CLINICAL PHARMACOLOGY MEMORANDUM

BLA	125-289 Serials 353, 357, and 360
Submission Dates	August 22, 2016; October 14, 2016, and November 3, 2017
Brand Name	SIMPONI
Generic Name	Golimumab
Reviewer	S.W. Johnny Lau, R.Ph., Ph.D.
Team Leader	Anshu Marathe, Ph.D.
OCP Division	Clinical Pharmacology 2
OND Division	Pulmonary, Allergy, and Rheumatology Products
Sponsor	Janssen Biotech, Inc.
Available Dosage Form; Strengths	Solution for injection; 100 mg/mL and 50 mg/0.5 mL
Previously Approved Indications	Treatment of moderately to severe rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), moderate to severe ulcerative colitis (UC) in adults

Executive Summary

Golimumab is a human tumor necrosis factor alpha blocker indicated for the treatment of adult patients with:

- Moderately to severely active RA in combination with methotrexate (MTX)
- Active PsA alone, or in combination with MTX
- Active AS
- Moderate to severe UC

In this submission, the sponsor conducted Study CNTO148JIA3001 titled "A Multicenter, Double-Blind, Randomized-Withdrawal Trial of Subcutaneous Golimumab, a Human Anti-TNFα Antibody, in Pediatric Patients with Active Polyarticular Course Juvenile Idiopathic Arthritis (JIA) Despite Methotrexate Therapy" under the Pediatric Research Equity Act to fulfill the PMR #1 that was issued with BLA 125-289's approval letter dated April 24, 2009 for subcutaneously (SC) administered SIMPONI. The required study is listed below:

1. Assess the pharmacokinetics, safety, immunogenicity, and efficacy of golimumab in pediatric patients 2 to 16 years of age with active polyarticular juvenile idiopathic arthritis (pJIA).

The primary objective of Study CNTO148JIA3001 was to assess the clinical efficacy of SC administration of golimumab in pediatric patients (ages 2 to less than 18 years) with pJIA manifested by ≥5 joints with active arthritis despite MTX therapy for ≥3 months. The secondary objectives of this study were to evaluate golimumab in pediatric patients with pJIA with respect to safety, physical function, health-related quality of life, disease activity status over time, pharmacokinetics (PK), immunogenicity, and pharmacodynamics. The primary endpoint (the proportion of patients who were ACR Ped 30 responders at Week 16 and did not experience a flare of disease between Week 16 and Week 48) and major secondary endpoints were assessed at Week 48.

All patients received SC 30 mg golimumab/m^2 (maximum 50 mg) every 4 weeks plus MTX in the active treatment portion of the study from Week 0 through Week 12, followed by randomization of ACR Ped 30

responders at Week 16 to receive placebo + MTX or golimumab + MTX. Patients received commercial MTX weekly at the same numerical dose as what they were receiving at the time of study entry. Patients also received the US-licensed and marketed golimumab 100 mg/mL solution in this study. The sponsor collected serum samples at Weeks 4, 8, 12, 16, 20, 24, and 48 as well as to final database lock for the determination of golimumab concentration.

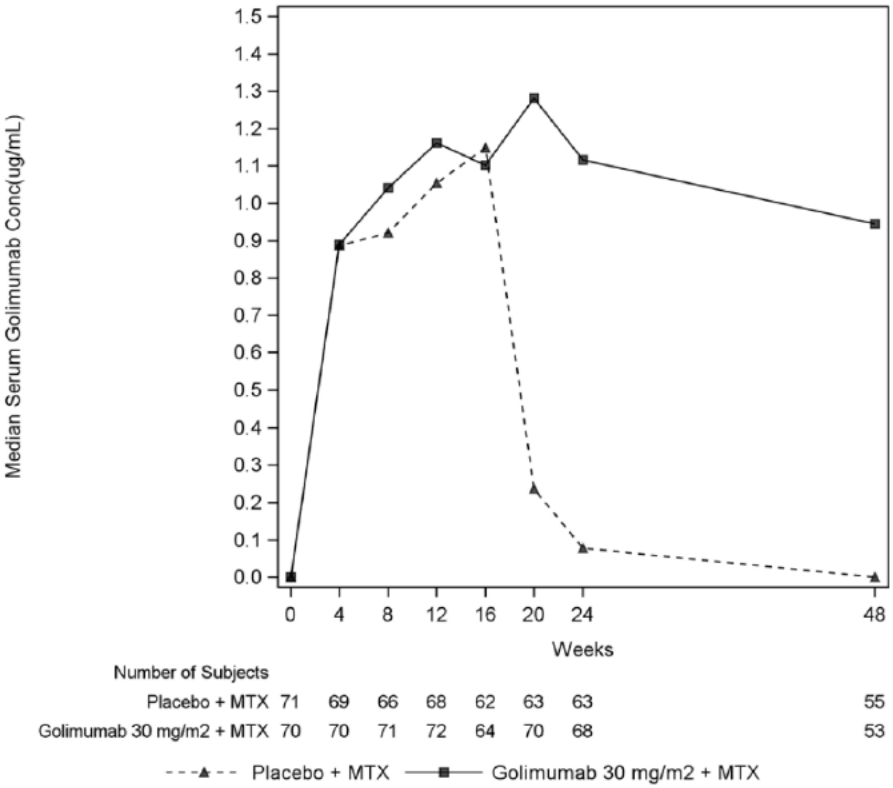
Following the analyses of data through Week 48, the Sponsor decided [redacted] (b) (4)

Later, the Sponsor sought FDA's feedback on the adequacy of the data from Study CNTO148JIA3001 to support an indication in pJIA via a Type C meeting. FDA issued a written feedback on December 17, 2015. Overall, FDA did not agree that the results from Study CNTO148JIA3001 would be sufficient to support an indication for SIMPONI in pJIA. Therefore, in this submission the Sponsor does not seek an indication for SIMPONI for patients with pJIA. The sponsor has updated Section 8.4 (Pediatric Use) of the SIMPONI label. There is no change in the label pertaining to Clinical Pharmacology. For the efficacy and safety findings from Study CNTO148JIA3001, refer to the Clinical Review. For descriptive summary of serum golimumab concentrations, see the following section.

