DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125509

BLA APPROVAL - ANIMAL EFFICACY

Elusys Therapeutics, Inc.
Attention: Robin L. Conrad
Vice President, Regulatory Affairs
25 Riverside Drive, Unit 1
Pine Brook, NJ 07058

Dear Ms. Conrad:

Please refer to your Biologics License Application (BLA) dated March 20, 2015, received March 20, 2015, submitted under section 351(a) of the Public Health Service Act for Anthim (obiltoxaximab) injection, 600 mg/6 mL.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 1907 to Elusys Therapeutics, Inc., Pine Brook, New Jersey, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Anthim (obiltoxaximab). Anthim is indicated for the treatment of adult and pediatric patients with 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.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture obiltoxaximab drug substance at (b) (4) (b) (4) The final formulated product will be manufactured, filled, labeled, and packaged at (b) (4)
You may label your product with the proprietary name, Anthim, and market it in a single-dose vial containing 600 mg/6 mL injection.

DATING PERIOD

The dating period for Anthim finished drug product shall be 18 months from the date of manufacture when stored at 2°C to 8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for Anthim drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C to (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Anthim 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 Anthim, 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, as amended, 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.

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 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be 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.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your March 2, 2016, submission containing final printed carton and container labels.

ADVISORY COMMITTEE

Your application for Anthim (obiltoxaximab) was not referred to an FDA Advisory Committee because this drug is not the first monoclonal antibody directed against PA that has been approved and the animal models of infection utilized are similar to a previously approved drug. There were no specific questions regarding efficacy that warranted Advisory Committee input and the drug's safety profile can be adequately addressed in the product labeling.

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 Anthim (obiltoxaximab) can be safely used without restrictions on distribution or use, as the risk of hypersensitivity reactions, including anaphylaxis, and need to administer Anthim (obiltoxaximab) in medically monitored settings are adequately described in labeling.

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 Anthim (obiltoxaximab) 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 note your agreement, in a letter dated February 26, 2016, to conduct a field study to evaluate the safety and efficacy of Anthim (obiltoxaximab) for the treatment of inhalational anthrax, and to submit a protocol on or before November 30, 2016.

We remind you of your postmarketing requirement specified in your submission dated February 26, 2016. This requirement, along with any agreed upon completion dates, is listed below.

3050-1 Conduct a Field Study to evaluate the clinical response, pharmacokinetics, and safety profile of Anthim (obiltoxaximab) when used in the treatment of suspected or confirmed cases of inhalational anthrax due to *B. anthracis* in the United States.

Final Protocol Submission:	11/30/16
Study/Trial Completion:	To be determined should an event occur
Final Report Submission:	To be determined should an event occur

Submit final reports to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirements**."

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.

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

We remind you of your postmarketing commitments:

3050-2 Conduct a study to qualify the bioburden test for the primary recovery samples using the increased sample volume (10 mL).

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion:	08/31/2016
Final Report Submission:	11/30/2016

3050-3 Re-evaluate and establish final (b) (4) bioburden and endotoxin limits for all the sampling points.

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion:	01/31/2019
Final Report Submission:	03/31/2019

3050-4 Develop reduced and non-reduced SDS-based assays capable of providing quantitative data for the evaluation of size related product impurities and implement these assays in the release and stability program for obiltoxaximab drug substance and drug product after sufficient data have been acquired to set appropriate acceptance criteria. Provide the analytical procedure, validation report, proposed acceptance criteria, and data used to set the proposed acceptance criteria.

The timetable you submitted on March 4, 2016, states that you will conduct this study according to the following schedule:

Final Report Submission for Drug Substance (DS): 03/2019
Final Report Submission for Drug Product (DP): To be determined based on when data from 20 lots of DP becomes available or 03/2021, whichever comes first.

3050-5 Conduct a validation study to confirm the shipper is suitable for maintaining critical quality attributes during shipping of obiltoxaximab drug products. This should include consideration for worst case shipping routes. The study will include monitoring of temperature during the shipment, as well as testing of pre- and post-shipping samples of obiltoxaximab drug product quality (e.g., appearance, protein concentration, purity by SEC-HPLC, reduced and non-reduced SDS-PAGE, icIEF, visible and sub-visible particulates and potency).

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion: 04/2016
Final Report Submission: 05/2016

3050-6 Conduct a study to confirm compatibility of the drug product with syringe infusion components used for administration. These studies will include monitoring samples for protein concentration, purity by SEC-HPLC, icIEF, visible and sub-visible particulates and potency.

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion: 05/2016
Final Report Submission: 06/2016

3050-7 Conduct a study to support the worst case cumulative hold times in obiltoxaximab drug substance manufacturing process to demonstrate that the worst case cumulative hold time will not adversely affect the product quality of obiltoxaximab drug substance. These data are expected to demonstrate that there is no adverse impact to product quality when the manufacturing of a drug substance batch involves (b) (4)

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion: 01/2018
Final Report Submission: 03/2018

3050-8 Re-evaluate obiltoxaximab drug substance lot release and stability specifications after 20 lots have been manufactured using the commercial manufacturing process. Provide the final report, the corresponding data, the analysis, and the statistical plan used to evaluate the specifications.

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion: 01/2019
Final Report Submission: 03/2019

3050-9 Re-evaluate obiltoxaximab drug product lot release and stability specifications after 20 lots have been manufactured using the commercial manufacturing process. Provide the final report, the corresponding data, the analysis, and the statistical plan used to evaluate the specifications.

The timetable you submitted on March 4, 2016, states that you will conduct this study according to the following schedule:

Final Report Submission: To be determined based on when data from 20 lots of DP becomes available or 03/2021, whichever comes first.

3050-10 Establish a permanent control limit for (b) (4) of production (b) (4) and (b) (4) of (b) (4) unit operations after (b) (4) control points have been analyzed. The (b) (4) limits and supportive data should be submitted to the BLA.

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Study Completion: 01/2019
Final Report Submission: 03/2019

3050-11 Conduct drug substance specific leachable and extractable studies (b) (4) (b) (4) (b) (4) The drug substance manufacturing processes will be optimized, as needed, based on results.

The timetable you submitted on February 26, 2016, states that you will conduct this study according to the following schedule:

Final Report Submission: 04/2016

Submit clinical protocols to your IND 012285 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**."

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 Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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

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 APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval 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.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ('the Program'). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

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 M. 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
03/18/2016