ATOPIC ECZEMA/DERMATITIS

TREATMENT WITHDRAWAL AND RETREATMENT WITH UPADACITINIB IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS FROM A PHASE 2B, RANDOMIZED, CONTROLLED TRIAL

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Introduction and Objective: Effect of withdrawal/retreatment with upadacitinib (UPA; selective JAK-1 inhibitor) was evaluated during the week-32 pre-specified interim analysis from the phase-2b trial in atopic dermatitis (AD) patients.

Materials and Methods: Adults with moderate-to-severe AD enrolled in Period 1 (16-week, randomized, placebo [pbo]-controlled), and at Week 16 were re-randomized within their Period 1 treatment groups, to blinded treatment in Period 2; the 8 groups were (Period 1/Period 2 doses): pbo/pbo, pbo/UPA30mg, UPA7.5mg/pbo, UPA7.5mg/7.5mg, UPA15mg/pbo, UPA15mg/15mg, UPA30mg/pbo, UPA30mg/30mg. Patients with a <50% improvement from baseline in EASI (<EASI 50) response starting 4 weeks after re-randomization were rescued with UPA30 (blinded). Efficacy is reported as observed.

Results: Of 167 enrolled, 126 were re-randomized in Period 2 to continue or switch to pbo (63) or UPA (63). 80.1% (51/63) who were re-randomized to pbo and 42.9% (27/63) re-randomized to UPA were rescued with UPA30. In Period 2, EASI 75 response rate [% (n/N)] at re-randomization (Week 16) was 0% (0/8) pbo/pbo, 0% (0/1) pbo/UPA30, 23.1% (3/13) UPA7.5/pbo, 9.1% (1/11) UPA7.5/7.5, 64.7% (11/17) UPA15/pbo, 50.0% (6/12) UPA15/15, 76.9% (10/13) UPA30/pbo, 66.7% (2/3) UPA30/30. Response rate 8 weeks post-rescue with UPA30 was 50.0% (4/8) pbo/pbo, 100% (1/1) pbo/UPA30, 58.3% (7/12) UPA7.5/pbo, 30.0% (3/10) UPA7.5/7.5, 93.8% (15/16) UPA15/pbo, 55.6% (5/9) UPA15/15, 69.2% (9/13) UPA30/pbo, 33.3% (1/3) UPA30/30. Among all re-randomized to pbo, the overall response rate after 8 weeks of rescue with UPA30 was 71.4% (35/49). The most

common category of adverse events (AEs) in both periods was non-serious infection; rates were higher for UPA (all doses) vs pbo. AEs of interest for JAK inhibitors occurred infrequently.

Conclusions: The majority re-randomized to pbo, lost clinical response, requiring protocol-mandated rescue with blinded UPA30 (80.1%), and after 8 weeks, achieved EASI 75 (71.4%). No new safety signal was identified.