equivalents. In future filings, we propose to disclose in a footnote to our financial statements the amount of short-term investments held by Symphony Icon considered to be cash and cash equivalents, and the amount considered to be short-term investments, or available-for-sale securities.

c. Please revise your disclosure to explain how you valued your purchase option to acquire all the equity of Symphony Icon. In this regard, it appears that you may have valued this option by subtracting the $15 million cash you received from the $23.6 million fair value of the 7,650,622 shares of your common stock issued to Symphony Icon Holdings LLC based on the closing price of your stock on the date of this transaction. If this is true, please explain why there is no apparent fair value for the option in excess of the value of the shares you issued.

Response: We valued the purchase option by subtracting the $15 million cash we received from the $23.6 million fair value of the common stock we issued to Holdings.

We considered the fair value of the transaction to be the estimated fair value of the consideration received or the consideration given, whichever is more clearly evident. We believe the fair value of the consideration given — the common stock with a value of $23.6 million — was more clearly evident than the fair value of the purchase option. As a result, we based the value of the purchase option on the difference between the fair value of the common stock and the cash received. In future filings, we propose to disclose in a footnote to our financial statements the following statement:

> The Company calculated the value of the Purchase Option as the difference between the fair value of the common stock issued to Holdings of $23.6 million and the $15 million in cash received from Holdings for the issuance of the common stock.

d. Please explain to us why it is appropriate to charge the $8.6 million assigned to the purchase option and the $2.2 million of Symphony Icon structuring and legal fees to noncontrolling interest on your balance sheet. Please reference for us the authoritative literature you rely upon to support your accounting.

Response: We have determined that it is appropriate to record the purchase option as an offset to noncontrolling interest as a result of our belief that the purchase option should not be recorded as an acquisition in accordance with EITF 00-6, paragraph 8(a), which states that if a parent enters into a forward contract to purchase outstanding common shares (that is, minority interest) of its subsidiary at a future date, the parent should not record the acquisition of the subsidiary's shares until the forward contract is settled and the shares are received. During the period of the contract, the parent should continue to allocate subsidiary income or loss to the minority interest to be acquired. Furthermore, under paragraph 20 of EITF 00-6 and paragraph 21 of SFAS 150, forward purchase contracts that require physical settlement by repurchase of a fixed number of shares (minority interest) in exchange for cash shall be measured initially at the fair value of the shares, adjusted for any consideration or unstated rights or privileges, with an initial reduction to equity (minority interest) equal to the fair value of the shares at inception. Therefore, as we have not determined if we will exercise the purchase option, we have reduced the noncontrolling interest by the fair value of the purchase option.

We consider the structuring and legal fees to be the costs of entering into the overall Symphony transaction and, therefore, we concluded that the best method to record these fees was an allocation between the two primary funding elements of the transaction: (1) $15 million we received as partial consideration for the issuance of our common stock and (2) $45 million received by Symphony Icon to fund the development of the programs. In order to allocate the fees in proportion to such funding, we determined 25% of such fees ($15 million divided by the total funding amount of $60 million) should be allocated to the sale of our common stock and the remaining 75% should be allocated to the noncontrolling interest.

e. Please revise your disclosure to clarify whether you have charged any license fees or are recording any revenue from Symphony Icon.

Response: We propose to revise our disclosure related to Symphony Icon in future filings to clarify whether we have charged any license fees or are recording any revenue from Symphony Icon. To date, we have not charged any licenses fees and are not recording any revenue from Symphony Icon. Also, we do not expect any future license fees or revenue from Symphony Icon based on the current agreements with Symphony Icon and Holdings.

Note 8: Agreements with Invus, L.P., page 10

4. You disclose that you issued 50,824,986 shares of common stock to Invus and permitted Invus to require that you conduct certain rights offerings in the future for $205.4 million in gross proceeds. Please address the following comments:

a. Although you indicate that the warrants you issued to Invus automatically terminated upon the closing of the transaction, it appears from your proxy materials filed initially on June 18, 2007 that Invus exercised these warrants and that the shares are included in the 50.8 million shares identified above. Please revise your disclosure to clarify.

