DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 761066

BLA APPROVAL

Samsung Bioepis Co., Ltd.
c/o Biologics Consulting Group, Inc.
1555 King Street, Suite 300
Alexandria, VA 22314

Attention: Norman W. Baylor, PhD
President & CEO, Biologics Consulting Group, Inc.

Dear Dr. Baylor:

Please refer to your Biologics License Application (BLA) dated May 25, 2017, received May 25, 2017, and your amendments, submitted under section 351(k) of the Public Health Service Act for Eticovo (etanercept-ykro) injection 25 mg/0.5 mL and 50 mg/mL.

We acknowledge receipt of your resubmission dated October 25, 2018, which constituted a complete response to our March 23, 2018, action letter.

LICENSING

We have approved your BLA for Eticovo (etanercept-ykro) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Eticovo under your existing Department of Health and Human Services U.S. License No. 2046. Eticovo is indicated for:

- Rheumatoid Arthritis
- Polyarticular Juvenile Idiopathic Arthritis in patients aged 2 years or older
- Psoriatic Arthritis (PsA)
- Ankylosing Spondylitis (AS)
- Plaque Psoriasis (PsO) in patients 4 years or older

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Eticovo drug substance (b) (4) (b) (4). The final formulated drug product will be manufactured and filled (b) (4) (b) (4), and labeled and packaged (b) (4) (b) (4). You may label your product with the proprietary name, Eticovo, and market it in single-dose prefilled syringes containing 25 mg/0.5 mL or 50 mg/mL injection.

DATING PERIOD

The dating period for Eticovo shall be 36 months from the date of manufacture when stored at 5±3°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored (b) (4).

We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating period of your drug substance **and** drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Eticovo and each kit component 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 Eticovo, 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.

APPROVAL AND LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 Prescribing Information, Instructions for Use, and Medication Guide). 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 CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761066**." Approval of this submission by FDA is not required before the labeling is used.

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

We remind you of your postmarketing commitments:

3608-1 Implement (b) (4) monitoring during sterile filtration of the Eticovo (etanercept-ykro) drug product (b) (4).

The timetable you submitted on April 10, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/31/2020

3608-2 Implement (b) (4) monitoring during sterile filtration of the Eticovo (etanercept-ykro) drug product (b) (4).

The timetable you submitted on April 10, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/31/2020

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 (which includes new salts and new fixed combinations), 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.

We are waiving the pediatric studies requirement for the following indications:

- Psoriatic Arthritis because studies are impossible or highly impractical due to the difficulty of making the diagnosis in the pediatric population.

- Ankylosing Spondylitis because studies are impossible or highly impractical due to the difficulty of making the diagnosis in the pediatric population.

- Polyarticular Juvenile Idiopathic Arthritis (pJIA) for ages 0 to 1 year 11 months because studies are impossible or highly impractical due to the rarity of the disease in this age group.

- Pediatric Plaque Psoriasis for ages 0 to 3 years 11 months because studies are impossible or highly impractical due to the rarity of the disease in this age group.

We are deferring the required pediatric assessment for pJIA and plaque psoriasis pediatric patients <63 kg. See Deferred Pediatric Assessment below.

Deferred Pediatric Assessments

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

3608-3 Develop a presentation that can be used to accurately administer Eticovo (etanercept-ykro) to pediatric patients who weigh less than 63 kg.

The timetable you submitted on April 17, 2019 states that you will conduct this study according to the following schedule:

Final Report Submission: 09/30/23

Submit the study to an IND for this presentation with a cross-reference letter to this BLA, if needed.

Reports of this required pediatric postmarketing study must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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

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 4207
Silver Spring, MD 20903

If you have any questions, call Brandi Wheeler, Regulatory Project Manager, at (301)796-4495.

Sincerely,

{See appended electronic signature page}

Sally Seymour, MD
Acting Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

NIKOLAY P NIKOLOV
04/25/2019 02:58:52 PM
Signed under the authority delegated by Dr. Sally Seymour, Acting Division Director, DPARP.