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Long-Term Efficacy and Safety of Remibrutinib in Patients With Chronic Spontaneous Urticaria in the Phase 3 REMIX-1 and REMIX-2 Studies

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Late ORAL Abstract Session on Clinical Trials (L-OAS-CT 01)

Clinical Trials

Friday 31 May 2024, 16:45-18:15 CET

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Disclosures and Acknowledgements

In relation to this presentation, the following real or perceived conflicts of interest were declared:

MMetz is or recently was a speaker and/or advisor for AbbVie, Amgen, AstraZeneca, argenx, Bayer, Beiersdorf, Celldex, Celltrion, Escient, Galderma, gsk, Incyte, Jasper, Novartis, Pharvaris, Pfizer, Regeneron, Sanofi, Teva, ThirdHarmonicBio, Vifor. **AG-A** reports roles as a medical advisor for Uriach, Sanofi, Genentech, Novartis, FAES, GSK, Amgen, and Thermo Fisher and has research grants supported by Uriach, Novartis and Instituto de Salud Carlos III, FEDER; she also participates in educational activities for Uriach, Novartis, Genentech, Menarini, LEO Pharma, GSK, MSD, Ammirall, Avène, and Sanofi. **MH** has received lecture and/or consultation fees from Japan Tabaclo, Kaken Pharmaceutical, Kyorin Pharmaceutical, Kyowa Kirin, Meiji Seika, Mitsubishi Tanabe Pharma, Nippon Zoki, Novartis, Sanofi, TAIHO Pharmaceutical, and Teikoku Seiyaku. **VJ** has consulted as/or advised and/or received research funding from Pediapharm, Medexus, Sanofi, Regeneron, Bausch, Novartis, AbbVie, Aralez, ALK, Celgene, Amgen, Leo Pharma, Mylan, Pfizer, Covis Pharma, Galderma, Eli Lilly, GSK, Incyte, Arcutis, Janssen, and AstraZeneca. **AK** has been a consultant for and/or has received honoraria and/or investigator fees from AbbVie, Actelion, Ammirall, Amgen, Basilea, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Forward Pharma, GlaxoSmithKline, Galderma, Genentech, Janssen, La Roche Posay, LEO Pharma, Medac, Merck Sharp & Dohme, Novartis, Pierre Fabre Dermatologie, Pfizer, Regeneron, Roche, Sanofi and UCB Pharma. **ML** is an employee of Mount Sinai and receives research funds from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant Sciences, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc., and is a consultant for Aditum Bio, Ammirall, AltruBio Inc., AnaptysBio, Arcutis, Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd., LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica. **MP** serves as a speaker for AstraZeneca, CSL Behring, Grifols, Regeneron, Sanofi Genzyme and Amgen. **SS** has received grant/research/clinical trial support from the National Institutes of Health, Novartis, Sanofi, Amgen, and Regeneron and is a consultant/advisory board member for Allakos, Granular Therapeutics, Novartis, Aquestive, Regeneron, Escient, Innate, Celltrion, and Sanofi. **GS** has received research support from Aimmune, Amgen, AstraZeneca, DBV Technologies, Genentech, Kedrion S.p.A, Leo Pharma, Novartis, Nuvo Pharmaceuticals, Sanofi, Stallergenes, Merck, Schering Plough, Regeneron, and ALK; is a medical advisor and/or has received payment for lectures from Merck, Novartis, CSL Behring, Pfizer, Anaphylaxis Canada, the Allergy Asthma and Immunology Society of Ontario, and the Canadian Hereditary Angioedema Network. **ES** has acted as a speaker/consultant/advisor for Sanofi, Pfizer, Abbvie, Novartis, Lilly and Johnson&Johnson. **RS** serves as a speaker for AstraZeneca and Pharming, and has received clinical trial support and/or consulting fees from Genentech, Sanofi, Arcutis, AstraZeneca, GSK, Abbvie, Amgen, Novartis, and Regeneron. **IWH** has received lecture and/or consultation fees from Novartis, Sanofi, AbbVie, Leo Pharma, Pfizer, Eli Lilly, and AstraZeneca, Ammirall, Boehringer Ingelheim, GlaxoSmithKline, Janssen, Medac, UCB Pharma, Boehringer Ingelheim. **HW** has served as a Principle Investigator for Novartis, Sanofi, Astra-Zeneca, Areteia, Chiesi, and Teva. **SH, KL, PGPM, E-DM, NS, PW, and AZ** are employed by Novartis. **MMaurer** is or recently was a speaker and/or advisor for and/or has received research funding from Amgen, Allakos, Aralez, AstraZeneca, Celldex, FAES, Genentech, GI Innovation, Kyowa Kirin, LEO Pharma, Menarini, Novartis, Moxie, MSD, Roche, Sanofi, Third Harmonic, UCB, and Uriach.

