Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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

MEDIA & INVESTOR RELEASE

FDA approves Novartis Kesimpta® (ofatumumab), the first and only self-administered, targeted B-cell therapy for patients with relapsing multiple sclerosis

- *Kesimpta delivers powerful efficacy with a favorable safety profile and can be self-administered at home, addressing significant unmet needs for people living with relapsing forms of multiple sclerosis (RMS)*[1]
- *Approval based on two Phase III ASCLEPIOS studies demonstrating significant reductions in risk of relapses, confirmed disability progression, Gd+ T1 brain lesions and new/enlarging T2 lesions*[1]
- *Kesimpta may halt new disease activity in RMS patients as shown in a post hoc analysis, with 47.0% and 87.8% of patients treated with ofatumumab achieving no evidence of disease activity (NEDA-3) within the first (0–12 months) and second year (12–24 months) of treatment, respectively*[2]

Basel, August 20, 2020 — Novartis today announced that the US Food and Drug Administration (FDA) has approved Kesimpta® (ofatumumab, formerly OMB157) as an injection for subcutaneous use for the treatment of relapsing forms of multiple sclerosis (RMS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that has shown superior efficacy with a similar safety profile compared with teriflunomide and is a first-choice treatment option for RMS patients[1]. Kesimpta is the first B-cell therapy that can be self-administered once monthly at home via the Sensoready® autoinjector pen[3].

“This approval is wonderful news for patients with relapsing multiple sclerosis. In the key clinical studies, this breakthrough treatment produced a profound reduction in new brain lesions, reducing relapses and slowing underlying disease progression[1],” said Professor Stephen L. Hauser, Director of the UCSF Weill Institute for Neurosciences and co-chair of the steering committee for the ASCLEPIOS I and II studies. “Through its favorable safety profile and well-tolerated monthly injection regimen, patients can self-administer the treatment at home, avoiding visits to the infusion center[1].”

One of the goals when managing RMS is to preserve neurological function to slow down the worsening of disability[4]. Despite the availability of several disease-modifying therapies (DMTs) for the treatment of RMS, the majority of individuals with RMS continue to experience disease activity[5]. Evidence suggests early initiation of high-efficacy treatment can improve long-term outcomes for patients with RMS[6].

“Multiple sclerosis (MS) is a complex disease, and response to disease modifying treatment will vary among individuals,” said Bruce Bebo, PhD, Executive Vice President of Research at the National MS Society. “This makes it important to have a range of treatments available with different mechanisms of action and routes of administration. We are pleased to have an additional option approved for the treatment of relapsing forms of MS.”

Traditionally, B-cell treatments, which bind to and deplete B-cells associated with disease activity in MS, have predominantly been available in hospitals or infusion treatment centers, which can add costs to the healthcare system and present a lifestyle burden for some patients[7,8]. Kesimpta provides patients the flexibility of self-administering via once-monthly subcutaneous dosing requiring no premedication, eliminating the need to travel to an infusion center. The positive results from the APLIOS study—an open-label Phase II study to determine the bioequivalence of subcutaneous delivery of Kesimpta via a prefilled syringe and a Sensoready pen in patients with RMS—and the ASCLEPIOS studies show Kesimpta to be a highly effective B-cell therapy that can be easily self-administered at home[1,3].

“At Novartis, we challenge treatment paradigms and strive to offer the best treatment choice for patients,” said Marie-France Tschudin, President, Novartis Pharmaceuticals. “When treating patients with RMS, Kesimpta is a meaningful treatment option that delivers both high efficacy and safety with the ability for patients to have more freedom in managing their disease. The development of Kesimpta is a great example of our commitment, knowledge and understanding of multiple sclerosis, which enabled us to identify a targeted treatment that can significantly improve patient outcomes and experience.”

