Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

MEDIA & INVESTOR RELEASE

Novartis receives positive CHMP opinion for Kesimpta®* (ofatumumab), a self-administered treatment for adult patients with relapsing multiple sclerosis

- *Kesimpta is a targeted B-cell therapy that delivers superior efficacy with a similar safety and tolerability profile compared with teriflunomide, a first-line treatment in MS*[1]

- *CHMP opinion is based on two Phase III ASCLEPIOS studies that met the primary endpoints where Kesimpta showed a reduction of the annual relapses by over 50% versus teriflunomide and achieved more than 30% relative risk reduction of 3-month confirmed disability progression (CDP)* [1]

- *In a post hoc analysis, nearly nine out of 10 patients treated with Kesimpta achieved no evidence of disease activity (NEDA-3) in their second year of treatment*[2]

- *If approved, Kesimpta will be the first and only self-administered, targeted B-cell therapy for patients with relapsing multiple sclerosis in Europe*

Basel, January 29, 2021 — Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion and recommended granting marketing authorization of Kesimpta® (ofatumumab) for the treatment of relapsing forms of multiple sclerosis (RMS) in adults with active disease defined by clinical or imaging features. Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that has shown superior efficacy with a similar safety profile compared with teriflunomide, a first-line treatment in MS[1]. Kesimpta has the potential to become a first-choice treatment option for patients with RMS that can be self-administered once-monthly at home via the Sensoready® autoinjector pen[3].

“In MS, one of the main goals of treatment is to achieve no evidence of disease activity as early on and for as long as possible[4],” said Dr. Xavier Montalban, Multiple Sclerosis Centre of Catalonia (Cemcat), Vall d'Hebron University Hospital. “Knowing that early initiation of high-efficacy treatments can improve long-term outcomes[5], it’s exciting to see that Kesimpta has the potential to halt new disease activity and help people to preserve neurological function and slow down the worsening of disability[2].”

“The positive CHMP opinion for Kesimpta underscores its potential to provide people living with RMS in Europe with a new treatment that combines powerful efficacy with a favorable

safety profile and can be taken at home[1,3]," said Marie-France Tschudin, President, Novartis Pharmaceuticals. "By removing the need to go to an infusion center, Kesimpta has the capability to reduce the burden not only for patients, but also for physicians and the healthcare system[6,7]. Kesimpta is a testament to our commitment to reimagine medicine for the MS community and we will work closely with the regulatory authorities to ensure it is available for people living with MS as soon as possible."

The CHMP opinion is based on results from the Phase III ASCLEPIOS I and II studies, in which Kesimpta demonstrated superiority versus teriflunomide in significantly reducing the annualized relapse rate (ARR, primary endpoint), 3-month confirmed disability progression (CDP), and the number of gadolinium-enhancing (Gd+) T1 and new or enlarging T2 lesions[1]. Results from these two studies were published in the August 6, 2020 issue of *The New England Journal of Medicine*.

A separate post hoc analysis demonstrated that Kesimpta may halt new disease activity in RMS patients, with nearly nine out of 10 patients treated with Kesimpta achieving no evidence of disease activity (NEDA-3) in their second year of treatment[2].

The CHMP recommended approval for Kesimpta with an indication for the treatment of adult patients with RMS with active disease defined by clinical or imaging features. The European Commission will review the CHMP recommendation and deliver its final decision in approximately two months.

In August 2020, the US Food and Drug Administration approved Kesimpta as an injection for subcutaneous use for the treatment of RMS, to include clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease, in adults. On January 25, 2021, Kesimpta was approved in Canada for the treatment of relapsing remitting multiple sclerosis (RRMS).

