Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Arthritis Advisory Committee Meeting
July 13, 2016

Location: The FDA White Oak Campus, Building 31, The Great Room (Rm. 1503), White Oak Conference Center, Silver Spring, Maryland.

Topic: The committee discussed biologics license application 761042, for GP2015, a proposed biosimilar to Amgen Inc.'s ENBREL (etanercept) submitted by Sandoz, Inc. The proposed indications (uses) for this product are: (1) Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (in combination with methotrexate (MTX) or used alone); (2) reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 and older; (3) reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis (in combination with MTX in patients who do not respond adequately to MTX alone); (4) reducing signs and symptoms in patients with active ankylosing spondylitis; and (5) treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

These summary minutes for the July 13, 2016 meeting of the Arthritis Advisory Committee of the Food and Drug Administration were approved on August 24, 2016.

I certify that I attended the July 13, 2016 meeting of the Arthritis Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Moon Hee V. Choi, PharmD
Acting Designated Federal Officer, AAC

/s/
Daniel Solomon, MD, MPH
Acting Chairperson, AAC

Summary Minutes of the Arthritis Advisory Committee Meeting
July 13, 2016

The following is an internal report (which has not been reviewed) of the Arthritis Advisory Committee meeting held on July 13, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Pulmonary, Allergy, and Rheumatology Products and posted on the FDA website at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/ucm481975.htm.

All external requests for the meeting transcripts should be submitted to the CDER Freedom of Information Office.

The Arthritis Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on July 13, 2016, at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, The Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Sandoz, Inc. The meeting was called to order by Daniel Solomon, MD, MPH (Acting Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Acting Designated Federal Officer). There were approximately 175 people in attendance. There were 14 Open Public Hearing (OPH) presentations.

Issue: The committee discussed biologics license application 761042, for GP2015, a proposed biosimilar to Amgen Inc's ENBREL (etanercept) submitted by Sandoz, Inc. The proposed indications (uses) for this product are (1) Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA)((in combination with methotrexate (MTX) or used alone); (2) reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 and older; (3) reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis (in combination with MTX in patients who do not respond adequately to MTX alone); (4) reducing signs and symptoms in patients with active ankylosing spondylitis; (5) treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Attendance:

Arthritis Advisory Committee Members Present (Voting): Mara L. Becker, MD, MSCE; Jennifer Horonjeff, PhD (Consumer Representative); Beth L. Jonas, MD; Donald R. Miller, PharmD, FASHP; Andreas M. Reimold, MD

Arthritis Advisory Committee Members Not Present (Voting): Liron Caplan, MD, PhD; Jeffrey Curtis, MD, MPH; Veena K. Ranganath, MD, MS; Eric J. Tchetgen Tchetgen, BS, PhD; Therese M. Wolpaw, MD, MHPE

Arthritis Advisory Committee Members Not Present (Non-Voting): James B. Chung, MD, PhD

Temporary Members (Voting): Diane Aronson, BS in Ed (Patient Representative); Wilma F. Bergfeld, MD, FAAD; Warren B. Bilker, PhD; Erica Brittain, PhD; William Hancock, PhD, DSc; Donald E. Mager, PharmD, PhD; David J. Margolis, MD, PhD; Alyce M. Oliver, PhD, MD; June K. Robinson, MD; Jose U. Scher, MD; Joseph Shiloach, PhD; Richard Siegel, MD, PhD; Daniel Solomon, MD, MPH (Acting Chairperson); Scott A. Waldman, MD, PhD, FCP, FAHA; Yihong Ye, MD, PhD

Acting Industry Representative to the Committee (Non-Voting): Sean P. Curtis, MD

FDA Participants (Non-Voting): Leah Christl, PhD; Badrul Chowdhury, MD, PhD; Nikolay P. Nikolov, MD; Steven Kozlowski, MD; Peter L. Adams, PhD

