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MEDIA & INVESTOR RELEASE

Novartis Kesimpta® six-year efficacy data show substantial benefits in recently diagnosed treatment-naïve people with relapsing multiple sclerosis

- *Continuous Kesimpta® treatment for up to six years showed sustained efficacy in recently diagnosed (≤3 years) treatment-naïve people living with relapsing multiple sclerosis (RMS) in an analysis of the ALITHIOS open-label extension study*[1]

- *Similar efficacy outcomes were demonstrated in a separate analysis of continuous Kesimpta treatment for up to six years in the overall ALITHIOS study population*[2]

- *Switch from teriflunomide to Kesimpta resulted in significant improvements across several efficacy outcomes such as annualized relapse rate and MRI lesion activity in both analyses*[1,2]

- *Treatment with Kesimpta for up to six years continues to be well tolerated with consistent safety outcomes, supporting the favorable benefit-risk profile of Kesimpta in RMS*[2]

Basel, April 17, 2024 – Novartis today announced data from the ALITHIOS open-label extension study showing sustained efficacy of first-line, continuous Kesimpta® (ofatumumab) treatment for up to six years in recently diagnosed – defined as starting treatment within three years of initial diagnosis – treatment-naïve people living with relapsing multiple sclerosis (RMS).[1] These efficacy outcomes included 44% fewer relapses; 96.4% and 82.7% reductions in MRI lesions (Gd+ T1 and neT2), respectively; and 24.5% and 21.6% fewer 3- and 6-month confirmed disability worsening (CDW) events, respectively, versus those who switched to Kesimpta from teriflunomide.[1] A separate analysis of the overall ALITHIOS population showed similar efficacy with continuous Kesimpta treatment, which was also well-tolerated with a consistent safety profile up to six years.[2] These data will be presented at the American Academy of Neurology (AAN) 2024 Annual Meeting held in Denver, Colorado and virtually on April 13-18, 2024.

“Our analysis of treatment-naïve people who were recently diagnosed with relapsing multiple sclerosis found that first-line use of Kesimpta for up to six years provided long-term benefits, including fewer relapses, profoundly suppressed MRI lesion activity, and fewer disability worsening events,” said principal investigator Gabriel Pardo, MD, Founding Director of the Multiple Sclerosis Center of Excellence at Oklahoma Medical Research Foundation. “While measurable improvements were also seen in patients switching to Kesimpta later on, the delay in irreversible disability worsening was not fully realized in the switch group compared to those starting on Kesimpta first, reinforcing the value of introducing the treatment to patients earlier.”

“We are extremely pleased to share the new data from ALITHIOS, which adds to the growing body of evidence of Kesimpta as an efficacious and well-tolerated option for people living with RMS,” said Norman Putzki, Development Unit Head, Neuroscience & Gene Therapy, Development, Novartis Pharmaceuticals Corporation. “Novartis is committed to addressing the biggest challenges for people living with MS through relentless discovery, development, and delivery of potentially transformative medicines with the goal of achieving complete disease control.”

Study Results

In the first analysis, the low annualized relapse rate (ARR) experienced by recently diagnosed treatment-naïve (RDTN) people living with RMS receiving continuous Kesimpta during the core Phase III trials was further reduced in the ALITHIOS open-label extension study, from 0.104 to 0.050 (52.0% reduction), corresponding to an adjusted ARR of one relapse per 20 years.[1] Rates of 3- and 6-month progression independent of relapse activity (PIRA) with first-line Kesimpta were also lower versus switch.[1] The observed rapid increase in the proportion of participants with no evidence of disease activity (NEDA-3) with continuous first-line Kesimpta treatment was maintained up to six years.[1]

In RDTN people living with RMS initially randomized to teriflunomide, improvements across several efficacy outcomes were seen after switching to Kesimpta, including significant reductions in ARR (71.3%) and in MRI lesion activity (Gd+ T1: 98.5% reduction; neT2: 93% reduction), and rapid increase in rates of NEDA-3.[1] However, rates of 3- and 6-month CDW events remained higher compared to patients receiving continuous Kesimpta, indicating that the efficacy benefit of first-line Kesimpta on delaying disability worsening was not fully achieved in the switch group.[1] Across both continuous and switch groups, nine out of 10 participants achieved NEDA-3 at Year 6.[1]

Similar results were seen in the second analysis, which looked at the overall ALITHIOS population.[2] Data showed sustained efficacy of continuous Kesimpta up to six years, including low ARR (49.9% reduction between core Phase III trials and extension phase), suppression of MRI lesion activity (Gd+ T1: 56.7% reduction; neT2: 89.3% reduction), sustained reduction of 6-month CDW events (14.1%, relative to the switch group), lower rates of 6-month PIRA, and sustained high rates of NEDA-3.[2] People switching from teriflunomide to Kesimpta experienced reductions in ARR (73.8%) and MRI lesion activity (Gd+ T1: 97.7% reduction; neT2: 91.8% reduction) and a rapid increase in NEDA-3 rates during the extension period.[2] Six-month CDW rates remained higher compared to patients receiving continuous Kesimpta, again highlighting an efficacy benefit of first-line Kesimpta on delaying disability worsening that was not fully achieved in the switch group.[2] At Year 6, NEDA-3 status was achieved in nine out of 10 participants in both the continuous and switch groups.[2]