**Brand name Kesimpta provisionally approved by EMA*.

About Kesimpta® (ofatumumab)
Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that provides the flexibility of self-administration for adults with RMS. It is an anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly injection, delivered subcutaneously[1,3]. Initial doses of Kesimpta are given at Weeks 0, 1 and 2, with the first injection performed under the guidance of a healthcare professional. As shown in preclinical studies, Kesimpta is thought to work by binding to a distinct epitope on the CD20 molecule inducing potent B-cell lysis and depletion[8]. The selective mechanism of action and subcutaneous administration of Kesimpta allows precise delivery to the lymph nodes, where B-cell depletion in MS is needed, and preclinical studies have shown that it may preserve the B-cells in the spleen[9]. Once-monthly dosing of Kesimpta differs from other anti-CD20 therapies as it allows faster repletion of B-cells, offering more flexibility in MS management[10]. Ofatumumab was originally developed by Genmab and licensed to GlaxoSmithKline. Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015[11].

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 Kesimpta 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 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[1]. The studies were conducted in over 350 sites in 37 countries[12]. Kesimpta demonstrated a significant reduction in ARR by 51% (0.11 vs 0.22) and 59% (0.10 vs 0.25) compared with teriflunomide (P<.001 in both studies) in ASCLEPIOS I and II, respectively (primary endpoint). Kesimpta also showed a relative risk reduction of 34.4% (P=.002) in 3-month CDP compared with teriflunomide, as defined in ASCLEPIOS[1].

Kesimpta 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 (98% and 94% relative reduction in ASCLEPIOS I and II, respectively, both *P*<.001) and new or enlarging T2 lesions (82% and 85% relative reduction in ASCLEPIOS I and II, respectively, both *P*<.001) vs teriflunomide[1].

Kesimpta had a similar safety profile to teriflunomide, with the frequency of serious infections and malignancies also being similar across both treatment groups. Upper respiratory tract infection, headache, injection-related reactions and local injection site reactions were the most commonly observed adverse reactions with Kesimpta (incidence greater than 10%)[1].

A separate post hoc analysis demonstrated that Kesimpta 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 Months 0–12 (47.0% vs 24.5% of patients; *P*<.001) and >8-fold higher at Months 12–24 (87.8% vs 48.2% of patients; *P*<.001)[2].

Overall Kesimpta, an antibody targeting CD20 positive B-cells, delivered superior efficacy and demonstrated a safety and tolerability profile with infection rates similar to teriflunomide[1].

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 Kesimpta subcutaneous monthly injections and the bioequivalence of subcutaneous administration of Kesimpta via a prefilled syringe—as used in ASCLEPIOS I and II—and a Sensoready pen in patients with RMS. Patients were randomized according to injection device and site including the abdomen and 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, Kesimpta 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. Kesimpta 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[3].

The ASCLEPIOS and APLIOS studies form part of the AXIOS Program, the overarching ofatumumab clinical development program, which will expand the evidence of ofatumumab in MS.

About Multiple Sclerosis
Multiple sclerosis is a chronic inflammatory disease of the central nervous system characterized by myelin destruction and axonal damage in the brain, optic nerves and spinal cord[13]. MS, which affects approximately 2.8 million people worldwide[14], can be characterized into four main types of MS: CIS, relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS)[15]. The various forms of MS can be distinguished based on whether a patient experiences relapses (clearly defined acute inflammatory attacks of worsening neurological function), and/or whether they experience progression of neurologic damage and disability from the onset of the disease[13].

Novartis in Neuroscience
Novartis has a long heritage and strong ongoing commitment to neuroscience and to bringing innovative treatments to patients suffering from neurological and neuropsychiatric conditions where there is a high unmet need. We are committed to supporting patients and physicians with our ambition to pioneer, develop and deliver treatments across four pillars: multiple sclerosis, pediatric neurology, neurodegeneration and neuropsychiatry.

