Long-term safety and efficacy of roflumilast cream 0.15% in adults and children aged ≥6 years with mild to moderate atopic dermatitis: a 52-week, phase 3, open-label extension trial

Eric L. Simpson,1 Lawrence F. Eichenfield,2 Kim A. Papp,3 Seth Forman,4 Adelaide A. Hebert,5 Mercedes E.Gonzalez,6 Melinda Gooderham,7 H. Chih-ho Hong,8 Vimal H. Prajapati,9 Emma Guttman,10 Jonathan Silverberg,11 Melissa Seal,12 David Krupa,12 Patrick Burnett,12 Scott Synder,12 David H. Chu,12 Robert C. Higham,12 David R. Berk12

1Oregon Health & Science University, Portland, OR, USA; 2Rady’s Children’s Hospital-San Diego, Departments of Dermatology and Pediatrics, University of California San Diego, San Diego, CA, USA; 3Probity Medical Research and Alliance Clinical Trials, Waterloo, ON, Canada, and University of Toronto, Toronto, ON, Canada; 4ForCare Medical Center, Tampa, FL, USA; 5UT Health McGovern Medical School, Houston, TX, USA; 6Pediatric Skin Research, LLC Miami, FL, USA; 7SKiN Centre for Dermatology, Probity Medical Research, and Queen’s University, Peterborough, ON, Canada; 8Probity Medical Research and University of British Columbia, Department of Dermatology and Skin Science, Surrey, BC, Canada; 9Dermatology Research Institute, Probity Medical Research, Skin Health & Wellness Centre, and University of Calgary, Calgary, AB, Canada; 10Icahn School of Medicine at Mount Sinai, New York, NY, USA; 11Department of Dermatology, The George Washington University School of Medicine and Health Sciences, Washington, DC, USA; 12Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA.

Background: Roflumilast, a highly potent phosphodiesterase-4 inhibitor, is being investigated as a non-steroidal, once-daily cream for atopic dermatitis (AD).
**Methods:** INTEGUMENT-OLE (NCT04804605) was an open-label 52-week safety trial. Patients (N=658) with mild to moderate AD who completed a 4-week randomized vehicle-controlled phase 3 trial of roflumilast cream continued or switched to once-daily roflumilast cream 0.15% in this open-label extension trial. Starting at Week 4, patients achieving Validated Investigator Global Assessment for AD (vIGA-AD) score of 0 (Clear) switched to twice-weekly (BIW) maintenance dosing. The primary endpoint was safety; secondary endpoints included vIGA-AD, Worst Itch-Numeric Rating Scale (WI-NRS), and Eczema Area and Severity Index (EASI). “Disease control” was defined as duration of vIGA-AD=0/1 on BIW dosing following achievement of vIGA-AD=0.

**Results:** With cumulative treatment up to 56 weeks, 36.7% of patients reported treatment-emergent adverse events (AEs); most were mild to moderate in severity. Overall, 4.7% of patients had AEs deemed treatment-related and 3.0% discontinued due to AEs. The most common AEs (>2%) were COVID-19, upper respiratory tract infection, nasopharyngitis, and headache. At Week 52, 55.7%, 61.1%, and 53.6% of patients achieved vIGA-AD=0/1 (Clear/Almost Clear), ≥75% reduction in EASI, and ≥4-point reduction in WI-NRS (among patients aged ≥12 years with baseline WI-NRS ≥4), respectively. Of the 130 (19.8%) patients who achieved disease control, 50% maintained “disease control” for at least 281 days.

**Conclusion:** Treatment with roflumilast cream 0.15% demonstrated long-term safety in patients with AD consistent with parent trials and durable efficacy through 52 weeks, including patients who switched to BIW dosing.

**Keywords:** Atopic dermatitis, long-term, roflumilast cream, safety