The study also found that treatment with Kesimpta for up to six years was well-tolerated with no unexpected safety signals identified.[2] The rates of adverse events (AEs), serious AEs, serious infections, and malignancies remained stable with no increased risks over six years.[2]

The overall rates of AEs and serious AEs up to six years of Kesimpta treatment were consistent between the core Phase III trials and the ALITHIOS extension study.[2] The most common AEs were infections (COVID-19 [34.3%], nasopharyngitis [20.6%], upper respiratory tract infection [14.9%], and urinary tract infection [14.4%]).[2] The incidence of serious infections remained stable over time and did not increase with Kesimpta treatment up to six years.[2]

Mean serum immunoglobulin G (IgG) levels remained stable up to six years of treatment and the majority of patients (97.2%) had lgG levels above the lower limit of normal (LLN).[2] Mean serum immunoglobulin M (IgM) levels decreased over time but remained above the LLN for the majority of patients (65.9%).[2] No clinically meaningful association was observed between IgG/IgM levels below the LLN and risk of serious infections.[2]

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.[3] MS, which affects around 2 million people worldwide, can be characterized into four main types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS).[4,5] 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.[3]

About Kesimpta® (ofatumumab)
Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that provides the flexibility of self-administration for adults with relapsing forms of multiple sclerosis (RMS). Kesimpta is the first fully human anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly injection, delivered subcutaneously (SC) in RMS.[6, 7, 8]

The treatment regimen was designed and tested to enhance safety and tolerability and minimize the risk of systemic injection-related reactions.[6] Initial doses of Kesimpta are at Weeks 0, 1 and 2, with the first injection performed under the guidance of a healthcare professional. Monthly Kesimpta 20 mg doses are associated with rapid reduction and near-complete peripheral B-cell depletion, with no significant effect on pharmacokinetics due to body weight.[6] 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 SC 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.[10]

Data from the ASCLEPIOS I/II core studies demonstrate Kesimpta's efficacy and favorable safety and tolerability profile in RMS participants and the ALITHIOS open-label extension study provides additional support with up to 6 years of data.[2,11] The at-home administration of Kesimpta by monthly doses of 20 mg/0.4mL with an autoinjector (Sensoready®) also matches the preferences of many people living with MS due to its ease of use and supports patients to be compliant with, and persistent on the therapy over time.[6] Kesimpta was originally developed by Genmab and licensed to GlaxoSmithKline; Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015.[12]

Kesimpta has been approved for the treatment of relapsing forms of multiple sclerosis in over 90 countries worldwide with more than 100,000 patients treated as of March 2024.

Novartis in Neuroscience
At Novartis, in Neuroscience, we are committed to understanding and solving some of the most burdensome neurological conditions to improve the quality of life for patients and their caregivers, and to make a positive impact on society. We aim to lead the discovery, development and delivery of innovative medicines to create a transformational impact for people living with severe neurological conditions by changing the course of disease progression.

Through innovation, partnerships and community engagement, we have been tackling neurological conditions for >80 years, launching transformative treatments which have made meaningful differences to millions of people worldwide. We continue to collaborate on the development of industry-leading innovative medicines for multiple sclerosis, and in the areas of neuroimmunology, neurodegeneration, and neuromuscular/rare diseases.

To ensure patients everywhere can benefit from these life-changing therapies, we work closely with key stakeholders across the world to ensure rapid access and sustainable accessibility to our medicines, with the aim of providing the best treatment choices for each person's unique journey.

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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,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved 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. 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; 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; 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 an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people’s lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

References

1. Pardo G, Hauser SL, Bar-Or A, et al. Longer-term (up to 6 Years) Efficacy of Ofatumumab in People with Recently Diagnosed and Treatment-Naïve Relapsing Multiple Sclerosis. Oral presentation at the American Academy of Neurology (AAN) 2024 Annual Meeting; April 13-18, 2024; Denver, CO.
2. Wiendl H, Hauser SL, Nicholas J, et al. Longer-term Safety and Efficacy of Ofatumumab in People With Relapsing Multiple Sclerosis for Up to 6 Years. Poster presentation at the American Academy of Neurology (AAN) 2024 Annual Meeting; April 13-18, 2024; Denver, CO.
3. Guthrie EW. Multiple sclerosis: A primer and update. Adv Studies Pharm. 2007;4(11):313-317.
4. 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
5. National MS Society. Types of MS. Accessed January 18, 2023. https://www.nationalmssociety.org/What-is-MS/Types-of-MS
6. Hauser SL, Kappos L, Bar-Or A, et al. The Development of Ofatumumab, a Fully Human Anti-CD20 Monoclonal Antibody for Practical Use in Relapsing Multiple Sclerosis Treatment. Neurol Ther. 2023;12(5):1491-1515. doi:10.1007/s40120-023-00518-0
7. Kesimpta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corp; September 2022.

8. 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.
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. 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.
11. Cohen, JA, Hauser SL, Zielman R., et al. Effect of Longer-term Ofatumumab Treatment on Disability Progression and Brain Volume Change. Poster presentation at: AAN; April 2023; Boston, US.
12. Genmab Press Release: Genmab announces completion of agreement to transfer remaining ofatumumab rights. December 21, 2015. Accessed January 18, 2023. https://ir.genmab.com/static-files/9d491b72-bb0b-4e46-a792-dee6c29aaf7d

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