DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125349/0

BLA APPROVAL – ANIMAL EFFICACY

Human Genome Sciences, Inc.
Attention: Sally Bolmer, PhD, RAC
Senior Vice President, Development and Regulatory Affairs
14200 Shady Grove Road
Rockville, MD 20850

Dear Dr. Bolmer:

Please refer to your Biologics License Application (BLA) dated June 15, 2012, received June 15, 2012, submitted under section 351 of the Public Health Service Act for raxibacumab.

We acknowledge receipt of your amendments dated August 2, 29 and 30 (2), September 4, 5 and 17, October 1, 3, 4 and 31, and November 6, 13 and 20, December 7 (2) and 12, 2012.

The June 15, 2012, submission constituted a complete response to our November 14, 2009, action letter.

We have approved your BLA for raxibacumab effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, raxibacumab under your existing Department of Health and Human Services U.S. License No. 1820. Raxibacumab is indicated for treatment of inhalational anthrax due to *Bacillus anthracis* in combination with appropriate antibacterial drugs, and for prophylaxis of inhalational anthrax when alternative therapies are not available or are not appropriate.

Under this license, you are approved to manufacture raxibacumab drug substance at Human Genome Sciences, Inc. in Rockville, Maryland. The final formulated product will be manufactured, filled, labeled, and packaged at (b) (4). You may label your product with the proprietary name raxibacumab and will market it in 1700 mg vials.

The dating period for raxibacumab shall be 60 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of (b) (4) of the formulated drug product. The dating period for your drug substance shall be (b) (4) from the date of manufacture when stored at 2-8°C. Protocol No. M2109001 (Version 3.0) is approved as the stability protocol for commercial final drug product (FDP). Protocol No. M2109002 (Version 4.0) is approved as the stability protocol for commercial bulk drug substance (BDS).

You are not currently required to submit samples of future lots of raxibacumab to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2.

We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of raxibacumab, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

We are approving this application, under the provisions of 21 CFR 601, Subpart H (Approval of Biological Products When Human Efficacy Studies Are Not Ethical or Feasible), for use as recommended in the enclosed agreed-upon labeling text and required patient labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced animal efficacy regulations.

We note that your December 12, 2012, submission includes final printed labeling (FPL) for your package insert and patient package insert. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert and text for the patient package insert. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA 125349**."

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 7, 2012, submission containing final printed carton and container labels.

SUBPART H APPROVAL REQUIREMENTS

Approvals under 21 CFR Part 601, Subpart H (Approval of Biological Product When Human Efficacy Studies Are Not Ethical or Feasible) are subject to three requirements:

1. *Approval with restrictions to ensure safe use.* This subsection permits the Agency to require postmarketing restrictions as are needed to ensure safe use of the drug product,

commensurate with the specific safety concerns presented by the drug product. We have concluded that raxibacumab can be safely used without restrictions on distribution or use.

2. *Information to be provided to patient recipients.* This subsection requires applicants to prepare labeling to be provided to patient recipients for drug products approved under this subpart. We have concluded that the FDA-Approved Patient Labeling for raxibacumab meets the requirements of this subsection. We remind you that the Patient Labeling must be available with the product to be provided, when possible, prior to administration or dispensing of the drug product for the use approved under this subpart.

3. *Postmarketing Studies.* This subsection requires you to conduct postmarketing studies, such as field studies, to verify and describe the biological product's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. We refer to your letter dated December 7, 2012, stating that you agree to conduct a field study to evaluate the efficacy and safety of raxibacumab use for *Bacillus anthracis* in the United States and to submit a protocol on or before June 13, 2013.

POSTMARKETING REQUIREMENTS

We remind you of your postmarketing requirement specified in your submission dated December 7, 2012. The requirement is listed below.

1. Conduct a field study to evaluate the efficacy, pharmacokinetics, and safety of raxibacumab use for *Bacillus anthracis* in the United States.

Final Protocol Submission:	June 15, 2013
Study/Trial Completion:	To be determined should an event occur
Final Report Submission:	To be determined should an event occur

Submit your clinical protocol to IND 011069. Submit final reports to the BLA as supplemental applications. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirements**."

We remind you of your postmarketing commitments specified in your submission dated December 17, 2012. These requirements, along with any agreed upon completion dates, is listed below.

POSTMARKETING COMMITMENT FOR THE PROPHYLAXIS INDICATION (SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B)

2. Conduct a Phase 4 study to evaluate the effect of raxibacumab on immunogenicity of anthrax vaccine.

Final Protocol Submission:	November 1, 2014
Study/Trial Completion:	October 1, 2016

Final Report Submission: October 1, 2017

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

3. Perform spiking studies of undiluted formulated bulk drug substance during which the samples are assayed initially and at periodic time points after spiking, simulating worst-case manufacturing conditions (hold time and temperature) to evaluate whether endotoxin masking occurs over time in undiluted samples.

   Final Protocol Submission: August 29, 2013
   Study/Trial Completion: November 30, 2013
   Final Report Submission: December 15, 2013

4. Develop and validate a new (b) (4) assay that has improved sensitivity and capability to detect a greater range of potentia (b) (4) contaminants compared to the current assay and to provide this information as a prior approval supplement to the BLA by June 30, 2015.

   Final Protocol Submission: December 31, 2014
   Study/Trial Completion: April 30, 2015
   Final Report Submission: June 30, 2015

Submit clinical protocols to your IND 011069 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

This product is appropriately labeled for use in all relevant pediatric populations. Therefore, no additional pediatric studies are needed at this time.

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4206
Silver Spring, MD 20903

PROMOTIONAL MATERIALS

Under 21 CFR 601.94, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of

Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 601.94, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved package insert (PI)/Medication Guide/patient PI (as applicable).

Send each submission directly to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotions (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST-ACTION FEEDBACK MEETING

New molecular entities and new biologics qualify for a post-action feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Jane A. Dean, RN, MSN, Regulatory Health Project Manager, at (301) 796-1202.

Sincerely,

{See appended electronic signature page}

Edward Cox, MD, MPH
Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

EDWARD M COX
12/14/2012