Response: We entered into a warrant agreement with Invus under which we issued warrants to purchase up to 16.5 million shares of our common stock for a purchase price of $3.09 per share. The warrant agreement provided that the warrants would terminate concurrently with the closing of the initial investment as defined in our securities purchase agreement with Invus. Pursuant to the securities purchase agreement, and subject to shareholder approval and certain other conditions, Invus separately agreed to purchase shares of our common stock in the initial investment in two separate tranches: (1) the number of shares that remained subject to the warrants at the time of the initial investment at a purchase price of $3.09 per share and (2) an additional 34.3 million shares at a purchase price of $4.50 per share. Invus did not exercise any of the warrants prior to the closing of the initial investment. As a result, at the closing of the initial investment, Invus purchased (a) 16.5 million shares of our common stock at a purchase price of $3.09 per share and (b) 34.3 million shares of our common stock at a purchase price of $4.50 per share, in each case pursuant to the securities purchase agreement. Simultaneously with such closing, all warrants issued under the warrant agreement terminated unexercised according to their terms. In future filings, we propose to revise our disclosure in order to clarify the mechanics relating to the termination of the warrants.

b. Please revise your disclosure to clarify your accounting for your rights offering grant to Invus. In addition, please reference for us the authoritative literature you rely upon to support your accounting. In your response, please explain to us how you evaluated the provision that permits Invus to settle rights offering price between $4.50 and the then-current market price of your common stock. In this regard, please explain the applicability of paragraphs 19 to 24 of EITF 00-19 and, if applicable, how your accounting complies.

Response: We have considered EITF 00-19 when determining how to account for a potential rights offering initiated by Invus. If a rights offering is conducted at fair value, then it is considered a physical settlement under EITF 00-19, as there would be no gain or loss. If a rights offering is conducted at a price below fair value, then it is considered a net-share settlement. In accordance with EITF 00-19, it is presumed that if a company does not have enough shares to settle under a net-share settlement, that company would have to settle in cash and, therefore, the transaction would be recorded as a liability.

Pursuant to the securities purchase agreement, Invus has the right, but not the obligation, to require us to issue shares of our common stock at a price per share to be designated by Invus in a range between $4.50 and the then current market price. However, as described in more detail below, in no event under the securities purchase agreement would we be required to settle any rights offering using cash. As a result, we believe that any rights offering under the securities purchase agreement should be considered a net-share settlement under EITF 00-19, which would require classification of the transaction as equity on our balance sheet rather than a liability, provided the following conditions listed in paragraphs 14 through 32 of EITF 00-19 are also satisfied:

(1) The contract permits the company to settle in unregistered shares:

The securities purchase agreement permits settlement in unregistered shares. Invus has certain registration rights with respect to shares it holds or acquires, but those would be considered under FSP EITF 00-19-2 rather than under the criteria in EITF 00-19.

(2) The company has sufficient authorized and unissued shares available to settle the contract after considering all other commitments that may require issuance of stock during the maximum period the derivative contract could remain outstanding:

As of the date of the securities purchase agreement, which was subject to shareholder approval, we did not have sufficient authorized and unissued shares to settle any reasonably anticipated rights offering. However, as our obligation to conduct a rights offering was contingent upon a number of closing conditions, including shareholder approval of both the Invus transaction and an amendment to our charter increasing the number of authorized shares of common stock, we believe that this condition should be reviewed after factoring in such increase in authorized shares, because only upon that vote of the shareholders to approve the transaction and associated incremental share authorization could any settlement under the securities purchase agreement actually occur. Following shareholder approval, the filing of the charter amendment and the closing of the initial investment on August 28, 2007, we had 300,000,000 shares of common stock authorized, 136,790,235 shares outstanding, 16,643,039 shares reserved for issuance upon exercise of currently outstanding options and warrants, and 861,889 additional

