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MEDIA & INVESTOR RELEASE

Novartis announces new late-breaking ofatumumab data at EAN demonstrating robust efficacy and safety in the treatment of relapsing forms of multiple sclerosis (RMS)

- *Rapid and profound depletion of B-cells contributed to a halt in disease activity in RMS patients*[1]
- *A post hoc analysis showed 47.0% and 87.8% of patients treated with ofatumumab achieved no evidence of disease activity (NEDA-3) within the first (0–12 months) and second year (12–24 months) of treatment, respectively*[1]
- *Regulatory action for ofatumumab in RMS in the US is expected in June 2020*
- *If approved, ofatumumab has the potential to become a first-choice treatment for RMS patients and the first B-cell therapy that can be self-administered at home using an autoinjector pen*

Basel, May 27, 2020 — Novartis announced today that new ofatumumab data from the Phase III ASCLEPIOS trials and the Phase II APLIOS trial were presented virtually at the 6th Congress of the European Academy of Neurology (EAN). The data continue to demonstrate ofatumumab (OMB157) as a potential novel treatment option for patients with RMS. The safety profile was comparable to teriflunomide[2].

Ofatumumab is a targeted B-cell therapy that, if approved, addresses a clinical unmet need as the first B-cell therapy that can be self-administered at home through an autoinjector pen[2]. In addition to being presented virtually, the data were also published in the *European Journal of Neurology,* Volume 27, Supplement 1, May 2020.

A post hoc analysis from the Phase III ASCLEPIOS I and II trials (n=1882) assessed the odds of patients achieving NEDA-3 with ofatumumab versus teriflunomide within the first (Month 0–12) and second year (Month 12–24) of treatment[1]. NEDA-3 is a comprehensive composite measure commonly used to assess treatment outcomes in patients with RMS. It is defined as an absence of three measures of disease activity: relapses; disease progression, measured as 6-month confirmed disability worsening (CDW), and gadolinium enhancing (Gd+) T1 lesions[3]. The study results showed that compared with teriflunomide, a greater proportion of patients treated with ofatumumab achieved NEDA-3 in year 1 (47.0% vs 24.5%; *P*<.001) and in year 2 (87.8% vs 48.2%; *P*<.001)[1].

“Achieving no evidence of disease activity is widely recognized as an important treatment goal for multiple sclerosis therapies,” said Professor Ludwig Kappos, University Hospital Basel.

“These data suggest that halting new disease activity is possible by targeted B-cell therapy in RMS.”

A separate analysis from the APLIOS trial (n=284) showed ofatumumab treatment led to rapid and sustained depletion of both CD20+ B- and T-cells in patients with RMS. Ofatumumab depleted different B- and T-cell subsets including memory B-cells and naïve B-cells, as well as a subset of T-cells that are known to exhibit an activated phenotype. However, CD3+ T-cells that do not express the CD20 receptor, were largely unaffected[4].

“These results are encouraging and support our belief that, if approved, ofatumumab could have the potential to significantly improve the lives of people with RMS,” said Krishnan Ramanathan, Neuroscience Global Program Head at Novartis. “These data are a testament to our commitment to reimagining medicine and advancing innovative treatments that help people with this serious and progressive disease.”

Regulatory action for ofatumumab in the US is expected in June 2020. Novartis is committed to bringing ofatumumab to patients around the world, and additional regulatory filings are currently under way.

About ofatumumab
Ofatumumab (OMB157) is a fully human anti-CD20 monoclonal antibody (mAb) in development for RMS that is self-adminstered by a once-monthly injection, delivered subcutaneously[2,5]. As shown in preclinical studies, ofatumumab is thought to work by binding to a distinct epitope on the CD20 molecule inducing potent B-cell lysis and depletion[6]. The selective mechanism of action and subcutaneous administration of ofatumumab allows precise delivery to the lymph nodes, where B-cell depletion in MS is needed, and may preserve the B-cells in the spleen, as shown in preclinical studies[7]. Once-monthly dosing of ofatumumab also allows fast repletion of B-cells and offers more flexibility[8]. Ofatumumab was originated by Genmab and licensed to GlaxoSmithKline; Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015[9].

