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MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis Phase III ASCLEPIOS trials demonstrate robust efficacy of ofatumumab in patients with relapsing multiple sclerosis

- *Both ASCLEPIOS I and II studies met their primary endpoints in patients with relapsing forms of MS (RMS)[1]; overall ofatumumab (OMB157), a subcutaneous, potent, fully-human antibody targeting CD20 positive B-cells, delivered efficacy with a favorable safety profile[1]*

- *RMS patients on ofatumumab had a reduction in annualized relapse rate (ARR) by 50.5% (0.11 vs. 0.22) and 58.5% (0.10 vs. 0.25) compared to Aubagio®* (teriflunomide) (both studies p<0.001) in ASCLEPIOS I and II studies respectively[1]*

- *Ofatumumab showed highly significant suppression of gadolinium (Gd) T1 lesions when compared to Aubagio®, demonstrating a profound suppression of new inflammatory activity[1]*

- *Ofatumumab showed a relative risk reduction of 34.4% in 3-month confirmed disability progression (CDP†) (p=0.002) and 32.5% in 6-month CDP (p=0.012) versus Aubagio® in pre-specified pooled analyses[1]*

- *Ofatumumab, if approved, will potentially become a treatment for a broad RMS population and the first B-cell therapy that is easy to start and manage in a monthly self-administered injection at home*

Basel, September 13, 2019 – Novartis, a global leader in neuroscience, today presented positive results of the Phase III ASCLEPIOS I and II studies at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Stockholm, Sweden. Data from both studies show ofatumumab (OMB157) was superior to Aubagio®* (teriflunomide) in patients with relapsing forms of MS (RMS)[1]. 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 20mg monthly subcutaneous injections versus Aubagio® 14mg oral tablets taken once daily in adults with RMS[2,3].

Both studies met the primary endpoints where ofatumumab showed a highly significant and clinically meaningful reduction in the number of confirmed relapses, evaluated as the annualized relapse rate (ARR)[1]. Patients treated with ofatumumab had an ARR of 0.11 and 0.10 compared to Aubagio® (ARR of 0.22 and 0.25) in ASCLEPIOS I and II respectively, corresponding to a reduction in ARR by 50.5% and 58.8% with ofatumumab (p<0.001 in both studies)[1]. Ofatumumab showed highly significant suppression of both Gd+ T1 lesions and new or enlarging T2 lesions compared to Aubagio®, demonstrating a profound suppression of new inflammatory activity[1]. Additionally, ofatumumab showed a relative risk reduction of 34.4% (p=0.002) in 3-month confirmed disability progression (CDP†) and 32.5% (p=0.012) in 6-

month CDP versus Aubagio® in pre-specified pooled analyses[1]. Overall ofatumumab, a potent, fully-human antibody targeting CD20 positive B-cells, delivered efficacy with a favorable safety profile[1]. The safety profile of ofatumumab as seen in the ASCLEPIOS studies is in line with the observations from Phase II results[1,4]. Novartis plans to initiate submissions to health authorities by end of 2019.

“It is clear that early initiation of highly effective treatment for MS improves long-term outcomes, and there is great need for potent, safe, and convenient therapy that can be used to treat MS from the start,” said Professor Stephen L. Hauser, Director of the UCSF Weill Institute for Neurosciences. “The results from ASCLEPIOS are wonderful news for patients who would like to take an extremely effective B-cell therapy with low requirement for monitoring, avoiding visits to an infusion center.”

“Ofatumumab showed high efficacy and a favorable safety profile in people with RMS, offering a potential first B-cell therapy that can be self-administered in the home,” said John Tsai, Head of Global Drug Development and Chief Medical Officer, Novartis. “This is a big step forward in our relentless efforts to advance and reimagine treatment in the MS journey of each patient.”

The ASCLEPIOS I and II studies enrolled 1,882 patients with MS, between the ages of 18 and 55 years, with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[2,3]. The studies were conducted in over 350 sites in 37 countries. Additional secondary endpoints included confirmed disability improvement at 6 months, serum levels of neurofilament light chain (NfL), and rate of brain volume loss[2,3]. Safety and the pharmacokinetic properties of ofatumumab were also measured throughout the treatment period[2,3].

About ofatumumab
Ofatumumab is a fully human anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly subcutaneous injection that is in development for MS. Ofatumumab works by binding to the CD20 molecule on the B-cell surface and inducing potent B-cell lysis and depletion. Positive Phase IIb results in MS patients were presented in 2014 and showed a marked significant reduction in the number of new brain lesions in the first 24 weeks after ofatumumab administration[4]. Novartis initiated a Phase III program for ofatumumab in RMS in August 2016. Novartis obtained rights for ofatumumab from Genmab in all indications, including MS, in December 2015. Novartis released first interpretable results from the ASCLEPIOS studies at the end of August 2019.

About Multiple Sclerosis
MS disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[5]. MS, which affects approximately 2.3 million people worldwide[6], is often characterized into three forms: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS – often defined as cognitive and physical changes, and an overall accumulation of disability[7]) and primary progressive MS (PPMS)[8]. Approximately 85% of patients initially present with relapsing forms of MS[6].

About Novartis in MS
The Novartis multiple sclerosis portfolio includes Gilenya® (fingolimod, an S1P modulator), which is indicated in European Union for the treatment of adult patients and children and adolescents 10 years of age and older with RMS. In the United States, Gilenya is approved for the treatment of adults with relapsing forms of MS, to include clinically isolated syndrome (CIS‡), relapsing remitting disease and active secondary progressive disease.

In March 2019, the US Food and Drug Administration approved Mayzent® (siponimod) for the treatment of relapsing forms of MS, to include CIS, relapsing remitting disease and active secondary progressive disease. The approval is based on the Phase III EXPAND trial, the

largest controlled clinical study of SPMS patients, showing Mayzent significantly reduced the risk of disease progression, including impact on physical disability and cognitive decline[9]. Novartis is committed to bringing Mayzent to patients worldwide, and additional regulatory filings are currently underway with other health authorities outside the US for secondary progressive MS.

Extavia® (interferon beta-1b for subcutaneous injection) is approved in the US for relapsing forms of MS, to include CIS, relapsing remitting disease and active secondary progressive disease. In Europe, Extavia is approved to treat people with RRMS, SPMS with active disease and people who have had a single clinical event suggestive of MS.

In the US, the Sandoz Division of Novartis markets Glatopa® (glatiramer acetate injection) 20mg/mL and 40mg/mL, generic versions of Teva's glatiramer acetate.

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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 more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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*Aubagio® is a registered trade mark of Genzyme, a Sanofi company.
†CDP synonymously used for confirmed disability worsening (CDW).
‡ Clinically isolated syndrome (CIS) is defined as a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination in the central nervous system[10].

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