shares reserved for issuance pursuant to our stock option plans, resulting in 145,704,837 authorized and unissued shares available for issuance pursuant to any rights offering. Based on such share amounts, we had a sufficient number of authorized and unissued shares available, as of August 28, 2007, to allow for the issuance of shares with an aggregate value of $345 million (the maximum amount issuable pursuant to any rights offerings under the securities purchase agreement) at a price of $2.37 per share. As the per share issuance price with respect to any rights offerings will be unknown until the time of such rights offerings, we cannot state with certainty that the current number of authorized shares will be sufficient to settle our obligations pursuant to any rights offering, raising a question as to whether net cash settlement could be required outside our control. We have concluded, however, that this transaction will never require net cash settlement and, therefore, that this condition is satisfied. Please see paragraph 3 below for further comment.

(3) The contract contains an explicit limit on the number of shares to be delivered in a share settlement.

As the number of shares to be issued pursuant to any rights offering under the securities purchase agreement will be based on the price per share designated by Invus at such time, the number of shares to be delivered pursuant to any rights offering will be unknown until the time of such rights offering.

However, if the market price of our common stock is below $4.50 per share at the time of any rights offering, then the purchase price of any shares issued pursuant to the rights offering would be no less than the market value as of that date. As described in paragraph 2 above, we may not have a sufficient number of authorized and unissued shares to settle our obligations pursuant to any rights offering if the market price of our common stock were below $2.37 per share at that time. However, there would be no gain or loss on the transaction in that instance, as the transaction would be conducted at the market price — a transaction at the then fair value has no gain or loss. Therefore, there would be no amount to be net settled — that is, no net settlement in either cash or shares is possible. If the market price of our common stock is greater than $2.37 at the time of any rights offering, then there would be a sufficient number of authorized and unissued shares available for the transaction.

The only circumstance that could lead to a net settlement at the time of any rights offering would be in the case where the market price of our common stock is in excess of $4.50 per share. In such case, a purchaser would be in a position to purchase shares at a price less than market value, resulting in positive value to the holder that could be net settled. However, at such market price, we would have a sufficient number of authorized and unissued shares to settle our obligations pursuant to any rights offering. There is no scenario under the securities purchase agreement that would require us to settle any rights offering in cash and,

based on the discussion above, no situation in which a net cash settlement could result despite there being no explicit limit on the number of shares to be issued under the securities purchase agreement. This is a result of the unique pricing mechanism for the rights offering. As such, we have concluded that this transaction will never require settlement in cash, and that the conditions described in paragraphs 2 and 3 are satisfied.

(4) There are no required cash payments to the counterparty in the event the company fails to make timely filings with the SEC.

This condition is met as there are no required cash payments to Invus.

(5) There are no required cash payments to the counterparty if the shares initially delivered upon settlement are subsequently sold by the counterparty and the sales proceeds are insufficient to provide the counterparty with the full return of the amount due (that is there are no cash settled “top-off” or “make whole” provisions).

This condition is met as there are no required cash payments to Invus.

(6) The contract requires net-cash settlement only in specific circumstances in which holders of shares underlying the contract also would receive cash in exchange for their shares.

This condition is met as there are no provisions in the securities purchase agreement which would require net-cash settlement.

(7) There are no provisions in the contract that indicate that the counterparty has rights that rank higher than those of a shareholder of the stock underlying the contract.

This condition is met as there are no provisions in the securities purchase agreement that allow for rights ranking higher than a common stockholder.

(8) There is no requirement in the contract to post collateral at any point for any reason.

This condition is met as there is no requirement in the securities purchase agreement to post collateral at any point for any reason.

Based on the above analysis, we believe that it is appropriate to classify any rights offering transaction under the securities purchase agreement as an equity transaction.

To clarify the accounting for any rights offering initiated by Invus, we propose to include in our disclosure in future filings a statement that we have determined that any rights offerings should be treated as equity instruments in accordance

with EITF 00-19, and accordingly has not recorded a liability for the future settlement of any rights offerings.

As requested by the staff, we are providing the following acknowledgements:

- we are 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
- we 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.

If you have any further questions or require additional information, please do not hesitate to contact me at (281) 863-3321.