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 CHMP opinion,” “potential,” “can,” “will,” “could,” “expectations,” “ongoing,” “commitment,” “committed,” “investigational,” “recommended,” “to provide,” “to reduce,” “to ensure,” “goals,” “to achieve,” “to preserve,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Kesimpta, or regarding potential future revenues from Kesimpta. 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 Kesimpta will be submitted or approved for sale or for any additional indications or labeling in any additional markets, or at any particular time. Nor can there be any guarantee that Kesimpta will be commercially successful in the future. In particular, our expectations regarding Kesimpta 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; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity 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 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 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at **https://twitter.com/novartisnews**
For Novartis multimedia content, please visit **https://www.novartis.com/news/media-library**
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Hauser S, Bar-Or A, Cohen J, et al. Ofatumumab versus teriflunomide in relapsing multiple sclerosis. *N Engl J Med*. 2020;383(6):546-557.
2. Hauser S, Bar-Or A, Cohen J, et al. Ofatumumab versus teriflunomide in relapsing multiple sclerosis: analysis of no evidence of disease activity (NEDA-3) from ASCLEPIOS I and II trials. Eur J Neurol. 2020;27(S1):85-86.
3. Bar-Or A, Fox E, Goodyear A, et al. Onset of B-cell depletion with subcutaneous administration of ofatumumab in relapsing multiple sclerosis: results from the APLIOS bioequivalence study. Poster presentation at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum; February 27-29, 2020; West Palm Beach, FL.
4. Winkelmann A, Loebermann M, Reisinger EC, Hartung HP, Zettl UK. Disease-modifying therapies and infectious risks in multiple sclerosis. Nat Rev Neurol. 2016;(4):217-33.
5. Stankiewicz J, Weiner H. An argument for broad use of high efficacy treatments in early multiple sclerosis. *Neurol Neuroimmunol Neuroinflamm*. 2020;7(1):e636.

6. Lehmann-Horn K, Kronsbein HC, Weber MS. Targeting B cells in the treatment of multiple sclerosis: recent advances and remaining challenges. *Ther Adv Neurol Disord*. 2013;6(3):161-173.
7. Dieguez G, Engel T, Jacobson N. Site of service and cost dispersion of infused drugs [online]. Available from: https://www.milliman.com/insight/2019/Site-of-Service-and-Cost-Dispersion-of-Infused-Drugs/ [Last accessed: January 2021].
8. Smith P, Kakarieka A, Wallstroem E. Ofatumumab is a fully human anti-CD20 antibody achieving potent B-cell depletion through binding a distinct epitope. Poster presentation at the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) Congress; September 14-17; 2016; London, UK.
9. Smith P, Huck C, Wegert V, et al. Low-dose, subcutaneous anti-CD20 therapy effectively depletes B-cells and ameliorates CNS autoimmunity. Poster presentation at ECTRIMS; September 2016; London, UK.
10. Savelieva M, Kahn J, Bagger M, et al. Comparison of the B-cell recovery time following discontinuation of anti-CD20 therapies. ePoster presentation at ECTRIMS; October 25-28, 2017; Paris, FR.
11. Genmab Press Release: Genmab announces completion of agreement to transfer remaining ofatumumab rights [online] December 21, 2015. Available from: https://ir.genmab.com/static-files/9d491b72-bb0b-4e46-a792-dee6c29aaf7d [Last accessed: January 2021].
12. Kappos L, Bar-Or A, Cohen J, et al. Ofatumumab versus teriflunomide in relapsing multiple sclerosis: baseline characteristics of two pivotal phase 3 trials (ASCLEPIOS I and ASCLEPIOS II). Poster presentation at ECTRIMS; October 2018; Berlin, Germany.
13. Guthrie E. Multiple sclerosis: a primer and update. *Adv Studies Pharm.* 2007;4(11):313-317.
14. Multiple Sclerosis International Federation. Atlas of MS 2020-Mapping multiple sclerosis around the world. Available from: https://www.msif.org/wp-content/uploads/2020/10/Atlas-3rd-Edition-Epidemiology-report-EN-updated-30-9-20.pdf [Last accessed: January 2021].
15. National MS Society. *Types of MS*. Available from: https://www.nationalmssociety.org/What-is-MS/Types-of-MS [Last accessed: January 2021].

# # #

Novartis Media Relations
E-mail: media.relations@novartis.com

Antonio Ligi
Novartis External Communications
+41 79 723 3681 (mobile)
antonio.ligi@novartis.com

Meghan O'Donnell
Novartis Global Pharma Communications
+41 79 797 9102
meghan.odonnell@novartis.com

Eric Althoff
Novartis US External Communications
+1 862 778 3243
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		