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Remibrutinib is a novel, highly selective, oral BTK inhibitor

- Despite treatment with standard-dose second-generation H₁-AHs, >50% of patients with CSU remain symptomatic¹
- Updosing of second-generation H₁-AHs, up to 4X the standard dose, provides no or only partial relief in 75% of these patients²
- In the phase 3 REMIX-1 and REMIX-2^a studies, remibrutinib demonstrated statistically significant superiority in both primary endpoint scenarios (UAS7 and ISS7/HSS7 at week 12) vs placebo in patients with CSU remaining symptomatic with second-generation H₁-AHs³

This figure has been published in the New England Journal of Medicine.
It can be found by clicking here: [Metz M, et al. N Engl J Med. 2025;392\(10\):984-94.](#)

Saini S, et al. Abstract presented at ACAAI Annual Scientific Meeting 2023. Abstract LB001. Reprinted with permission by the author.

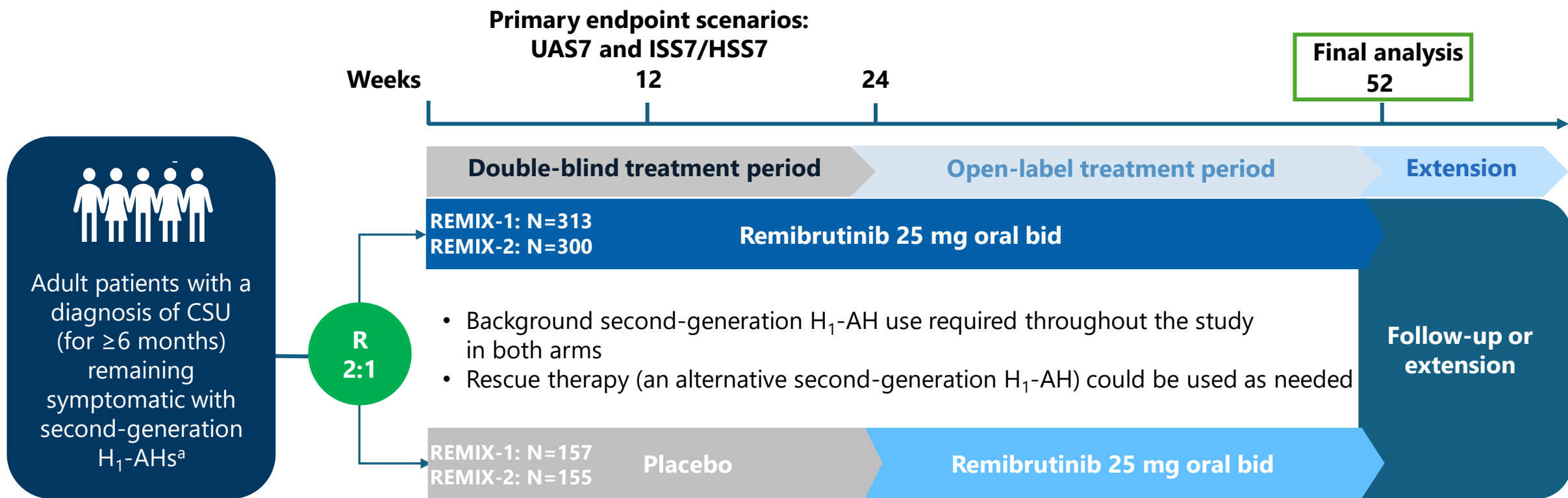
Objective: To present the final, long-term (week 52) analysis of the REMIX-1 and REMIX-2 studies

AH, antihistamine; BTK, Bruton's tyrosine kinase; CSU, chronic spontaneous urticaria; FcεRI, high-affinity IgE receptor; H1, histamine-1; HSS7, weekly Hives Severity Score; Ig, immunoglobulin; ISS7, weekly Itch Severity Score; LYN, LCK/YES novel tyrosine kinase; SYK, spleen tyrosine kinase; UAS7, weekly Urticaria Activity Score.

