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MEDIA UPDATE

Novartis data show rapid and effective disease activity control with remibrutinib (LOU064) in patients with chronic spontaneous urticaria

- *Results from a Phase IIb study show all remibrutinib doses provided significant improvements in UAS7 change from baseline at week 4 and week 12 compared to placebo, and a favorable safety profile across the entire dose range tested*

- *All doses provided clinically meaningful improvements with respect to the proportion of patients achieving UAS7=0 (complete absence of hives and itch) and UAS7≤6 (well-controlled disease activity) vs. placebo over the treatment period, starting as early as Week 1*

- *Remibrutinib is a highly selective, potent oral BTK inhibitor with a potential best-in-class profile, under investigation for a number of immune-mediated conditions; Phase III studies in CSU are expected to begin enrolling patients by the end of 2021*

- *Novartis datasets at EADV 2021 demonstrate our continued commitment to innovation in immuno-dermatology, aiming to ease the burden of these life-limiting diseases*

- *CSU is a distressing and unpredictable disease that remains inadequately controlled for many, highlighting the importance of pursuing new modes of action*

Basel, September 30, 2021 — Novartis today announced positive Phase IIb data showing remibrutinib (LOU064), a potentially best-in-class oral BTK inhibitor, demonstrated rapid and effective disease control in patients with inadequately controlled chronic spontaneous urticaria (CSU). The data were presented as a late-breaking abstract at the European Academy of Dermatology and Venereology (EADV) 30th Anniversary Congress.

This randomized, double-blind, placebo-controlled study (NCT03926611) evaluated the efficacy and safety of remibrutinib over 12 weeks in patients inadequately controlled with antihistamines. Patients (n=311) were randomized to placebo or different doses of remibrutinib, taken orally. The primary endpoint was achieved with remibrutinib showing a statistically significant dose-response compared to placebo with respect to change from baseline in UAS7 score at Week 4[1].

All remibrutinib doses provided significant improvements with respect to change from baseline in UAS7 at Week 4 and at Week 12 ($p<0.0001$ for all doses vs placebo) and demonstrated a

rapid improvement as of Week 1. Compared with placebo, more patients receiving any remibrutinib dose achieved a complete control with absence of hives and itch (UAS7=0) or well-controlled disease (UAS7≤6) until Week 12 (end of treatment). Remibrutinib showed a favorable safety profile and good tolerability across the entire dose range tested, with no dose-dependent pattern.

“Up to one percent of the world’s population is affected by CSU[2] and we are proud of our contribution to advancing treatment. Despite these advances, there continues to be a need for new CSU therapies and we are committed to challenge the boundaries of innovation,” said Angelika Jahreis, M.D., Ph.D., Novartis Global Head Development Unit Immunology, Hepatology & Dermatology. “The fast-onset of control achieved with this novel oral agent in patients with previously inadequately-controlled CSU is compelling, and we are excited to rapidly develop remibrutinib.”

CSU is a distressing and unpredictable disease, characterized by the occurrence of itchy wheals (hives), angioedema, or both for 6 weeks or more without specific external stimuli[3,4] and can have a major negative impact on patients’ quality of life[2]. It most commonly persists for 1-5 years, but in some cases even longer. Despite existing treatments, the disease remains inadequately controlled in a large portion of patients[5].

Remibrutinib is a highly selective, potent oral BTK inhibitor discovered within Novartis[6,7] and being developed in a number of clinical and early settings. With an unmet need for new CSU therapies, highlighting the importance of targeting new modes of action, BTK inhibition may be an attractive therapeutic option for CSU, due to its pivotal role in FcεR1-mediated (high affinity receptor of IgE) signalling of mast cells and basophils and their relevance to CSU pathogenesis.

About the study
NCT03926611 is a Phase IIb, dose-finding, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of remibrutinib over 12 weeks of treatment in patients with at least moderately active CSU, inadequately controlled by second generation H1-antihistamines. Eligible patients had CSU for ≥6 months and a weekly urticaria activity score (UAS7) ≥16 at randomization. The primary aim was to establish a dose-response relationship for remibrutinib with respect to change from baseline (CFB) in UAS7 at Week 4. Secondary endpoints included CFB in UAS7 over time; UAS7=0 (complete absence of hives and itch) over time, UAS7≤6 (well-controlled disease response) over time and recording of adverse events (AEs) to assess safety[1].

Novartis in chronic spontaneous urticaria (CSU)
Novartis is curious about the science beneath the skin and dedicated to reimagining the care of patients with diseases that can severely limit quality of life such as CSU, psoriasis, acne, and atopic dermatitis. Novartis is committed to developing medicines that will advance the treatment of CSU, so patients are able to live their lives without the distressing and unpredictable symptoms of this debilitating disease. These include ligelizumab (QGE031) a next generation high-affinity monoclonal anti-immunoglobulin (Ig) E antibody and remibrutinib (LOU064) a potentially best-in-class oral BTK inhibitor. It is intended that these investigational therapies will complement Xolair, our existing approved add-on therapy for CSU.

In the US, Novartis and Genentech, a member of the Roche Group, work together to develop and co-promote Xolair. Outside the US, Novartis markets Xolair and records all sales and related costs.

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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.

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References

1. Maurer, M, Berger, W, et al. *The Bruton's Tyrosine Kinase Inhibitor Remibrutinib (LOU064) in Chronic Spontaneous Urticaria: Top Line Results of a Phase 2b Dose-Finding Study*. Presented at the EADV Congress 2021.
2. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA^{2}LEN task force report. *Allergy*. 2011;66(3):317-330.
3. Grattan, C. The urticarias: pathophysiology and management. Clin Med (Lond) 2012;12(2):164-7. (http://www.ncbi.nlm.nih.gov/pubmed/22586795).
4. Zuberbier, T, Aberer W, Asero R, et al. The EAACI/GA(2)LEN/EDF/WAO guideline for definition, classification, diagnosis and management of urticaria. Allergy 2018;73(7): 1393-1414.DOI:10.1111/all.13397.
5. Kaplan A, Ferrer M, Bernstein JA, et al. Timing and duration of omalizumab response in patients with chronic idiopathic/spontaneous urticaria. J Allergy Clin Immunol 2016;137(2):474-81. DOI:10.1002/j.jaci.2015.08.023
6. Angst D, Gessier F, Janser P, et al. Discovery of LOU064 (Remibrutinib), a Potent and Highly Selective Covalent Inhibitor of Bruton's Tyrosine Kinase. Journal of Medicinal Chemistry 2020, 63, 10, 5102-5118 https://doi.org/10.1021/acs.jmedchem.9b01916

7. Kaul M, End P, Cabanski M,et al. Remibrutinib (LOU064): A selective potent oral BTK inhibitor with promising clinical safety and pharmacodynamics in a randomized phase I trial. *Clin Transl Sci*. 2021;00:1–13. https://doi.org/10.1111/cts.13005

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