Summary of Golimumab Exposure in pJIA

Figure 1 shows that all patients received golimumab up to the randomized withdrawal at Week 16 with comparable median trough serum golimumab concentrations at each visit between the 2 groups of patients who were subsequently randomized to placebo and 30 mg golimumab/m^2 at Week 16. Median trough serum golimumab concentrations were maintained for patients who continued on active treatment, and median trough serum golimumab concentrations dropped to low concentrations for patients who were randomized to placebo + MTX.

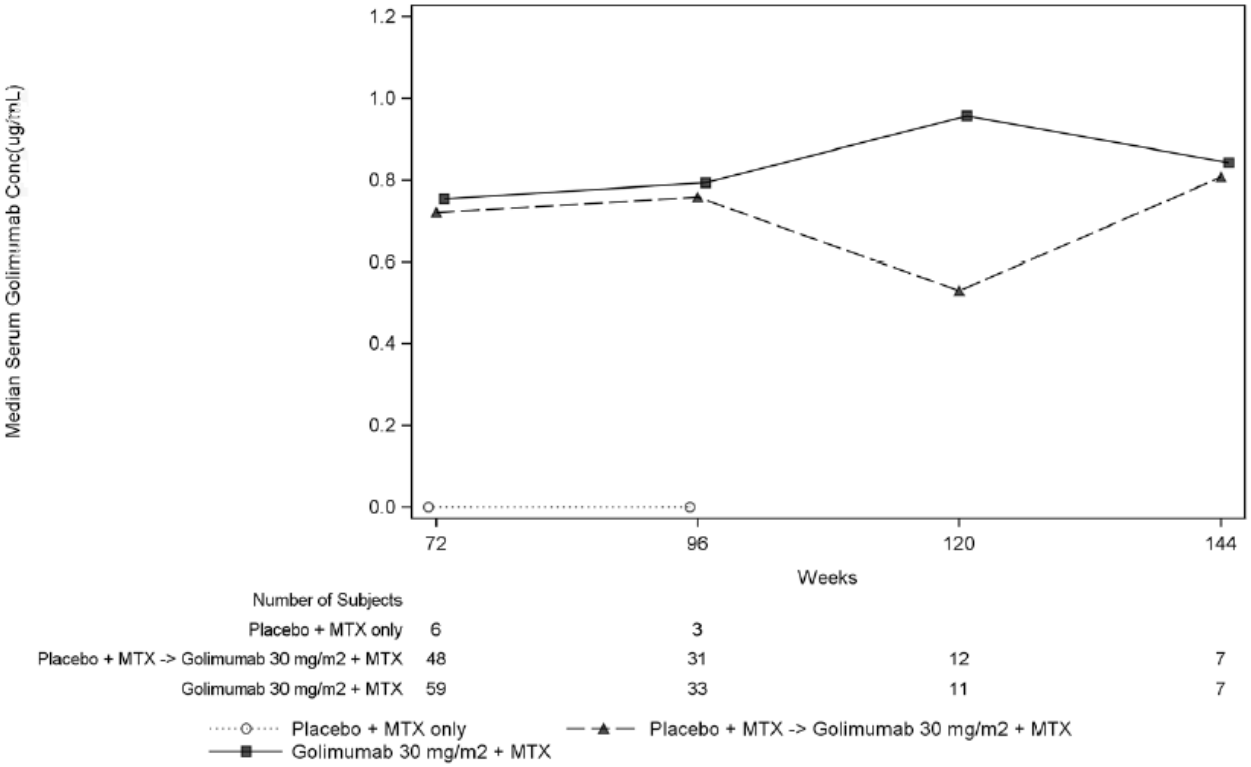
Figure 1. Median trough serum golimumab concentration (µg/mL) through Week 48; treated patients who were randomized at Week 16.



Source: Study CNTO148JIA3001's 48-Week study report Page 69/1344 submitted on December 10, 2015

Figure 2 shows that the median trough serum golimumab concentrations were maintained through the final database lock for patients who received SC 30 mg golimumab/m^2 every 4 weeks and continued on active treatment or were switched to active treatment from the placebo group.

Figure 2. Median trough serum golimumab concentration (µg/mL) after Week 48 through the final data base lock; treated patients who were randomized at Week 16.



Source: Study CNTO148JIA3001's final study report Page 46/791 submitted on August 22, 2016

The sponsor used the electrochemiluminescent immunoassay on a Meso Scale Discovery Platform to measure serum golimumab concentration. The validation of bioanalytical assay to measure golimumab in serum samples for Study CNTO148JIA3001 are reasonable as the following:

Bioanalytical Validation for Study CNTO148JIA3001	
Analyte	Golimumab
Matrix	Serum
Sample volume, µL	10
Lower limit of quantitation, µg/mL	0.03905 at 1:5 serum dilution
Validated assay range, µg/mL	0.03905 – 2.5 at 1:5 serum dilution
Assay precision (%CV)	
Inter-assay	2.6 – 5.47
Intra-assay	1.06 – 4.87
Assay accuracy (% bias)	-23.43 – 0.59
Storage stability demonstrated	-70°C for 5 years
Stability (freeze/thaw cycles)	Up to 8

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/s/

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05/18/2017

ANSHU MARATHE
05/18/2017