^a REMIX-1: NCT05030311; REMIX-2: NCT05032157.

1. Guillen-Aguinaga S, et al. British J Derm. 2016;175:1153-1165. 2. Bernstein J, et al. Oral presentation at: ACAAI 2023 Annual Scientific Meeting; November 9-13, 2023; Anaheim, CA. Abstract D006. 3. Saini S, et al. Oral presentation at: ACAAI 2023 Annual Scientific Meeting; November 9-13, 2023; Anaheim, CA. Abstract LB001.

REMIX-1 and REMIX-2: Week 52 Analysis



- REMIX-1 and -2 are identical, randomized, placebo-controlled studies of oral remibrutinib 25 mg bid conducted in parallel; efficacy is assessed for each study, safety data is from a pooled analysis of both studies

bid, twice daily; CSU, chronic spontaneous urticaria; H₁, histamine 1; HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; UAS7, weekly Urticaria Activity Score.

^a Presence of itch and hives for ≥6 consecutive weeks prior to screening despite the use of a second-generation H₁-antihistamine; UAS7 score ≥16, ISS7 score ≥6, and HSS7 score ≥6 during the 7 days prior to randomization (day 1).

**This table has been published in the New England Journal of Medicine.
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Patients
randomized

REMIX-1
N=470

Remibrutinib
n=313

Placebo→
remibrutinib
n=157

REMIX-2
N=455

Remibrutinib
n=300

Placebo→
remibrutinib
n=155

Discontinued treatment, n (%) ^a	Remibrutinib n=313	Placebo→ remibrutinib n=157	Remibrutinib n=300	Placebo→ remibrutinib n=155
Patient decision	57 (18.2)	30 (19.1)	65 (21.7)	41 (26.5)
AE	31 (9.9)	18 (11.5)	36 (12.0)	18 (11.6)
Unsatisfactory therapeutic effect	15 (4.8)	5 (3.2)	13 (4.3)	8 (5.2)
Physician decision	4 (1.3)	3 (1.9)	4 (1.3)	7 (4.5)
Lost to follow-up	4 (1.3)	2 (1.3)	7 (2.3)	2 (1.3)
Protocol deviation	3 (1.0)	1 (0.6)	0	3 (1.9)
Pregnancy	0	1 (0.6)	5 (1.7)	1 (0.6)
	0	0	0	2 (1.3)

- Rates of treatment discontinuation were comparable between remibrutinib and placebo



Remibrutinib Demonstrated Significant Improvement in UAS7 vs Placebo

**This figure has been published in the New England Journal of Medicine.
It can be found by clicking here: [Metz M, et al. N Engl J Med. 2025;392\(10\):984-94](#).**

- Remibrutinib demonstrated superiority vs placebo for the primary endpoint of change from baseline in UAS7 at week 12
- Significant improvements with remibrutinib vs placebo were sustained at week 24

bid, twice daily; BL, baseline; LS, least squares; UAS7, weekly Urticaria Activity Score.

^a Full analysis set; imputed data. Statistical significance (one-sided p value) in change from baseline in UAS7 with remibrutinib vs placebo at week 12 was assessed using a linear mixed model with repeated measures.

Remibrutinib Demonstrated Significant Improvement in Itch and Hives vs Placebo

This figure has been published in the New England Journal of Medicine.
It can be found by clicking here: [Metz M, et al. N Engl J Med. 2025;392\(10\):984-94\).](#)



