

MEDIA & INVESTOR RELEASE

Novartis remibrutinib Phase III trials met their primary endpoints and showed rapid symptom control in chronic spontaneous urticaria

Ad hoc announcement pursuant to Art. 53 LR

- *The Phase III REMIX-1 and REMIX-2 studies met all primary and secondary endpoints, showing rapid, clinically meaningful improvements across urticaria disease activity scores¹*
- *Patients on remibrutinib saw rapid improvement as early as 2 weeks after treatment initiation¹*
- *Remibrutinib, a highly selective oral BTK inhibitor, was well-tolerated and demonstrated a favorable safety profile, including balanced liver function tests in active and placebo arms across both studies¹*
- *Final (52 weeks) readout and submission in 2024; full data will be presented at upcoming medical meetings*
- *If approved, remibrutinib has the potential to become the first of a new class of chronic spontaneous urticaria (CSU) treatment in a decade, offering a simple and effective option for the 60% of patients uncontrolled by H1-antihistamines²*

Basel, August 09, 2023 — Novartis today announced positive top-line results from the Phase III REMIX-1 and REMIX-2 studies evaluating remibrutinib 25 mg b.i.d., a Bruton's tyrosine kinase (BTK) inhibitor, in patients with chronic spontaneous urticaria (CSU) whose symptoms are inadequately controlled by H1-antihistamines¹. Both Phase III studies met their primary endpoint of absolute change from baseline in weekly urticaria activity score (UAS7) at Week 12, demonstrating clinically meaningful and statistically significant improvements in disease activity¹. The studies will continue until Week 52. Remibrutinib also demonstrated a rapid onset of action as illustrated by the improvement of UAS7 at Week 2 in the REMIX-1 and REMIX-2 studies¹. These data support the potential of remibrutinib as a new, effective and fast-acting oral treatment option for those uncontrolled by first-line H1-antihistamines¹.

“CSU is a distressing and unpredictable disease, and patients urgently need effective, convenient and well-tolerated treatments that can provide rapid and sustained relief from the relentless itching and deep tissue swelling that greatly impact their daily lives,” said Shreeram Aradhye, M.D., President, Global Drug Development and Chief Medical Officer, Novartis.

“These positive top-line results from the Phase III REMIX studies confirm that remibrutinib, a highly selective BTK inhibitor, has the potential to be a first-in-class, oral treatment for people living with CSU whose symptoms are refractory despite use of antihistamines.”

CSU is the medical term for chronic hives that last for 6 weeks or longer, where the underlying cause is internal rather than external exposure to any allergen^{3,4}. Affecting 40 million people worldwide, CSU is characterized by itchy hives (wheals) and/or deep tissue swelling (angioedema), which can occur on the face, throat, hands and feet³⁻⁶. Patients may experience burning, stinging and soreness on the skin where hives occur, causing a severe impact on their quality of life^{2,3,7,8}.

H1-antihistamines are the first-line treatment in CSU². Approximately 60% of patients are inadequately controlled with antihistamines alone and continue to live with the distressing symptoms of CSU². While injectable biologic therapies are an effective option for those whose CSU is uncontrolled by antihistamines, less than 20% of patients worldwide are treated with them¹. BTK is an enzyme central to the release of histamine, and when spontaneously activated plays a critical role in the debilitating symptoms associated with CSU⁹.

Discovered and developed by Novartis, remibrutinib is a highly selective oral BTK inhibitor that has the potential to provide rapid, sustained control of CSU within 2 weeks of initiation. It continues to show a favorable safety profile across several immune-mediated conditions including multiple sclerosis, hidradenitis suppurativa and food allergy¹⁰⁻¹³. Patients currently enrolled in REMIX-1 and REMIX-2 will continue to receive treatment up to Week 52 and will have the opportunity to continue in a long-term extension trial^{14,15}.

Novartis will present the REMIX data at an upcoming medical meeting and intends to submit to global health authorities starting in 2024.

About remibrutinib

Remibrutinib is a highly selective, oral Bruton's tyrosine kinase (BTK) inhibitor that blocks the BTK cascade and prevents the release of histamine that causes itch, hives/welts and swelling^{9,16}. In Phase II studies, remibrutinib demonstrated fast onset of action and sustained efficacy in patients with moderate to severe chronic spontaneous urticaria (CSU)⁹. Remibrutinib has been shown to be well-tolerated across all doses studied in Phase II⁹. These results have now been confirmed by the Phase III REMIX data¹. In addition to CSU, remibrutinib is being investigated in other immune-mediated conditions, such as multiple sclerosis, hidradenitis suppurativa, food allergy and Sjögren's syndrome^{10-13,17}. If approved, remibrutinib has the potential to become an effective oral option to complement Xolair® (omalizumab), the first and only injectable biologic indicated for CSU¹⁸. In the US, Novartis Pharmaceuticals Corporation and Genentech, a member of the Roche Group, work together to develop and co-promote Xolair.

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^{14,15}. Both studies are designed to establish the efficacy, safety and tolerability of remibrutinib in adult participants with chronic spontaneous urticaria that is inadequately controlled by second generation H1-antihistamines compared with placebo^{14,15}. The primary outcome measures include absolute change from baseline in the weekly urticaria activity score, absolute change in itch severity score and hive severity score at Week 12^{14,15}. Patients currently enrolled in REMIX-1 and REMIX-2 will continue to receive treatment up to Week 52 and will have the opportunity to continue in a long-term extension trial^{14,15}.

About chronic spontaneous urticaria (CSU)

CSU affects approximately 40 million people worldwide^{4,5}. CSU is characterized by the sudden appearance of itchy hives (wheals) and/or deep tissue swelling (angioedema) for

more than 6 weeks, affecting all ages but most frequently between 20–40 years, with women affected nearly twice as often as men^{3,4}. CSU causes significant emotional distress, with the majority of patients suffering from sleep deprivation, and high rates of mental disorders, such as anxiety or depression⁴. There are currently limited effective treatment options for CSU, with many patients not achieving full control from the first-line treatment, antihistamines^{2,3,7}.

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,” “investigational,” “continue,” “to assess,” “to establish,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for remibrutinib, or regarding potential future revenues from remibrutinib. 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 remibrutinib 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 remibrutinib will be commercially successful in the future. In particular, our expectations regarding remibrutinib 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

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