Ofatumumab was first approved by the FDA in 2009 for the treatment of chronic lymphocytic leukemia (CLL) as an intravenous infusion with a high dose, administered by a healthcare provider. Ofatumumab was then investigated in an entirely new development program in RMS, as B-cells are known to play a critical role in the development of autoimmune diseases, such as MS[7]. The clinical development program for ofatumumab in RMS took 10 years and has involved more than 2,300 patients around the world as part of rigorous studies that were reflective of the broad patient population. Kesimpta was found to work through a distinct mode of action, and the treatment regimen (dosing)—which was specifically designed for RMS—plays a critical role in the outcome[9]. This is a different dosing regimen and route of administration than was previously approved for the CLL indication.

The approval of Kesimpta 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 recently published in the August 6, 2020 issue of *The New England Journal of Medicine*.

Kesimpta is expected to be available in the United States in early September.* Additional regulatory filings are currently underway across the world, and regulatory approval for Kesimpta in Europe is expected by Q2 2021.

**Time of availability may vary as healthcare providers integrate Kesimpta into their practices.*

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[10]. 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 in pre-specified meta-analysis, 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[1]. 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 Kesimpta may halt new disease activity in RMS patients. It showed the odds of achieving no evidence of disease activity (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 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 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, 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].

About Kesimpta® (ofatumumab, formerly OMB157)
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 loading 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[9]. 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[11]. Once-monthly dosing of Kesimpta also allows faster repletion of B-cells and offers more flexibility[12]. 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[13].

About Multiple Sclerosis
Multiple sclerosis (MS) 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[14]. MS, which affects approximately 2.3 million people worldwide[15], can be characterized into four main types of MS: clinically isolated syndrome (CIS), relapsing remitting (RRMS),

secondary progressive (SPMS) and primary progressive (PPMS)[16]. 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[14].

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.

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 “potential,” “can,” “will,” “may,” “could,” “expected,” “committed,” “commitment,” “promising,” “pipeline,” “addressing,” “underway,” “to include,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Kesimpta, or regarding the timing of availability of Kesimpta in the United States, or regarding regulatory approval of Kesimpta in Europe, 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 Europe or in any other markets, or at any particular time. Neither can there be any guarantee that Kesimpta will be available in early September, or in any other time frame, in the United States. 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, including European regulatory authorities not approving Kesimpta in the expected time frame, or at all; 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.

Dr. Hauser’s statements reflect his professional opinion and not necessarily the views of The Regents of the University of California. Nothing in his statements shall be construed to imply any support or endorsement of Novartis, or any of its products, by The Regents of the University of California.

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 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. Kesimpta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corp; August 2020.
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).
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: ACTRIMS; February 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. The Multiple Sclerosis Coalition. The use of disease-modifying therapies in multiple sclerosis: principles and current evidence. Accessed August 12, 2020. http://ms-coalition.org/the-use-of-disease-modifying-therapies-in-multiple-sclerosis-updated/
6. Cree BA, Mares J, Hartung HP. Current therapeutic landscape in multiple sclerosis: an evolving treatment paradigm. *Curr Opin Neurol.* 2019;32(3):365-377.
7. 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.
8. Dieguez G, Engel T, Jacobson N. Site of service and cost dispersion of infused drugs. Accessed August 12, 2020. https://www.milliman.com/insight/2019/Site-of-Service-and-Cost-Dispersion-of-Infused-Drugs/
9. 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: ECTRIMS; September 2016; London, UK.
10. 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.
11. 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.
12. 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 2017; Paris, FR.
13. Genmab Press Release: Genmab announces completion of agreement to transfer remaining ofatumumab rights. December 21, 2015. Accessed August 12, 2020. https://ir.genmab.com/static-files/9d491b72-bb0b-4e46-a792-dee6c29aaf7d
14. Guthrie E. Multiple sclerosis: a primer and update. *Adv Studies Pharm*. 2007;4(11):313-317.
15. Multiple Sclerosis International Federation. Atlas of MS 2013-Mapping Multiple Sclerosis Around the World. Accessed August 12, 2020. http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf
16. National MS Society. Types of MS. Accessed August 12, 2020. https://www.nationalmssociety.org/What-is-MS/Types-of-MS

# # #

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

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

Michael Amos
Novartis Global Pharma Communications
+41 79 123 7806 (mobile)
michael.amos@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		