Background: Remibrutinib, a novel, potent, highly selective, covalent, oral Bruton's tyrosine kinase inhibitor, is currently being investigated in phase 3 trials for the treatment of multiple sclerosis (MS; NCT05147220/NCT05156281). Remibrutinib showed a favorable selectivity and potency profile in vitro, with the potential to minimize off-target toxicity and associated adverse events (AEs).

Objectives: To report an overview of the safety of remibrutinib from phase 2 clinical trials in various autoimmune disorders.

Methods: Data from a final analysis of phase 2 trials in chronic spontaneous urticaria (CSU; NCT03926611), Sjögren syndrome (SjS; NCT04035668), and asthma (NCT03944707), and an interim analysis of the open-label extension (OLE) in CSU (NCT04109313) were included in this analysis. Safety assessments comprised AEs, including serious AEs and AEs of special interest (AESIs), vital signs, electrocardiograms (ECGs), and laboratory parameters.

Results: A total of 363 patients (CSU, 267; SjS, 49; asthma, 47) who received various doses (10-100 mg qd/bid) of remibrutinib for 12 to 52 weeks were included. For CSU, 267 patients received different doses in the 12-week core study; in the 52-week OLE study, 183 received 100 mg bid. Safety of remibrutinib in the core CSU study was similar across dose levels. Likewise, in the OLE CSU study, safety of remibrutinib 100 mg bid was comparable to any dose in the core study. Across the CSU, SjS, and asthma studies, the most frequently reported grouped AEs (≥10%) were Infections and infestations, Skin and subcutaneous tissue disorders, Gastrointestinal diseases, and Nervous system disorders. Overall, AEs observed were similar to placebo in controlled studies across indications; except for skin disorders in CSU, where post-treatment CSU flares caused an imbalance. There were no increases in infection rates. Infections, as well as other AESIs, including bleeding (all minor) and cytopenia, were comparable across indications, also with long-term treatment in CSU extension study. No safety concerns were noted in the analysis of laboratory parameters, ECGs, and vital signs.

Conclusions: Remibrutinib demonstrated a favorable safety profile and was well tolerated at all doses studied in phase 2 trials and the 52-week OLE (up to 100 mg bid), supporting its development in phase 3 clinical trials in MS.