Very truly yours,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
Executive Vice President and
General Counsel

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

Appendix A

Lexicon has derived substantially all of its revenues from drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, government grants and contracts, technology licenses, subscriptions to its databases and compound library sales.

Drug Discovery Alliances

Lexicon has entered into the following alliances for the discovery and development of therapeutics based on its *in vivo* drug target discovery efforts:

Bristol-Myers Squibb Company: Lexicon established an alliance with Bristol-Myers Squibb in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. Lexicon initiated the alliance with a number of drug discovery programs at various stages of development and is continuing to use its gene knockout technology to identify additional drug targets with promise in the neuroscience field. For those targets that are selected for the alliance, Lexicon and Bristol-Myers Squibb are working together, on an exclusive basis, to identify, characterize and carry out the preclinical development of small molecule drugs, and will share equally both in the costs and in the work attributable to those efforts. As drugs resulting from the collaboration enter clinical trials, Bristol-Myers Squibb will have the first option to assume full responsibility for clinical development and commercialization.

Lexicon received an upfront payment of $36.0 million and research funding of $30.0 million in the initial three years of the agreement , or the target function discovery term. This funding was in consideration for access to Lexicon's technology and infrastructure and for Lexicon's production and specified phenotypic analysis of knockout mice in support of the target function discovery portion of the alliance. Bristol-Myers Squibb extended the target discovery term of the alliance in May 2006 for an additional two years in exchange for $20.0 million in additional research funding over the two year extension, which commenced in January 2007. This additional funding is in consideration for additional research and phenotypic analysis of knockout mice which supplements the phenotypic analysis conducted in the initial target function discovery term. Lexicon may receive additional cash payments for exceeding specified research productivity levels. Lexicon will also receive clinical and regulatory milestone payments for each drug target for which Bristol-Myers Squibb develops a drug under the alliance. Lexicon will earn royalties on sales of drugs commercialized by Bristol-Myers Squibb. The party with responsibility for the clinical development and commercialization of drugs resulting from the alliance will bear the costs of those efforts. The original upfront payment of $36.0 million and research funding of $30.0 million was recognized over the initial estimated period of service of three years. The additional research funding of $20.0 million is being recognized over the two additional years subject to the extension, beginning in January 2007.

The upfront payment of $36.0 million was not related to a deliverable with standalone value at inception, and Lexicon accounted for the entire agreement with Bristol-Myers Squibb as a single unit of accounting. Milestone payments received are in consideration for additional performance measures. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $xx million, $21.8 million and $21.8 million for the years ended December 31, 2007, 2006 and 2005, respectively.

Genentech, Inc. Lexicon established an alliance with Genentech in December 2002 to discover novel therapeutic proteins and antibody targets. Under the original alliance agreement, Lexicon used its target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Lexicon received an upfront payment of $9.0 million and funding under a $4.0 million loan in 2002. The terms of the loan are discussed in Note 8. In addition, Lexicon received $24.0 million in performance payments for its work in the collaboration as it was completed. The original upfront payment of $9.0 million was recognized over the initial estimated period of service of three years, which was subsequently extended to three and one-half years.

In November 2005, Lexicon and Genentech negotiated a new agreement expanding the alliance to include additional research, as well as the development and commercialization of new biotherapeutic drugs. Lexicon will receive a total of $25.0 million in upfront and milestone payments and research funding for the three-year advanced research portion of the expanded alliance. In the expanded alliance, Lexicon is conducting advanced research on a broad subset of targets validated in the original collaboration using Lexicon's proprietary gene knockout technology. The upfront payment under the new agreement is being recognized over the estimated period of service of three years.

Lexicon may develop and commercialize drugs for up to six of the targets included in the alliance. Genentech retains an option on the potential development and commercialization of these drugs under a cost and profit sharing arrangement, with Lexicon having certain conditional rights to co-promote drugs on a worldwide basis. Genentech is entitled to receive milestone payments in the event of regulatory approval and royalties on net sales of products commercialized by Lexicon outside of a cost and profit sharing arrangement. Lexicon will receive payments from Genentech upon achievement of milestones related to the development and regulatory approval of certain drugs resulting from the alliance that are developed and commercialized by Genentech. Lexicon is also entitled to receive royalties on net sales of these products, provided they are not included in a cost and profit sharing arrangement. Lexicon retains non-exclusive rights for the development and commercialization of small molecule drugs addressing the targets included in the alliance.

