Sandoz presents new long-term and switching data for biosimilars Zessly® (infliximab) and Erelzi® (etanercept) in rheumatoid arthritis

- Zessly® (infliximab) matched the reference medicine in terms of safety and efficacy at 54 weeks, even in patients who switched from the reference medicine to Zessly®.
- Switching from the reference medicine to Erelzi® (etanercept) did not impact efficacy and safety in patients with moderate to severe rheumatoid arthritis at 48 weeks.
- Nearly 320 million people in Europe are expected to have limited access to disease-modifying anti-rheumatic medicines, underscoring the value of Zessly and Erelzi®.

Holzkirchen, June 15, 2018 – Sandoz, a Novartis division and the pioneer and global leader in biosimilars, today announced the presentation of two long-term, Phase III studies: one each for biosimilar Zessly® (infliximab)\(^1\)\(^2\)\(^3\) and biosimilar Erelzi® (etanercept)\(^6\)\(^7\).

Research from the 54-week REFLECTIONS B537-02 study of Zessly and the 48-week EQUIRA study of Erelzi showed that each biosimilar matched its reference biologic in terms of safety, efficacy and quality, reinforcing previously-presented findings\(^1\)\(^2\)\(^8\)\(^9\). The research also indicated that switching from the reference medicine to the biosimilar did not affect safety, efficacy or immunogenicity\(^1\)\(^2\). Both studies are being presented at the Annual European Congress of Rheumatology (EULAR) in Amsterdam.

“We are very pleased with these data, which reinforce what well over 10 years of science and real-world evidence in Europe have shown – that biosimilars match their reference medicines in terms of safety, efficacy and quality,” said Mark Levick, MD, PhD, Global Head of Development, Biopharmaceuticals, Sandoz. “It is our hope that these studies will help healthcare providers and patients have confidence that switching to Zessly or Erelzi will continue to deliver the benefits they are receiving from their existing treatment.”

About the Zessly® (infliximab) Research (Poster FRI0137; 15 June, 11:45 – 13:30 CET)
“Efficacy, Safety and Immunogenicity from Week 30 to Week 54 in a Randomised, Double-Blind, Phase III Study Comparing an Infliximab Biosimilar (PF-06438179/GP1111) with Reference Infliximab”

REFLECTIONS B537-02 is a Phase III, double-blind, parallel-group, confirmatory study of Sandoz biosimilar Zessly (infliximab) versus reference Remicade® (infliximab) in combination with methotrexate in 650 biologic-naïve, adult patients with moderately to severely active rheumatoid arthritis who had an inadequate response to methotrexate therapy alone.

The study met its primary endpoint, a ≥20% improvement in American College of Rheumatology (ACR) response (ACR 20) at Week 14. The research demonstrated that there were no clinically-meaningful differences from 30 to 54 weeks in terms of safety, efficacy and immunogenicity between patients with rheumatoid arthritis remaining on Sandoz infliximab and reference infliximab. The same results were found when patients on reference infliximab were blindly re-randomized to switch to Sandoz infliximab or remained on reference therapy.

Patients were on a stable dose of methotrexate at initiation of treatment and randomized 1:1 to Sandoz infliximab (n=324) or reference infliximab (n=326) at a dose of 3 mg/kg IV at weeks 0, 2, 6, and then every 8 weeks, with one dose escalation to 5 mg/kg allowed at or after week 14 for inadequate responders for 30 weeks. At week 30, 566 patients entered the second treatment phase,
and 280 patients continued onto treatment with Sandoz infliximab. At week 30, patients (n=286) were blindly re-randomized (1:1) to remain on treatment (n=143) or switch to Sandoz infliximab (n=143).  

Incidence of adverse events (AEs) (36.8%, 33.6%, and 37.8%, respectively), serious AEs (4.6%, 7.7% and 2.8%, respectively) and infusion-related reactions (3.2%, 8.4% and 4.2%, respectively) were comparable among the Sandoz infliximab, reference infliximab, and switched treatment groups. Overall, post-dose anti-drug antibody (ADA) rates were comparable among the groups (52.1%, 60.1%, and 58.0% respectively).  