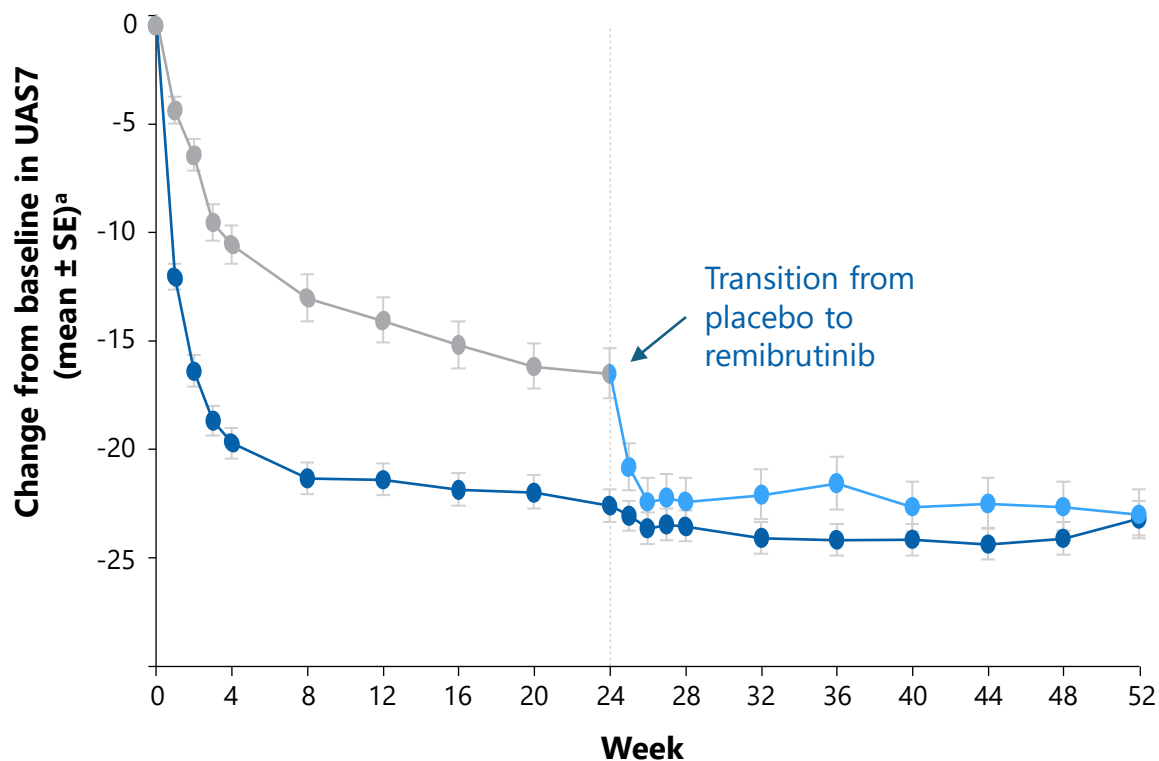
bid, twice daily; BL, baseline; HSS7, weekly Hives Severity Score; ISS7, weekly Itch Severity Score; LS, least squares.

^a Full analysis set; imputed data. Statistical significance (one-sided p value) in change from baseline in ISS7 and HSS7 with remibrutinib vs placebo at week 12 was assessed using a linear mixed model with repeated measures.