Acting Designated Federal Officer (Non-Voting): Moon Hee V. Choi, PharmD

Open Public Hearing Speakers: Andrew Spiegel, Esquire on behalf of Harry Gewanter, MD, FACR, FAAP (Alliance for Safe Biologic Medicines); Dennis R. Cryer, MD (Biologics Prescribers Collaborative); Richard M. Hodge (American Autoimmune Related Diseases Association); Andrew Spiegel, Esquire (Digestive Disease National Coalition); Jasey Cardenas on behalf of Lawrence A. La Motte (Patients for Biologic Safety and Access); Seth Ginsberg (Global Healthy Living Foundation and CreakyJoints); Emily Lemiska on behalf of Casey Cashman (U.S. Pain Foundation); Thair Phillips (RetireSafe); Andrew Spiegel, Esquire on behalf of Kathleen A. Arntsen (Lupus and Allied Diseases Association); Ali Boyle, MPH 9 The Advisory Board Company); Christine Simmon (The Biosimilars Council); Christine Schaefer (Central Dermatology); Matthew Banfield (Biosimilars Forum); Tiffany McCaslin (National Business Group on Health)

The agenda proceeded as follows:

Call to Order and Introduction of Committee	**Daniel Solomon, MD, MPH** Acting Chairperson, AAC
Conflict of Interest Statement	**Moon Hee Choi, PharmD** Acting Designated Federal Officer, AAC
Overview of the Regulatory Pathway and FDA's Guidance for the Development and Approval of Biosimilar Products in the US	**Leah Christl, PhD** Associate Director, Therapeutic Biologics Therapeutic Biologics and Biosimilars Staff Office of New Drugs (OND), CDER, FDA
Clarifying Questions to the FDA	

FDA Introductory Remarks	**Nikolay P. Nikolov, MD** Clinical Team Leader Division of Pulmonary, Allergy & Rheumatology Products (DPARP) Office of Drug Evaluation II (ODE-II) OND, CDER, FDA
APPLICANT PRESENTATIONS	**Sandoz, Inc.**
Introduction and Concept	**Mark McCamish, MD, PhD** Global Head of Development Sandoz Biopharmaceuticals
Analytical Demonstration of Similarity	**Martin Schiestl, PhD** Chief Science Officer, Sandoz Biopharmaceuticals
Non-clinical and Pharmacokinetic Characterization of GP2015	**Oliver von Richter, PhD, FCP** Clinical Pharmacologist, Global Clinical Development Sandoz Biopharmaceuticals
Clinical Confirmation of GP2015 Equivalence to Enbrel®	**Malte Peters, MD** Global Head of Clinical Development Sandoz Biopharmaceuticals
Use in Clinical Practice	**Jonathan Kay, MD** Timothy S. and Elaine L. Peterson Chair in Rheumatology Professor of Medicine Director of Clinical Research, Rheumatology University of Massachusetts Medical School
Conclusions	**Mark McCamish, MD, PhD**
Clarifying Questions to Applicant	
BREAK	
FDA PRESENTATIONS	
GP2015 Product Quality Review	**Peter L. Adams, PhD** CMC Product Quality Reviewer Division of Biotechnology Review and Research 1 Office of Biotechnology Products Office of Pharmaceutical Quality, CDER, FDA

FDA PRESENTATIONS (CONT.)

GP2015 Statistical Equivalence Testing for Bioactivity	**Meiyu Shen, PhD** CMC Statistical Reviewer Division of Biometrics VI Office of Biostatistics (OB) Office of Translational Sciences (OTS), CDER, FDA
GP2015 Product Quality Review (cont.)	**Peter L. Adams, PhD**
Clinical Pharmacology Review	**Yunzhao Ren, MD, PhD** Clinical Pharmacology Reviewer Division of Clinical Pharmacology II Office of Clinical Pharmacology, OTS, CDER, FDA
Clinical Efficacy Review	**Kathleen Fritsch, PhD** Mathematical Statistician Division of Biometrics III, OB, OTS, CDER, FDA
Clinical Safety and Immunogenicity Review, Considerations for Extrapolation and Summary of FDA Presentation	**Rachel Glaser, MD** Medical Officer DPARP, ODE-II, OND, CDER, FDA
Clarifying Questions to FDA	

