

Via Facsimile and U.S. Mail
Mail Stop 4720

November 30, 2009

Dr. Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer
Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands
San Diego, CA 92121

Re: Lexicon Pharmaceuticals, Inc.
Form 10-K for the Year Ended December 31, 2008
Filed March 6, 2009
File No. 000-30111
DEF14A
Filed March 13, 2009
File No. 000-30111

Dear Dr. Sands:

We have reviewed your filings and have the following comments.

In our comments, we ask you to provide us with information to better understand your disclosure. Where it requests you to revise disclosure, the information you provide should show us what the revised disclosure will look like and identify the annual or quarterly filing, as applicable, in which you intend to first include it. If you do not believe that revised disclosure is necessary, explain the reason in your response. After reviewing the information provided, we may raise additional comments and/or request that you amend your filing.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comment or on any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

FORM 10-K

Item 1. BUSINESS

Drug Discovery and Development Collaborations, page 5

1. With respect to each drug discovery and collaboration agreement referenced in this section, please disclose the upfront payments and research funding received to date, the aggregate potential milestone payments and the potential range of royalty payments (for example, “low-teens” or “high-teens”). We note that you have included some information regarding the upfront payments and research funding amounts with respect to these agreements in the notes to the financial statements but this is material information which should be consolidated in the Business section.

Patents and Proprietary Rights, page 9

2. Please revise your disclosure to include a discussion of all material patents or groups of patents and indicate whether such patents are held directly by you or licensed from a third party. For each material patent, the disclosure should include a discussion of the technologies that relate to such patent, the jurisdiction in which the patent is granted and the expiration date.
3. We note that you license your principal gene targeting technologies from GenPharm International, Inc. We further note the disclosure on page 28 of your filing indicating that there is a dispute with the University of Utah Research Foundation regarding your payment of royalties under this agreement. Please revise your disclosure to include the material terms of the licensing agreement with GenPharm International, Inc. and file the agreement as an exhibit or provide us with an analysis setting forth your determination that this agreement is not material to your business.

DEF14A

EXECUTIVE AND DIRECTOR COMPENSATION

Compensation Discussion and Analysis, page 24

4. We note your disclosure that payment of cash bonuses is determined by taking into account both pre-determined corporate and individual goals. While you have disclosed the corporate goals, whether or not those goals were achieved and how the achievement was tied to the level of bonus paid, you have not provided similar disclosure with respect to individual goals. Accordingly, please provide us with sample disclosure for inclusion in your next annual report or proxy statement which sets forth the individual goals for each executive officer, whether such goals were achieved and how the achievement of such goals was tied to the amount of bonus paid.

* * * *

Please respond to these comments within 10 business days or tell us when you will provide us with a response. Please furnish a cover letter that keys your response to our comment and provide any requested information. Detailed letters greatly facilitate our review. Please file your letter on EDGAR under the form type label CORRESP.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Exchange Act of 1934 and that they have provided all information investors require for an informed investment decision. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

In connection with responding to our comments, please provide, in your letter, a statement from the company acknowledging that:

- 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.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in our review of your filing or in response to our comment on your filing.

Please contact Nandini Acharya, Staff Attorney at (202) 551-3495 or me at (202) 551-3715 with any questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director