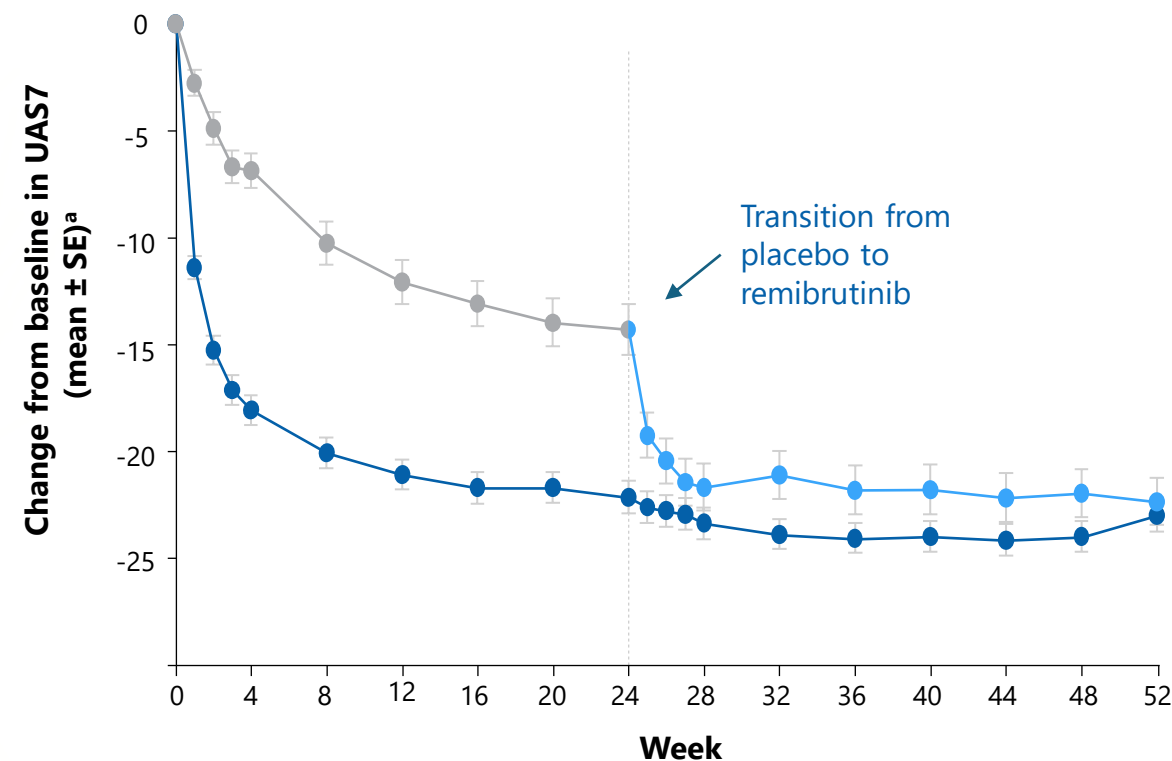
***P* < .001**

Improvements in UAS7 With Remibrutinib Were Observed as Early as Week 1 and Were Sustained to Week 52

REMIX-1



REMIX-2



Remibrutinib 25 mg bid Placebo \rightarrow remibrutinib 25 mg bid

bid, twice daily; UAS7, weekly Urticaria Activity Score.

^a Full analysis set; observed data.



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Significantly More Patients Achieved Well-Controlled Disease ($\text{UAS7} \leq 6$) With Remibrutinib vs Placebo at Weeks 2, 12, and 24

This figure has been published in the New England Journal of Medicine.
It can be found by clicking here: [Metz M, et al. N Engl J Med. 2025;392\(10\):984-94\).](#)



Significantly More Patients Achieved Complete Response (UAS7=0) With Remibrutinib vs Placebo at Weeks 12, and 24

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Complete Responses (UAS7=0) With Remibrutinib Were Observed Early and Were Sustained to Week 52

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Most Common AEs (>3% in any Treatment Group)

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- Respiratory tract infections were among the most common AEs and were comparable between remibrutinib and placebo during the double-blind treatment period
- Petechiae was reported more commonly with remibrutinib vs placebo during the double-blind treatment period; all were mild or moderate and were not associated with clinically significant platelet count decreases
- EAIRs of most common AEs did not increase with long-term treatment (up to week 52)



Liver Safety (Newly Occurring Transaminase Elevations)

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- Newly occurring liver transaminase (ALT or AST) elevations were infrequent and balanced between remibrutinib and placebo during the double-blind treatment period
- All observed liver transaminase (ALT or AST) elevations across both studies were asymptomatic and transient/reversible



- In the pivotal phase 3 studies REMIX-1 and -2, **improvements in symptoms with remibrutinib vs placebo were observed as early as week 1 and were sustained to week 52** in patients with CSU remaining symptomatic despite second-generation H₁-antihistamines
- Among **patients transitioning from placebo to remibrutinib** at week 24, **responses with remibrutinib were observed as early** as one week after transitioning **and were sustained** until the end of the study
- Overall, **remibrutinib demonstrated favorable safety and tolerability** across REMIX studies, **including long-term**, with up to 52 weeks of treatment
 - In the double-blind period, **rates of AEs**, including serious AEs and AEs leading to treatment discontinuation, **were comparable between remibrutinib and placebo**
 - **Exposure-adjusted incidence rates of AEs**, including SAEs and treatment discontinuation, **did not increase over time**
- **Remibrutinib** has the potential to become **a novel oral treatment** option that **provides fast** (observed as early as week 1) **and sustained symptom relief** for patients with CSU

