Arcutis Announces Publication of ZORYVE® (roflumilast) Cream 0.15% Pivotal Results from Phase 3 INTEGUMENT-1 and -2 Trials in Mild to Moderate Atopic Dermatitis in Journal of American Medical Association Dermatology

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- ZORYVE® (roflumilast) cream 0.15% improved atopic dermatitis (AD) across multiple efficacy endpoints while demonstrating favorable safety and tolerability
- Across both studies, approximately 31% of children and adults treated with ZORYVE cream achieved the primary efficacy endpoint of Investigator Global Assessment (IGA) Success at Week 4 compared to 14% for vehicle, with significant improvement as early as Week 1
- ZORYVE cream 0.15% rapidly and significantly reduced itch, the most bothersome symptom of AD
- Once-daily, ZORYVE cream 0.15% is approved to treat mild to moderate AD in adults and children down to age 6

WESTLAKE VILLAGE, Calif., Sept. 19, 2024 (GLOBE NEWSWIRE) -- Arcutis Biotherapeutics, Inc. (Nasdaq: ARQT), a commercial-stage biopharmaceutical company focused on developing meaningful innovations in immuno-dermatology, today announced that the *Journal of American Medical Association Dermatology (JAMA Dermatology)* published the positive results from two pivotal Phase 3 studies (INTEGUMENT-1 and INTEGUMENT-2) evaluating the efficacy and safety of ZORYVE® (roflumilast) cream 0.15% as a once-daily, steroid-free treatment for mild to moderate AD. ZORYVE cream, 0.15%, was approved in July 2024 by the U.S. Food and Drug Administration (FDA) for the topical treatment of mild to moderate AD in adult and pediatric patients 6 years of age and older and is available in pharmacies nationwide.

The article reported that treatment with ZORYVE cream resulted in significant improvements across multiple efficacy endpoints, including achieving a statistically significant improvement in the primary efficacy endpoint of IGA Success, as well as statistically significant improvements in key secondary endpoints, including itch and a reduction in Eczema Area and Severity Index score.

“AD is a chronic and burdensome disease that often leaves patients and caregivers searching for relief from intractable itch, the most reported symptom which leads to reduced quality of life and sleep disturbances,” said Eric Simpson, MD, MCR, FAAD, Professor of Dermatology at Oregon Health & Science University in Portland and lead author on the publication. “These compelling results reinforce the strong efficacy and safety profile of ZORYVE and its ability to provide rapid and significant itch relief. Skin barrier is another key consideration for the treatment of AD, and these data further demonstrate that ZORYVE may be relied upon to deliver results without concerns for further disrupting the skin barrier.”

INTEGUMENT-1 and INTEGUMENT-2 (The INterventional Trial EvaluatinG roflUMilast cream for the treatmENt of aTopic dermatitis) were two identical Phase 3, parallel group, double-blind, vehicle-controlled trials evaluating the safety and efficacy of ZORYVE cream 0.15% or vehicle applied once-daily for four weeks to 1,337 adults and children 6 years of age and older with mild to moderate AD.

As previously reported, both INTEGUMENT-1 and -2 studies met their primary endpoint of IGA Success, defined as a validated Investigator Global Assessment – Atopic Dermatitis (vIGA-AD) score of *Clear* or *Almost Clear* plus a 2-grade improvement from baseline at Week 4 (INTEGUMENT-1: 32.0% ZORYVE cream vs. 15.2% vehicle, P<0.0001; INTEGUMENT-2: 28.9% ZORYVE cream vs. 12.0% vehicle, P<0.0001). Other key findings included:

- Rapid improvement in itch was observed in individuals treated with ZORYVE cream within 24 hours of the first application, as measured by the change from baseline in daily Worst Itch-Numeric Rating Scale (WI-NRS) scores and compared with vehicle (nominal P<0.05).
- Over 30% of individuals treated with ZORYVE cream in each study achieved WI-NRS Success at Week 4 compared to vehicle (INTEGUMENT-1: 33.6% vs 20.7% P<0.01; INTEGUMENT-2: 30.2% vs 12.4% P<0.01), with significant improvements seen as early as Week 1. WI-NRS Success is defined as achievement of at least a 4-point reduction on the WI-NRS 0-10 scale (in individuals ages 12 and older who had a baseline WI-NRS score of ≥ 4).
- More than 40% of children and adults treated with ZORYVE cream achieved a 75% reduction in Eczema Area and Severity Index (EASI-75) score at Week 4 compared to vehicle (INTEGUMENT-1: 43.2% vs. 22.0%, P<0.0001; INTEGUMENT-2: 42.0% vs. 19.7%, P<0.0001). Significant improvements based on EASI-75 were observed with ZORYVE cream compared to vehicle as early as Week 1 in both studies (nominal P=0.0006; nominal P=0.0329).
- ZORYVE cream 0.15% was safe and well tolerated. The incidence of Treatment Emergent Adverse Events (TEAEs) was low in both active treatment and vehicle arms.
- At each time point, investigators noted 95% of ZORYVE-treated patients had no signs of irritation at the application site. More than 90% of ZORYVE-treated patients self-reported no sensation or mild sensation at the application site.

