

MEDIA & INVESTOR RELEASE

Novartis provides an update on Phase III ligelizumab (QGE031) studies in chronic spontaneous urticaria (CSU)

Ad hoc announcement pursuant to Art. 53 LR

- *Ligelizumab, a high-affinity anti-IgE antibody, demonstrated superiority compared with placebo at Week 12 in Phase III PEARL 1 and PEARL 2 trials, but not versus omalizumab¹*
- *Novartis is continuing to evaluate the PEARL data and will provide an update in due course as well as next steps for the program*

Basel, December 20, 2021 – Novartis today announced top-line results from PEARL 1 and PEARL 2 Phase III studies in chronic spontaneous urticaria (CSU), which showed that the studies met their primary endpoints of superiority for ligelizumab versus placebo at Week 12, but not versus omalizumab¹.

“We are disappointed that we have been unable to demonstrate superior efficacy for ligelizumab versus standard of care in the treatment of CSU,” said John Tsai, M.D., Head of Global Drug Development and Chief Medical Officer, Novartis. “We will continue to evaluate the potential for ligelizumab to bring benefit to patients in the areas of chronic inducible urticaria (CIndU) and food allergy, where there is significant unmet need.”

Full PEARL 1 and 2 Phase III data will be made publicly available after study completion in the second half of 2022.

CSU is an unpredictable, systemic skin disease, characterized by the spontaneous and recurrent appearance of itchy, painful hives (wheals) on the skin, angioedema or both for at least 6 weeks^{2,3} and affects up to 1% of the population at any one time². Approximately 60% of patients do not achieve complete control with first-line treatment antihistamines⁴⁻⁷.

Novartis recently began Phase III studies for remibrutinib (LOU064), a highly selective, potent oral BTK inhibitor that has previously shown rapid and effective CSU disease control^{8,9}.

Novartis in chronic spontaneous urticaria (CSU)

Novartis is 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 disease¹⁰. These include ligelizumab (QGE031) a high-affinity monoclonal anti-immunoglobulin E antibody and remibrutinib (LOU064), a highly selective, potent oral Bruton's tyrosine kinase (BTK) inhibitor with a potential best-in-class profile for the treatment of autoimmune disorders. Any new therapies will add to our portfolio of medicines that already includes Xolair[®] (omalizumab), our existing approved therapy for CSU.

About ligelizumab

Ligelizumab (QGE031) is a high-affinity, monoclonal anti-immunoglobulin (Ig) E antibody. In a Phase IIb dose-finding trial, more patients experienced complete resolution of wheals (hives) with ligelizumab compared with Xolair[®] (omalizumab)¹¹.

About PEARL 1 and PEARL 2

PEARL 1 and PEARL 2 (NCT03580369 and NCT03580356) are two identically designed Phase III, multicenter, randomized, double-blind, active- and placebo-controlled, parallel-group studies^{12,13}. The twin studies are designed to establish efficacy and safety of ligelizumab in adult and adolescent patients (≥12 years of age) with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1-antihistamine treatment by demonstrating better efficacy over placebo and Xolair[®] (omalizumab)^{12,13}. More than 2,000 adult and adolescent patients across 48 countries were randomized to ligelizumab 72 mg, ligelizumab 120 mg, omalizumab 300 mg or placebo with treatment given every 4 weeks for 1 year¹²⁻¹⁴. Patients initially randomized to placebo were switched to ligelizumab 120 mg from Week 24 until the end of the 52-week treatment period. The primary outcome measured the change from baseline in Urticaria Activity Score over 7 days (UAS7) at Week 12¹²⁻¹⁴.

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," "plan," "may," "could," "would," "expect," "anticipate," "seek," "look forward," "believe," "committed," "investigational," "pipeline," "launch," "dedicated," "continuing," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for ligelizumab, or regarding potential future revenues from ligelizumab. 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 ligelizumab 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 ligelizumab will be commercially successful in the future. In particular, our expectations regarding ligelizumab 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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at <https://www.novartis.com>.

