Pooled efficacy, patient-reported outcomes, and safety of roflumilast cream 0.15% from the INTEGUMENT-1 and INTEGUMENT-2 phase 3 trials of adults and children with atopic dermatitis

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Introduction: Roflumilast is a selective, highly potent phosphodiesterase 4 inhibitor under investigation as a nonsteroidal, once-daily cream for treatment of atopic dermatitis (AD).

Methods: We present pooled results from two identical phase 3 randomized controlled trials (INTEGUMENT-1: NCT04773587; INTEGUMENT-2: NCT04773600) of roflumilast cream 0.15%. Patients aged ≥6 years with mild to moderate AD were randomized 2:1 to
apply roflumilast (n=884) or vehicle (n=453) cream once-daily for 4 weeks. The primary endpoint was validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success (Clear/Almost Clear vIGA-AD plus ≥2-grade improvement from baseline) at Week 4. Patient-reported outcomes (PROs) were evaluated using the Worst Itch-Numeric Rating Scale (WI-NRS), SCORing AD (SCORAD), Patient-Oriented Eczema Measure, Dermatology Life Quality Index/Children’s Dermatology Life Quality Index, and the Dermatitis Family Impact questionnaire. Safety and tolerability were also evaluated.

**Results:** At Week 4, more roflumilast- than vehicle-treated patients achieved vIGA-AD Success (31.3% vs. 14.1%, P<0.0001), WI-NRS Success (≥4-point improvement on WI-NRS in patients aged ≥12 years with baseline WI-NRS ≥4; 31.9% vs. 16.6%, P<0.0001); and WI-NRS of 0/1 (in patients with baseline WI-NRS ≥2; 28.8% vs 18.5%, P=0.0087). At Week 4, roflumilast-treated patients improved more than vehicle-treated on the pruritus and sleep components of SCORAD (least squares mean percentage change −48.2% vs. −27.8%; [P<0.0001] and −47.9% vs. −22.9% [P<0.05], respectively). Differences favoring roflumilast were also seen for other secondary endpoints, including quality of life of the patient and family. Safety and local tolerability were favorable.

**Conclusion:** Once-daily, nonsteroidal roflumilast cream 0.15% improved PROs in patients with AD. Sponsored by Arcutis Biotherapeutics, Inc.

**Keywords:** Atopic dermatitis, efficacy, patient-reported outcomes, roflumilast cream, safety