About ASCLEPIOS I and II studies
The ASCLEPIOS I and II studies are twin, identical design, flexible duration (up to 30 months), double-blind, randomized, multi-center Phase III studies evaluating the safety and efficacy of ofatumumab 20 mg monthly subcutaneous injections versus teriflunomide 14 mg oral tablets taken once daily in adults with RMS. The ASCLEPIOS I and II studies enrolled 1882 patients with MS, between the ages of 18 and 55 years, with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[2]. The studies were conducted in over 350 sites in 37 countries[10]. Ofatumumab demonstrated a significant reduction in annualized relapse rate (ARR) by 50.5% (0.11 vs 0.22) and 58.5% (0.10 vs 0.25) compared with teriflunomide (*P*<.001 in both studies) in ASCLEPIOS I and II respectively (primary endpoint). Ofatumumab showed significant reduction of both Gd+ T1 lesions and new or enlarging T2 lesions. It significantly reduced the mean number of both Gd+ T1 lesions (97.5% and 93.8% relative reduction in ASCLEPIOS I and II, respectively, both *P*<.001) and new or enlarging T2 lesions (82.0% and 84.5% relative reduction in ASCLEPIOS I and II, respectively, (both *P*<.001).

Ofatumumab also showed a relative risk reduction of 34.4% (*P*=.002) in 3-month CDW and 32.5% (*P*=.012) in 6-month CDW compared with teriflunomide in pre-specified meta-analysis, as defined in ASCLEPIOS. Ofatumumab demonstrated that it lowered neurofilament light levels in serum at the first assessment at Month 3 compared with teriflunomide. There was no difference in slope of brain volume change from baseline between treatments. In a measure of 6-month confirmed disability improvement events, a favorable trend was seen but this did not reach significance. The frequency of serious infections and malignancies was similar across both treatment groups, and overall, ofatumumab had a similar safety profile to teriflunomide. Injection-related reactions, injection-site reactions and upper respiratory tract infection were the most commonly observed adverse events across both treatment groups, occurring in ≥10% of patients[2].

A separate post hoc analysis demonstrated ofatumumab may halt new disease activity in RMS patients. It showed the odds of achieving NEDA-3 (no relapses, no MRI lesions, and no disability worsening combined) with ofatumumab versus teriflunomide were >3-fold higher at Month (M) 0–12 (47.0% vs 24.5% of patients; *P*<.001) and >8-fold higher at M12–24 (87.8% vs 48.2% of patients; *P*<.001)[1]. Overall ofatumumab, a fully human antibody targeting CD20+ B-cells, delivered superior efficacy and demonstrated a safety and tolerability profile with infection rates similar to teriflunomide[2].

About APLIOS study

The APLIOS study is a 12-week, open-label, Phase II bioequivalence study to determine the onset of B-cell depletion with ofatumumab subcutaneous monthly injections and the bioequivalence of subcutaneous administration of ofatumumab via a pre-filled syringe—as used in ASCLEPIOS I and II—and an autoinjector pen in patients with RMS. Patients were randomized according to injection device and site including the abdomen and the thigh. B-cell depletion was measured nine times over 12 weeks and Gd+ lesion counts were assessed at baseline and at Weeks 4, 8 and 12. Regardless of injection device or site, ofatumumab 20 mg subcutaneous monthly injections resulted in rapid, close to complete and sustained B-cell depletion. The proportion of patients with B-cell concentrations of <10 cells/µL was >65% after the first injection by Day 7, 94% by Week 4 and sustained >95% at all following injections. Ofatumumab treatment reduced the mean number of Gd+ lesions from baseline (1.5) to 0.8, 0.3 and 0.1 by Weeks 4, 8 and 12, respectively. The proportion of patients free from Gd+ lesions at the corresponding time points were 66.5%, 86.7%, and 94.1%, respectively[4,5].

About Multiple Sclerosis

MS disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[11]. MS, which affects approximately 2.3 million people worldwide[12], is often characterized into three forms: primary progressive MS (PPMS)[13], relapsing remitting MS (RRMS), and secondary progressive MS (SPMS), which follows from an initial RRMS course and is characterized by physical and cognitive changes over time, in presence or absence of relapses, leading to a progressive accumulation of neurological disability[14]. Approximately 85% of patients initially present with relapsing forms of MS[12].

Novartis in Neuroscience

Novartis has a strong ongoing commitment to neuroscience and to bringing innovative treatments to patients suffering from neurological conditions where there is a high unmet need. We are committed to supporting patients and physicians in multiple disease areas, including MS, migraine, Alzheimer's disease, Parkinson's disease, epilepsy and attention deficit hyperactivity disorder, and have a promising pipeline in MS, Alzheimer's disease, spinal muscular atrophy and specialty neurology.

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About Novartis

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 145 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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