About the Erelzi® (etanercept) Research (Poster FRI0129; 15 June, 11:45 – 13:30 CET): “Switch Between Reference Etanercept (ETN) and GP2015, an Etanercept Biosimilar, did not Impact Efficacy and Safety in Patients With Moderate-To-Severe Rheumatoid Arthritis: 48-Week Results From the Phase 3 EQUIRA Study”

EQUIRA was a 48-week, randomized, double-blind Phase III study that compared the efficacy and safety of Sandoz biosimilar Erelzi® (etanercept) versus reference Enbrel® (etanercept), in the 376 adult patient population with moderate to severe rheumatoid arthritis, and evaluated the effects of switching from reference etanercept to Sandoz etanercept.

This new research demonstrated that switching rheumatoid arthritis patients from reference etanercept to Sandoz etanercept does not affect the overall therapy outcome in terms of efficacy, safety and immunogenicity.

A total of 376 patients with active rheumatoid arthritis and inadequate response to methotrexate were randomized 1:1 to 50 mg Sandoz etanercept or reference etanercept subcutaneously once weekly for 24 weeks, at which point the primary endpoint for equivalence (change from baseline in DAS28-CRP at Week 24) was met. Patients with at least moderate response at Week 24 either continued Sandoz etanercept treatment or, in the reference etanercept group, were switched to receive 50 mg Sandoz etanercept up to 48 weeks.

At Week 48, the EULAR and ACR 20/50/70 response rates were comparable between the two groups. Following week 24, treatment-emergent adverse events (AEs) occurred in 42.9% vs 38.0% patients in the continued Sandoz etanercept (n=175) versus the switched (n=166) groups; serious AEs occurred in 2.3% versus 2.4% patients. The mean change in DAS28-CRP from baseline to Week 48 was comparable between the group that continued and the group that switched to Sandoz etanercept.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “positive opinion,” “recommendation,” “proposed,” “potential,” “can,” “will,” “believe,” “committed,” “investigational,” “portfolio,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved biosimilar products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Neither can
there be any guarantee that, if approved, such biosimilar products will be approved for all indications included in the reference product's label. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; the particular prescribing preferences of physicians and patients; competition in general, including potential approval of additional biosimilar versions of such products; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; litigation outcomes, including intellectual property disputes or other legal efforts to prevent or limit Sandoz from selling its products; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Sandoz
Sandoz is a global leader in generic pharmaceuticals and biosimilars. As a division of the Novartis Group, our purpose is to discover new ways to improve and extend people's lives. We contribute to society’s ability to support growing healthcare needs by pioneering novel approaches to help people around the world access high-quality medicine. Our portfolio of approximately 1,000 molecules, covering all major therapeutic areas, accounted for 2017 sales of USD 10.1 billion. In 2017, our products reached well over 500 million patients. Sandoz is headquartered in Holzkirchen, in Germany's Greater Munich area.

Sandoz is on Twitter. Sign up to follow @Sandoz_global at http://twitter.com/Sandoz_Global.

Follow our blog at www.sandoz.com/makingaccesshappen.

References
1. Alten, R. Efficacy, safety and immunogenicity from week 30 to week 54 in a randomised, doubleblind Phase III study comparing a proposed infliximab biosimilar (PF-06438179/GP1111) with reference INFLIXIMAB. Poster session presented at the Annual European Congress of Rheumatology, Amsterdam, Netherlands. 2018 June.
Sandoz acquired infliximab (PF-06438179) development, commercialization and manufacturing rights from Pfizer in February 2016 for the 28 European Union countries plus Norway, Iceland and Liechtenstein that form the European Economic Area (EEA). Under the terms of the divestment, Pfizer retains commercialization and manufacturing rights to infliximab (PF-06438179) in countries outside the EEA.

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