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MEDIA & INVESTOR RELEASE

Novartis receives positive CHMP opinion for new Xolair® indication to treat severe chronic rhinosinusitis with nasal polyps

- *If approved, Xolair® (omalizumab) will provide patients who have severe chronic rhinosinusitis with nasal polyps, not adequately controlled by intranasal corticosteroids, with the first anti-immunoglobulin E (IgE) antibody specifically designed to target and block IgE, a key driver in the inflammatory pathway*

- *Decision based on results from the Phase III POLYP 1 and 2 studies, in which omalizumab* significantly reduced the size of nasal polyps (defined by Nasal Polyp Score) and improved nasal congestion (defined by Nasal Congestion Score) compared with placebo**[1]

- *Among secondary endpoints, omalizumab reduced post-nasal drip and runny nose, improved sense of smell, and patients reported an improvement in quality of life measures*[1]

- *Omalizumab has a well-established safety record from over 1.3 million patient years of exposure and real-world evidence in severe allergic asthma and chronic spontaneous urticaria*[1]

Basel, June 26, 2020 — Novartis today announced that the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the approval of Xolair® (omalizumab) as an add-on therapy with intranasal corticosteroids (INC) for the treatment of adults (18 years and above) with severe chronic rhinosinusitis with nasal polyps (CRSwNP), for whom therapy with INC does not provide adequate disease control. If approved, omalizumab will be the first treatment for nasal polyps specifically targeting and blocking immunoglobulin E (IgE), which helps to reduce the size of nasal polyps (as defined by Nasal Polyps Score; NPS) and improve symptoms. The European Commission reviews the CHMP recommendation and usually delivers its final decision within two months.

“Patients with chronic rhinosinusitis with nasal polyps suffer from persistent symptoms, such as nasal congestion, facial pain, loss of sense of smell and taste, difficulty breathing and sleep problems, which can significantly impair their quality of life. Unfortunately, many patients continue to experience symptoms despite standard-of-care, and multiple sinus surgeries,” said Professor Philippe Gevaert, Upper Airway Research Laboratory, Department of Otorhinolaryngology, Ghent University Hospital, Ghent, Belgium. “Omalizumab is specifically designed to block immunoglobulin E, which is a key driver in the inflammatory pathway; if approved, it will provide patients, for whom intranasal corticosteroids do not provide adequate

disease control, with a treatment option that has been shown to improve both symptoms and quality of life."

The CHMP positive opinion is based on results from the Phase III POLYP 1 and 2 studies, which were published in the *Journal of Allergy and Clinical Immunology* in June 2020[1]. These replicate studies demonstrated that patients treated with omalizumab achieved statistically significant improvements in mean NPS (POLYP 1: -1.08; p<0.0001, POLYP 2: -0.90; p=0.014) and daily Nasal Congestion Score (NCS; POLYP 1: -0.89; p=0.0004, POLYP 2: -0.70; p=0.0017) compared to placebo at Week 24[1] (co-primary endpoints). All patients received INC (mometasone nasal spray) as background therapy. In both studies, patients treated with omalizumab demonstrated significant improvements in NPS and NCS as early as first assessment (Week 4), compared to placebo[1].

Among secondary endpoints, improvements were observed in the Sino-Nasal Outcome Test-22 (SNOT-22; a health-related quality of life assessment), the University of Pennsylvania Smell Identification Test (UPSIT), the Total Nasal Symptom Score (TNSS) and in sense of smell. Additionally, reductions in post-nasal drip (posterior rhinorrhea) and runny nose (anterior rhinorrhea) were seen[1]. In the studies, omalizumab was generally well tolerated and its safety profile was consistent with previous studies[1].

"Novartis has a mission to reimagine and advance the care of respiratory patients by developing innovative treatment options that treat the disease, reduce symptoms and improve quality of life," said Linda Armstrong, MD, Respiratory Development Unit Head, Novartis Pharmaceuticals. "This CHMP positive opinion builds on the established efficacy and safety profile of omalizumab, which has over 1.3 million patient years of exposure and the potential to become an additional treatment option in the EU for patients with severe chronic rhinosinusitis with nasal polyps."

Novartis is committed to bringing omalizumab to patients with severe CRSwNP and additional regulatory filings are currently underway in multiple countries, including the US and Switzerland.

More broadly, Novartis is dedicated to addressing unmet needs in the wider respiratory area, developing innovative medicines for diseases, including asthma, chronic obstructive pulmonary disease (COPD) and more.

*All patients received INC (mometasone nasal spray) as background therapy.

About Xolair (omalizumab)
Xolair (omalizumab) is the only approved anti-immunoglobulin E (IgE) antibody treatment specifically designed to target and block IgE. By reducing free IgE, down-regulating high-affinity IgE receptors and limiting mast cell degranulation, Xolair minimizes the release of mediators throughout the allergic inflammatory cascade.