Novartis is on Twitter. Sign up to follow @Novartis at <https://twitter.com/novartisnews>

For Novartis multimedia content, please visit

<https://www.novartis.com/news/media-library>

For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Novartis Data on File.
2. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA2LEN task force report. *Allergy*. 2011;66:317-330.
3. Vestergaard C and Deleuran M. Chronic spontaneous urticaria: latest developments in aetiology, diagnosis and therapy. *Ther Adv Chronic Dis*. 2015;6:304-13.
4. Zuberbier T, Latiff A, Abuzakouk M, et al. The international EAACI/GA2LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. Published 2021 Sept 18. doi:10.1111/all.15090.
5. Kaplan AP. Chronic Spontaneous Urticaria: Pathogenesis and Treatment Considerations. *Allergy Asthma Immunol Res*. 2017;9(6):477-482. doi:10.4168/air.2017.9.6.477
6. Maurer M, Costa C, Gimenez Arnau A, et al. Antihistamine- resistant chronic spontaneous urticaria remains undertreated: 2-year data from the AWARE study. *Clin Exp Allergy*. 2020;50(10):1166-1175. doi:10.1111/cea.13716.
7. Guillén-Aguinaga S, Jáuregui Presa I, Aguinaga-Ontoso E, Guillén-Grima F, Ferrer M. Updosing non-sedating antihistamines in patients with chronic spontaneous urticaria: a systematic review and meta-analysis. *Br J Dermatol*. 2016;175(6):1153-1165. doi:10.1111/bjd.14768.
8. ClinicalTrials.gov. A Phase 3 Study of Efficacy and Safety of Remibrutinib in the Treatment of CSU in Adults Inadequately Controlled by H1 Antihistamines (REMIX-1). NCT05030311. Available from: <https://clinicaltrials.gov/ct2/show/NCT05030311>. [Last accessed: December 2021].
9. ClinicalTrials.gov. A Phase 3 Study of Efficacy and Safety of Remibrutinib in the Treatment of CSU in Adults Inadequately Controlled by H1- Antihistamines. NCT05032157. Available from: <https://clinicaltrials.gov/ct2/show/NCT05032157>. [Last accessed: December 2021].
10. Weller K, Maurer M, Grattan C, et al. ASSURE-CSU: a real-world study of burden of disease in patients with symptomatic chronic spontaneous urticaria. *Clin Transl Allergy*. 2015;5:29.
11. Maurer M, Giménez-Arnau AM, Sussman G, et al. Ligelizumab for Chronic Spontaneous Urticaria. *N Engl J Med*. 2019;381:1321-1332.
12. ClinicalTrials.gov. NCT03580369. A Phase III Study of the Efficacy and Safety of Ligelizumab in the Treatment of CSU in Adolescents and Adults Inadequately Controlled with H1-antihistamines [online] April 2020. Available from: <https://clinicaltrials.gov/ct2/show/NCT03580369> [Last accessed: December 2021].
13. ClinicalTrials.gov. NCT03580356. A Phase III Study of the Efficacy and Safety of Ligelizumab in the Treatment of CSU in Adolescents and Adults Inadequately Controlled with H1-antihistamines [online] March 2020. Available from: <https://clinicaltrials.gov/ct2/show/NCT03580356> [Last accessed: December 2021].
14. Severin T, Maurer M, Giménez-Arnau A, et al. Ligelizumab versus omalizumab in CSU: Phase 3 design and rationale. Presented at the 4th GA2LEN Global Urticaria Forum; December 5–6 2018; Berlin, Germany.

###

Novartis Media Relations

E-mail: media.relations@novartis.com

Michael Meo
Novartis Global Media Relations
+1 862 274 5414 (mobile)
michael.meo@novartis.com

Louise Clark
Novartis Global Communications
+41 79 123 8172 (mobile)
louise.clark@novartis.com

Julie Masow
Novartis US External Communications
+1 862 579 8456
julie.masow@novartis.com

Novartis Investor Relations

Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 345 4440
Thomas Hungerbuehler	+41 61 324 8425	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973-876-4912