# Innovation fueled by compassion

We're striving to help more people with chronic spontaneous urticaria—a skin condition marked by hives and distressful itching—return to their daily lives.

Dec 12, 2023

Picture it: a person lying awake at night, uncomfortable and unable to fall asleep, as hives start to materialize all over their body, a cruel symphony of itching that just won't stop.

Angelika Jahreis, Global Head, Development, Immunology, Novartis

They tried the standard-of-care, antihistamines, to address the problem, but it wouldn't subside, joining the large percentage of other patients with chronic spontaneous urticaria (CSU) who don't respond to those medications. So there they are in bed: Tired, feeling helpless, and possibly depressed or anxious[1,2].

> CSU is often not a life-threatening disease, but it can take a real emotional toll on you and your family because it never stops, and it's psychologically extremely difficult. That's why it has been so critical to find new therapeutic options for these patients—so they could live their daily lives.

**Angelika Jahreis**, Global Head, Development, Immunology, Novartis.

## Following the science

Inhibiting an essential protein known as Bruton's tyrosine kinase (BTK) started out as a treatment for certain blood cancers, but about 20 years ago, when researchers confirmed the abnormal role certain immune cells played tied to BTK can play in autoimmunity, as well, possibilities opened up[3].

Evidence suggested that BTK is a central player in the commonly accepted autoimmune or auto-allergic pathogenesis of CSU that ultimately leads to the histamine release causing itching hives and swelling, the main signs and symptoms of CSU[4].

Backed by emerging science, researchers at Novartis saw the potential in inhibiting BTK to treat autoimmune diseases, like CSU. They also knew they needed a different type of medicine, a more precise one that could specifically target and inhibit BTK for a longer period, while having minimal effect on other biological processes[5].

Thanks to innovative efforts from the chemistry team, notably Robert Pulz and Daniela Angst, of Biomedical Research's Chemistry Discovery group, Novartis developed a highly selective, oral therapy that, in preclinical studies, showed it could inhibit BTK and reduce inflammation[5].

"There was a lot of excitement around the early data that this could be something very meaningful," said Thomas Severin, a Global Program Head in Immunology for Novartis. "Not to mention a real ambition to move this into human studies and forward in a fast way."

## Accelerating for patients

CSU—which affects an estimated 40 million people around the world—leaves people with an unpredictable onset of long-lasting hives, itching, and deep tissue swelling that can impact their daily life, both at home and work[1].

Antihistamines are the first-line treatment in CSU; however, more than 50% of the people who don't respond continue to live with distressing symptoms[6,7,8].

Motivated by this high patient need, Novartis sought out innovative ways to keep the work moving as fast and efficiently as possible.

A positive early skin prick test in healthy volunteers with asymptomatic skin conditions allowed the team to skip ahead to a later stage trial that would go on to show encouraging results halfway through the study[9]. This also meant the team could quickly advance planning with health authorities and other groups across R&D to design and conduct the next, larger Phase III studies.

More than 900 participants from around the world would eventually take part.

"Developing new medicines can take a decade or longer," Jahreis said. "When there are opportunities to shave off some time in R&D, you take it. Because patients are waiting."

Bruno Cenni, Executive Director, Immunology, Biomedical Research

The momentum hasn't stopped.

Positive new data from these pivotal studies continue to emerge, paving the way for possibility after years of scientific rigor fueled by the desire to find better treatment options for patients in need—day and night[10,11,12,13].

"We believed in the approach throughout, from the first idea," said Bruno Cenni, Executive Director, Immunology, Biomedical Research. "So it's extremely gratifying to see how far we've come."

## Immunology

Working to create a world where the millions of people with immunological conditions, and those who treat them, can live without compromise.

Learn more

References:


1. 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.
2. Patients with Chronic Urticaria Remain Largely Undertreated: Results from the DERMLINE Online Survey. Dermatol Ther (Heidelb). 2021 Jun; 11(3): 1027–1039. doi: 10.1007/s13555-021-00537-5.
3. Jonathan C.W. Edwards, M.D., Leszek Szczepański, M.D., Ph.D., et al. Efficacy of B-Cell–Targeted Therapy with Rituximab in Patients with Rheumatoid Arthritis. N Engl J Med 2004; 350:2572-2581 doi: 10.1056/NEJMoa032534
4. Maurer M, Berger W, Gimenez-Arnau A, et al. Remibrutinib, a novel BTK inhibitor, demonstrates promising efficacy and safety in chronic spontaneous urticaria. J Allergy Clin Immunol. 2022;150:1498–1506.
5. Daniela Angst, François Gessier, Philipp Janser, et al. Discovery of LOU064 (Remibrutinib), a Potent and Highly Selective Covalent Inhibitor of Bruton's Tyrosine Kinase. J Med Chem 2020 May 28;63(10):5102-5118 doi: 10.1021/acs.jmedchem.9b01916.
6. 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.
7. Guillen-Aguinaga S, Jauregui Presa I, Aguinaga-Ontoso E, et al. Updosing nonsedating antihistamines in patients with chronic spontaneous urticaria: a systematic review and meta-analysis. Br J Dermatol. 2016;175:1153–1165.
8. The World Bank. Population, total. Available from: https://data.worldbank.org/indicator/SP.POP.TOTL [Last accessed: November 2023].
9. Martin Kaul, Peter End, Maciej Cabanski, 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 Sep; 14(5): 1756–1768. doi: 10.1111/cts.13005
10. Novartis remibrutinib Phase III trials met their primary endpoints and showed rapid symptom control in chronic spontaneous urticaria. Novartis; 2023. Accessed October 4, 2023. https://www.novartis.com/news/media-releases/novartis-remibrutinib-phase-iii-trials-met-their-primary-endpoints-and-showed-rapid-symptom-control-chronic-spontaneous-urticaria
11. ClinicalTrials.gov. NCT05030311. A Phase 3 Study of Efficacy and Safety of Remibrutinib in the Treatment of CSU in Adults Inadequately Controlled by H1 Antihistamines (REMIX-1). Available from: https://clinicaltrials.gov/study/NCT05030311 [Last accessed: November 2023].
12. ClinicalTrials.gov. NCT05032157. A Phase 3 Study of Efficacy and Safety of Remibrutinib in the Treatment of CSU in Adults Inadequately Controlled by H1- Antihistamines (REMIX-2). Available from: https://clinicaltrials.gov/study/NCT05032157 [Last accessed: November 2023].
13. Sarbjit S, Giménez-Arnau A, Hide M, et al. Fast Symptom Improvement and Favorable Safety Profile With Remibrutinib in Chronic Spontaneous Urticaria: REMIX-1/-2 Studies. Presented as a late-breaking abstract at ACAAI 2023.

---