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MEDIA & INVESTOR RELEASE

Novartis Phase III data confirm sustained efficacy and long-term safety of oral remibrutinib in chronic spontaneous urticaria

- *Patients treated with remibrutinib experienced improvements in weekly urticaria activity scores (UAS7) observed as early as Week 1 and sustained to 1 year (Week 52)*[1]

- *Remibrutinib, an oral Bruton's tyrosine kinase inhibitor, demonstrated a favorable and consistent safety profile up to 1 year, including balanced liver function tests versus placebo*[1]

- *Novartis intends to submit remibrutinib for approval in chronic spontaneous urticaria (CSU) to global health authorities starting in H2 2024, and continues to investigate remibrutinib in multiple immune-mediated conditions*

- *Data reaffirm the first-in-class potential of remibrutinib for the more than 50% of patients with CSU uncontrolled by H1-antihistamines who continue to live with painful and debilitating symptoms*[1,2]

Basel, May 31, 2024 – Novartis today announced new data that confirm the long-term efficacy and safety of remibrutinib, a highly selective Bruton's tyrosine kinase (BTK) inhibitor, in chronic spontaneous urticaria (CSU)[1]. In the pivotal Phase III studies, REMIX-1 and REMIX-2, remibrutinib treatment showed significant symptom improvement early, which was sustained up to Week 52, in patients with CSU who remained symptomatic despite second-generation H1-antihistamine use[1]. These data are being presented at the 2024 European Academy of Allergy and Clinical Immunology (EAACI) Congress in Valencia, Spain, May 31–June 3.

"A large majority of people with CSU are living with uncontrolled and debilitating symptoms, often trying to manage the condition by cycling through antihistamines at higher doses with no lasting respite, impacting heavily on their day-to-day lives," said Martin Metz, Professor of Dermatology, Charité – Universitätsmedizin Berlin, Germany. "Remibrutinib has become an important investigational treatment for CSU as it blocks the BTK cascade and inhibits the release of histamine. These data show that remibrutinib has the potential to offer patients and physicians a well-tolerated oral treatment that provides early and lasting efficacy."

New long-term Phase III REMIX-1 and REMIX-2 data assessed at Week 52 show that[1]:

- Significant improvements with remibrutinib versus placebo, as previously shown at Week 12, were confirmed at Week 24, including in weekly urticaria activity score (UAS7), weekly itch severity score (ISS7), and weekly hive severity score (HSS7)
- At Week 24, patients receiving placebo were transitioned to remibrutinib; responses with remibrutinib were observed as early as the first week after switching and were sustained until the end of the study (28 weeks of treatment)
- Almost half of patients were completely free of itch and hives (UAS7=0) as assessed at Week 52

“Living with CSU can be very distressing due to its unpredictable nature and never knowing when a flare-up may happen. Symptoms can occur on the face, throat, hands, and feet, and people may experience burning and pain on their skin,” said Tonya Winders, President and CEO, Global Allergy and Airways Patient Platform. “Unfortunately, many people continue to cope with uncontrolled symptoms. We welcome further research advancing our knowledge about chronic spontaneous urticaria.”

Remibrutinib was well-tolerated and demonstrated a favorable and consistent safety profile up to 52 weeks, including balanced liver function tests versus placebo[1]. Adverse events (AEs), including serious AEs and treatment discontinuations due to AEs, were comparable between remibrutinib and placebo during the 24-week placebo-controlled period[1]. In addition, exposure-adjusted rates did not increase with long-term treatment[1]. Liver transaminase elevations were balanced across the remibrutinib and placebo treatment groups; all were asymptomatic, transient, and reversible[1]. None of the serious AEs were considered related to study medication by investigators.