The upfront payment was not related to a deliverable with standalone value at inception and Lexicon accounted for the entire agreement with Genentech as a single unit of accounting. Milestone payments received are in consideration for additional performance measures. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones. During the year ended December 31, 2005, Lexicon received a nonrefundable milestone payment for the delivery of data from specified phenotypic analyses. Revenue recognized under this agreement was $xx million, $5.0 million and $22.6 million for the years ended December 31, 2007, 2006 and 2005, respectively.

N.V. Organon. Lexicon established an alliance with Organon in May 2005 to jointly discover, develop and commercialize novel biotherapeutic drugs. In the alliance, Lexicon is creating and analyzing knockout mice for up to 300 genes selected by the parties that encode secreted proteins or potential antibody targets, including two of Lexicon's existing drug discovery programs. The parties will jointly select targets for further research and development and will equally share costs and responsibility for research, preclinical and clinical activities. The parties will jointly determine the manner in which alliance products will be commercialized and will equally benefit from product revenue. If fewer than five development candidates are designated under the alliance, Lexicon's share of costs and product revenue will be proportionally reduced. Lexicon will receive a milestone payment for each development candidate in excess of five. Either party

may decline to participate in further research or development efforts with respect to an alliance product, in which case such party will receive royalty payments on sales of such alliance product rather than sharing in revenue. Organon will have principal responsibility for manufacturing biotherapeutic products resulting from the alliance for use in clinical trials and for worldwide sales.

Lexicon received an upfront payment of $22.5 million from Organon in exchange for access to Lexicon's drug target discovery capabilities and the exclusive right to co-develop biotherapeutic drugs for the 300 genes selected for the alliance. Organon will also provide Lexicon with annual research funding totaling up to $50.0 million for its 50% share of the alliance's costs during this same period.

The upfront payment of $22.5 million was not related to a deliverable with standalone value at inception, and Lexicon accounted for the entire agreement with Organon as a single unit of accounting. Revenue from the upfront payment is recognized on a straight-line basis over the four-year period that Lexicon expects to perform its obligations under the target function discovery portion of the alliance. Revenue from the research funding fees is recognized as Lexicon performs its obligations under the target function discovery portion of the alliance, reflecting the gross amount billed to Organon on the basis of shared costs during the period. Milestone payments received are in consideration for additional performance measures. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $xx million, $15.5 million and $11.8 million for the years ended December 31, 2007, 2006 and 2005, respectively.

Takeda Pharmaceutical Company Limited. Lexicon established an alliance with Takeda in July 2004 to discover new drugs for the treatment of high blood pressure. In the collaboration, Lexicon used its gene knockout technology to identify drug targets that control blood pressure. Takeda will be responsible for the screening, medicinal chemistry, preclinical and clinical development and commercialization of drugs directed against targets selected for the alliance, and will bear all related costs. Lexicon received an upfront payment of $12.0 million from Takeda for the initial, three-year term of the agreement. This payment was in consideration for access to Lexicon's technology and infrastructure during the target discovery portion of the alliance. Takeda will make research milestone payments to Lexicon for each target selected for therapeutic development. In addition, Takeda will make clinical development and product launch milestone payments to Lexicon for each product commercialized from the collaboration. Lexicon will also earn royalties on sales of drugs commercialized by Takeda.

The upfront payment of $12.0 million was not related to a deliverable with standalone value at inception, and Lexicon accounted for the entire agreement with Takeda as a single unit of accounting. Revenue was recognized from the upfront payment on a straight-line basis over the three-year period Lexicon expected to perform its obligations under the agreement. Milestone payments received are in consideration for additional performance measures. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $xx million, $9.0 million and $4.0 million for the years ended December 31, 2007, 2006 and 2005, respectively.