DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125433/0

**BLA APPROVAL**

Janssen Biotech, Inc.
Welsh & McKean Roads
P.O. Box 776
Spring House, PA 19477

Attention: Salvatore Morello
Director, Global Regulatory Affairs

Dear Mr. Morello:

Please refer to your Biologics License Application (BLA) dated and received September 18, 2012, submitted under section 351(a) of the Public Health Service Act for Simponi Aria (golimumab), 50 mg/4 mL vial.

We acknowledge receipt of your amendments dated October 19, November 8 and 13, and December 6, 14, and 21, 2012, and January 2 and 17, February 20, March 1, April 16, May 2, 7 (two), 10 (two), and 28, June 3, 5, 10, 14, 26, and 27, and July 1, 9, 12, and 17, 2013.

## LICENSING

We have approved your BLA for Simponi Aria (golimumab) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Simponi Aria under your existing Department of Health and Human Services U.S. License No. 1864. Simponi Aria is indicated for treatment of moderate to severely active Rheumatoid Arthritis (RA) in adults in combination with methotrexate.

## MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture golimumab (for infusion) drug substance at Janssen Biologics/Barnahely, Ringaskiddy, Co. in Cork, Ireland, and Janssen Biologics B.V. in Leiden, The Netherlands. The final formulated product will be (b) (4), labeled, and packaged at Cilag AG, Schaffhausen, Switzerland. The drug product may also be labeled and packaged at AndersonBrecon, Inc. at Rockford, Illinois, USA. You may label your product with the proprietary name, Simponi Aria, and will market it in single use sterile solution of 50 mg/4 mL vials.

## DATING PERIOD

The dating period for Simponi Aria shall be 24 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as (b) (4)

Any changes in the manufacturing, testing, packaging, or labeling of Simponi Aria, 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 & 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.

## 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. Content of labeling must be identical to the enclosed labeling (text for the package insert 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 IMMEDIATE CONTAINER LABELS

We acknowledge your July 12, 2013, submission containing final printed carton and container labels.

## ADVISORY COMMITTEE

Your application for golimumab (for intravenous infusion) was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues in the intended population.

## 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.

We are waiving the pediatric study requirement for neonates and infants up to 1 year and 11 months of age years because necessary studies are impossible or highly impracticable. This is because juvenile idiopathic arthritis (JIA) does not present at birth and a small number of children in this age group are diagnosed with JIA.

We are deferring submission of your pediatric study for children 2 years of age to 17 years and 11 months for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

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)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

PMR #1: To conduct a trial that will evaluate the safety, efficacy, PK/PD and immunogenicity of IV golimumab in pediatric patients between the ages 2 to 17 years and 11 months with active juvenile idiopathic arthritis (JIA) despite standard therapy with methotrexate.

The timetable you submitted on July 9, 2013, states that you will conduct this trial according to the following schedule:

| | |
|---|---|
| Final Protocol Submission: | 12/2013 |
| Trial Completion: | 06/2018 |
| Final Report Submission: | 12/2018 |

Submit the protocol(s) to your IND 9925, with a cross-reference letter to this BLA.

Report 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 this study. When submitting the report, 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.

We remind you of your postmarketing commitments:

PMC #2: Increase in-process control sample size to (b) (4) and adjust acceptance criteria to (b) (4) In addition, implement the new bioburden sample size action and alert limits after production of 10 batches. The Final Report Submission should include the new in-process limits.

The timetable you submitted on July 9, 2013, states that you will conduct this study according to the following schedule:

Final Report Submission: 07/2014

PMC #3: [redacted] (b) (4)

The timetable you submitted on July 9, 2013, states that you will conduct this study according to the following schedule:

Final Report Submission: 07/2014

PMC #4: Perform the Rabbit Pyrogen Test on two batches of Golimumab FVP (IV) DP. Submit the results as a CBE-0 supplement.

The timetable you submitted on July 9, 2013, states that you will conduct this study according to the following schedule:

Final Report Submission: 09/2013

PMC #5: Perform LAL spiking studies in undiluted golimumab FVP (IV) DP samples and test the samples after different hold times.

The timetable you submitted on July 9, 2013, states that you will conduct this study according to the following schedule:

Final Report Submission: 07/2014

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 study 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

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 package insert 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. For instruction on completing the Form FDA 2253, see page 2 of the Form. 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). 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.

If you have any questions, call Christine Chung, Regulatory Project Manager, at (301) 796-3420.

Sincerely,

*{See appended electronic signature page}*

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

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

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/s/

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SARAH K YIM
07/18/2013
Signing for Badrul Chowdhury, M.D., Ph.D.