“Urticaria is a disease that significantly impacts patients' quality of life and there is an urgent need for new treatment options,” said Angelika Jahreis, Global Head, Development, Immunology, Novartis. “The 52-week REMIX-1 and REMIX-2 Phase III data are significant as many patients who had moderate to severe urticaria at study start were completely free of itch and hives after 52 weeks of treatment and remibrutinib, a highly selective oral BTK inhibitor, continued to be well tolerated. These exciting long-term data will be submitted to global health authorities later this year.”

In addition to CSU, remibrutinib is being investigated in several other immune-mediated conditions, such as hidradenitis suppurativa, where it met its primary endpoint in a Phase II study[3]. It is also being investigated in food allergy, chronic inducible urticaria, and multiple sclerosis[4-8]. Novartis will submit remibrutinib for approval in CSU to global health authorities starting in H2 2024.

About remibrutinib
Remibrutinib is an investigational, highly selective, covalent, oral BTK inhibitor that blocks the BTK cascade and prevents the release of histamine that causes itchy hives (wheals) and swelling[9-11]. When remibrutinib is used alongside standard-dose antihistamines, it results in a “two-pronged approach” where two parts of the inflammatory pathway are targeted, with remibrutinib inhibiting histamine release and antihistamines inhibiting histamine receptors, reducing CSU symptoms[12,13]. In the pivotal Phase III studies, REMIX-1 and REMIX-2, remibrutinib met all primary endpoints in patients with CSU who remained symptomatic despite second-generation H1-antihistamine use[1]. Treatment with remibrutinib showed significant symptom improvement early, which was sustained up to Week 52[1]. Remibrutinib has been shown to be well-tolerated, with a favorable safety profile up to 52 weeks, including balanced liver function tests versus placebo[1]. Most commonly (≥5%) observed AEs in the Phase III REMIX studies were respiratory tract infections (including COVID-19 and nasopharyngitis) and headache, all comparable with placebo[1,14]. If approved in CSU, remibrutinib would offer an effective oral option within the Novartis immunology portfolio, which currently includes Xolair® (omalizumab), the first and only injectable biologic indicated for CSU[15]. In the US, Novartis Pharmaceuticals Corporation and Genentech, a member of the Roche Group, work together to develop and co-promote Xolair. In addition to CSU,

remibrutinib is being investigated in several other immune-mediated conditions and has the potential to be a pipeline in a product[4-8].

About REMIX-1 and REMIX-2

REMIX-1 (NCT05030311) and REMIX-2 (NCT05032157) are two identically designed, global, multicenter, randomized, double-blind, parallel-group, placebo-controlled Phase III studies, with REMIX-1 consisting of 470 participants and REMIX-2 consisting of 455 participants[16,17]. Both studies are designed to establish the efficacy, safety, and tolerability of twice-daily remibrutinib 25 mg treatment in adult participants with CSU that is inadequately controlled by second-generation H1-antihistamines compared with placebo[1,16,17]. The primary outcome measures were absolute change from baseline in weekly urticaria activity score (UAS7) as well as weekly itch severity score (ISS7) and weekly hive severity score (HSS7) at Week 12[16,17]. All participants were on a stable, local label-approved dose of a second-generation H1-antihistamine throughout the entire study[16,17].

About CSU

CSU is the medical term for chronic hives that last for 6 weeks or longer, where the underlying cause is internal rather than exposure to any allergen or external trigger[2,11,18]. CSU affects approximately 40 million people worldwide[2,19]. It is characterized by the sudden appearance of itchy hives (wheals) and/or deep tissue swelling (angioedema, which can occur on the face, throat, hands, and feet)[11,20]. CSU affects all ages but occurs most frequently between the ages of 20–40 years, with women affected nearly twice as often as men[2]. CSU causes significant emotional distress, with the majority of patients suffering from sleep deprivation, and high rates of mental disorders, such as anxiety or depression, as well as impacting on their work productivity[2]. Antihistamines are often prescribed for CSU as they block histamine receptors and prevent the pro-inflammatory action of histamine, which causes itching and swelling[13,18]. However, more than 50% of people with CSU are uncontrolled by H1-antihistamines alone[2].

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