An injectable prescription medicine, Xolair is approved for the treatment of moderate-to-severe or severe persistent allergic asthma in more than 100 countries, including the US since 2003 and the EU since 2005. Xolair is approved for the treatment of chronic spontaneous urticaria in over 90 countries including the EU and for chronic idiopathic urticaria (CIU), as it is known in the US and Canada. Xolair has over 1.3 million patient years of exposure. In addition, a liquid formulation of Xolair in pre-filled syringes has been approved in the EU and in more than 20 countries outside of the EU, including Canada, the US, and Australia. The self-administration indication for Xolair in pre-filled syringes was also approved in the EU in 2018, and has since been approved in several other countries, including Australia, Taiwan, Argentina and Brazil. In the US, Novartis and Genentech, Inc. work together to develop and co-promote Xolair. Outside of the US, Novartis markets Xolair and records all sales and related costs.

If approved, Xolair will be indicated as an add-on therapy with intranasal corticosteroids (INC) for the treatment of adults (18 years and above) with severe chronic rhinosinusitis with nasal polyps, for whom therapy with INC does not provide adequate disease control; the first approval in the world for omalizumab in this indication.

About POLYP 1 and POLYP 2[1]

POLYP 1 and POLYP 2 are replicate Phase III studies designed to determine the efficacy and safety of omalizumab compared with placebo in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) who have had an inadequate response to daily intranasal corticosteroid (INC) therapy. All patients received INC (mometasone nasal spray) as background therapy. Both trials were randomized, multicenter, double-blind and placebo-controlled. POLYP 1 involved 138 patients and POLYP 2 involved 127 patients, with and without a history of surgery or prior use of systemic corticosteroids. The co-primary endpoints for both trials were change from baseline in average daily Nasal Congestion Score (NCS), and change from baseline in Nasal Polyp Score (NPS) at Week 24. Patients in the studies were administered either omalizumab or placebo by subcutaneous injection every 2–4 weeks.

Secondary endpoints included change from baseline at Week 24 in Sino-Nasal Outcome Test-22 (SNOT-22), University of Pennsylvania Smell Identification Test (UPSIT), mean daily sense of smell, post-nasal drip, runny nose, and Total Nasal Symptom Score (TNSS); change from baseline at Week 16 in NPS and NCS; and percentage of patients requiring rescue therapy (systemic corticosteroids for ≥3 consecutive days and/or nasal polypectomy) by Week 24. Reduction in need for surgery through Week 24 was predefined as patients achieving NPS of ≤4 (≤2 for each nostril) and at least minimal clinically important difference improvement (≥8.9 points) in SNOT-22. The percentage of patients with comorbid asthma demonstrating minimal clinically important difference improvement (≥0.5 points) in Asthma Quality of Life Questionnaire (AQLQ) through Week 24 was also assessed.

Exploratory endpoints included percentage of patients in the pooled population achieving ≥2-point and ≥1-point improvement in NPS and ≥1-point improvement in NCS. Adverse events (AEs) were assessed for severity and potential causal relationship to the study drug. Patients were monitored to Week 28 as safety follow-up.

About Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

Chronic rhinosinusitis with nasal polyps (CRSwNP) impacts up to 4% of people worldwide. It is a potentially debilitating condition in adults that is characterized by inflammation of the nose and paranasal sinuses with the presence of benign inflammatory polyps (nasal polyps) on the lining of the nasal sinuses or nasal cavity, which can block normal airflow[2-4]. It is possible to have a single polyp or several, and the size of the polyps can vary from microscopic to several centimeters[5,6].

Symptoms can include nasal blockage/obstruction, nasal congestion, nasal discharge, facial pain/pressure and reduction in, or loss of, sense of smell[2,3]. CRSwNP is diagnosed by physical examination with endoscopy. The condition can be associated with asthma, cystic fibrosis and aspirin sensitivity[7]. It is also associated with significant morbidity and decreased health-related quality of life, with quality of life impairment[8-13]. Patients with CRSwNP experience significantly lower health-related quality of life than the general population, with a greater impact for patients with more severe disease, other conditions (comorbidities), or whose CRSwNP has not responded to treatment (refractory disease)[11].

Currently, after standard-of-care, surgery and systemic steroids are the main treatments for this disease all over the world. Many patients choose them; however, they are often not effective in controlling chronic symptoms over time, due to nasal polyps regrowth. After sinus surgery, nasal polyps recur in up to 80% of people, with approximately 40% requiring at least one additional surgery[8]. Approximately 80% of people remain uncontrolled 3–5 years after sinus surgery[14].

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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,” “seek,” “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 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 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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