“We are thrilled that *JAMA Dermatology,* a premier medical journal, has published the positive results of our two pivotal Phase 3 trials. These data highlight the robust efficacy of ZORYVE to rapidly relieve AD, including the most troublesome symptom of itch,” said Patrick Burnett, MD, PhD, FAAD, chief medical officer at Arcutis. “As an effective, safe, and well-tolerated once-daily cream, ZORYVE offers those living with AD and their caregivers a new treatment option for use anywhere on the body—and for any duration.”

About Atopic Dermatitis
AD is the most common type of eczema, affecting approximately 9.6 million children and 16.5 million adults in the United States.

AD is a chronic, relapsing inflammatory skin disease that is genetically pre-disposed and presents across the lifespan. The disease appears as a red, intensely itchy rash that can occur anywhere on the body and may present differently in children and adults. AD presentation can rapidly fluctuate and vary based on geographic location and environment.

About ZORYVE®
ZORYVE is a steroid-free topical phosphodiesterase-4 (PDE4) inhibitor approved to treat AD, seborrheic dermatitis, and plaque psoriasis. PDE4 — an established target in dermatology — is an intracellular enzyme that increases the production of pro-inflammatory mediators and decreases production of anti-inflammatory mediators.

ZORYVE (roflumilast) cream 0.15% is approved by the FDA for the treatment of mild to moderate AD in individuals 6 years of age and older and ZORVYE cream 0.3% for the topical treatment of plaque psoriasis in individuals 6 years of age and older. Another formulation, ZORYVE foam 0.3%, is available for the treatment of seborrheic dermatitis in adults and children ages 9 and older.

Roflumilast cream for AD is currently being evaluated at a lower dose of 0.05% for children aged 2 to 5 years. In addition, Arcutis has completed its clinical development program for ZORYVE foam 0.3% for the treatment of scalp and body psoriasis and submitted a supplemental New Drug Application (sNDA) to the FDA in July 2024.

INDICATIONS
ZORYVE cream, 0.3%, is indicated for topical treatment of plaque psoriasis, including intertriginous areas, in adult and pediatric patients 6 years of age and older.

ZORYVE cream, 0.15%, is indicated for topical treatment of mild to moderate atopic dermatitis in adult and pediatric patients 6 years of age and older.

ZORYVE foam, 0.3%, is indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older.

IMPORTANT SAFETY INFORMATION
ZORYVE is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C).

Flammability: The propellants in ZORYVE foam are flammable. Avoid fire, flame, and smoking during and immediately following application.

The most common adverse reactions (≥1%) for ZORYVE cream 0.3% for plaque psoriasis include diarrhea (3.1%), headache (2.4%), insomnia (1.4%), nausea (1.2%), application site pain (1.0%), upper respiratory tract infection (1.0%), and urinary tract infection (1.0%).

The most common adverse reactions (≥1%) for ZORYVE cream 0.15% for atopic dermatitis include headache (2.9%), nausea (1.9%), application site pain (1.5%), diarrhea (1.5%), and vomiting (1.5%).

The most common adverse reactions (≥1%) for ZORYVE foam 0.3% for seborrheic dermatitis include nasopharyngitis (1.5%), nausea (1.3%), and headache (1.1%).

Please see full **Prescribing Information** for ZORYVE cream and full **Prescribing Information** for ZORYVE foam.

About Arcutis
Arcutis Biotherapeutics, Inc. (Nasdaq: ARQT) is a commercial-stage medical dermatology company that champions meaningful innovation to address the urgent needs of individuals living with immune-mediated dermatological diseases and conditions. With a commitment to solving the most persistent patient challenges in dermatology, Arcutis has a growing portfolio including three FDA-approved products that harness our unique dermatology development platform coupled with our dermatology expertise to build differentiated therapies against biologically validated targets. Arcutis' dermatology development platform includes a robust pipeline with multiple clinical programs for a range of inflammatory dermatological conditions including scalp and body psoriasis, AD, and alopecia areata. For more information, visit **www.arcutis.com** or follow Arcutis on **LinkedIn**, **Facebook**, **Instagram**, and **X**.

Forward-Looking Statements
Arcutis cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on the Company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding the potential of real-world use results of roflumilast cream in AD, and the potential for roflumilast cream to advance the standard of care in AD and other inflammatory dermatological conditions. These statements are subject to substantial known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements. Risks and uncertainties that may cause our actual results to differ include risks inherent in our business, reimbursement and access to our products, and the impact of competition and other important factors discussed in the "Risk Factors" section of our Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) on February 27, 2024, as well as any subsequent filings with the SEC. You should not place undue reliance on any forward-looking statements in this press release. We undertake no obligation to revise or update information herein to reflect events or circumstances in the future, even if new information becomes available. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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