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee	**Nikolay P. Nikolov, MD**
Questions to the Committee and Committee Discussion	

BREAK

Questions to the Committee and Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Please discuss whether the evidence from analytical studies supports a demonstration that GP2015 is highly similar to US-licensed Enbrel, notwithstanding minor differences in clinically inactive components.

   Committee Discussion: *Most committee members agreed that the evidence from analytical studies supports a demonstration that GP2015 is highly similar to US-licensed Enbrel, notwithstanding minor differences in clinically inactive components.*

One committee member noted that excellent characterization information for GP2015 was presented, but because it is a very complex molecule, recommended a discriminating quality control program to make sure that it stays within specifications. Another committee member noted that in addition to the analytical data presented, the use of pharmacodynamic biomarkers would have been helpful to further support the demonstration that GP2015 is highly similar to US-licensed Enbrel. Please see the transcript for details of the committee discussion.

2. **DISCUSSION:** Please discuss whether the evidence supports a demonstration that there are no clinically meaningful differences between GP2015 and US-licensed Enbrel in the studied condition of use (plaque psoriasis (PsO)).

   Committee Discussion: *Most committee members agreed that the evidence supports a demonstration that there are no clinically meaningful differences between GP2015 and US-licensed Enbrel in the studied condition of use (plaque psoriasis (PsO)). One committee member agreed that that the results of the single clinical trial was good, but noted that the primary efficacy response rates were significantly higher in the comparative clinical study than in the two historic placebo controlled trials raising the question about the interpretability of the comparative clinical study. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION:** Please discuss whether the totality of the data provides adequate scientific justification to support a demonstration of no clinically meaningful differences between GP2015 and US-licensed Enbrel for the following additional indications for which US-licensed Enbrel is licensed:
   - Rheumatoid Arthritis (RA)
   - Juvenile Idiopathic Arthritis (JIA)
   - Psoriatic Arthritis (PsA)
   - Ankylosing Spondylitis (AS)

   If not, please state the specific concerns and what additional information would be needed to support such a demonstration. Please discuss by indication, if relevant.

   Committee Discussion: *The committee members generally agreed that the totality of the data provides adequate scientific justification to support a demonstration of no clinically meaningful differences between GP2015 and US-licensed Enbrel for the following additional indications for which US-licensed Enbrel is licensed (RA, JIA, PsA and AS). Even though not concerned with the extrapolation to JIA, one committee member expressed concerns about the lack of an age-appropriate presentation for administration of GP2015 in pediatric patients with JIA. Please see the transcript for details of the committee discussion.*

4. **VOTE:** Does the totality of the evidence support licensure of GP2015 as a biosimilar to US-licensed Enbrel for the following indications for which US-licensed Enbrel is currently licensed and for which Sandoz is seeking licensure (RA, JIA, AS, PsA, PsO)?

   Please explain the reason for your vote.

Vote Result: YES: 20 NO: 0 ABSTAIN: 0

Committee Discussion: *The committee members unanimously agreed that the totality of the evidence support licensure of GP2015 as a biosimilar to US-licensed Enbrel for the following indications for which US-licensed Enbrel is currently licensed and for which Sandoz is seeking licensure (RA, JIA, AS, PsA, PsO). Some committee members recommended mandatory postmarketing surveillance to assess long-term safety. One committee member noted that nonmedical switching is a major concern that needs greater clarification from the Agency. One committee member noted that the labeling should clearly indicate that GP2015 is a biosimilar and is not an interchangeable product. Some committee members also stressed the importance of patient education on biosimilars and interchangeability Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 3:06 p.m.