**Prix Galien Award Submission for Arcutis ZORYVE® (roflumilast)**

**Award**

Best Biotechnology Product

**Company Name**

Arcutis Biotherapeutics

**Product/Solution Name**

ZORYVE® (roflumilast)

**Compound/Tech Name**

Topical roflumilast

**Trade Name**

ZORYVE®

**Corporate Name**

ZORYVE® (roflumilast)

**Date of Approval**

December 15, 2023

**Indications**

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

ZORYVE® (roflumilast) 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® (roflumilast) 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® (roflumilast) topical foam, 0.3%, is indicated for the treatment of plaque psoriasis of the scalp and body in adults and adolescents 12 years of age and older.

**Therapeutic Areas**

Dermatology, Immunology

**Background** Information and need for drug/device (unlimited word count)

***Word count: 1,499***

Our skin is the largest and most visible organ of the body, and chronic immune-mediated skin diseases such as seborrheic dermatitis, atopic dermatitis, and plaque psoriasis can significantly affect a person's physical and mental well-being, negatively impact a person’s quality of life, and may lead to alterations in a person’s daily activities to avoid social stigma.[[1]](#endnote-2),[[2]](#endnote-3),[[3]](#endnote-4)

These inflammatory skin conditions are often highly itchy (pruritic). When scratching breaks the skin, secondary skin infections can occur, which is particularly problematic for infants and young children afflicted with nocturnal itch, which leads to loss of sleep for both patient and parents.[[4]](#endnote-5),[[5]](#endnote-6) Because of the chronic nature of these diseases, individuals may feel a sense of hopelessness and constantly live with fearful anticipation of an unexpected outbreak of symptoms on their skin or the skin of their children.1,2

In recent decades there’s been a lack of innovation in topical treatments that has left individuals living with immune-mediated skin diseases with few options. Traditional topical therapeutics used to treat immune-mediated skin conditions, including topical steroids, come with safety and efficacy concerns related to long-term use, especially for children and adolescents.[[6]](#endnote-7),[[7]](#endnote-8) Depending on the body location affected, such as hair-bearing regions like the scalp or sensitive areas including the face and skin folds, many traditional topical therapies must be avoided entirely or require complex rotational regimens.[[8]](#endnote-9)

For the most effective, super-potent topical corticosteroids, use for longer than two-weeks can cause the irreversible, serious side effects of skin thinning and striae (stretch marks) formation, and should generally be avoided entirely on sensitive areas.[[9]](#endnote-10) Although the use of emollient-rich ointment vehicles in some topicals may augment efficacy in immune-mediated skin diseases,[[10]](#endnote-11) lack of acceptable aesthetics and the staining of clothing and bedding has been shown to reduce dosing compliance leading to reduced therapeutic benefit. As recently as 2021, dermatologists were grappling with why non-prescription cosmetic creams were dramatically superior in texture and moisturization compared to pharmaceutical cream vehicles.[[11]](#endnote-12)

That’s where Arcutis Biotherapeutics stepped in. Steered by their mission and vision, Arcutis has worked tirelessly to drive meaningful innovation that addresses real patient needs. With extensive medical dermatology development expertise, and a deep understanding of what really matters to patients and healthcare professionals, Arcutis aims to simplify complex disease management and solve the most persistent challenges of treating chronic inflammatory diseases of the skin.

Seborrheic dermatitis (seb derm) is a common, chronic, and recurrent inflammatory skin disease affecting more than 10 million people in the United States.6,[[12]](#endnote-13) Seb derm causes red patches covered with large, greasy, flaking yellow-gray scales, and persistent itch.6 It occurs most often in areas of the body with oil-producing (sebaceous) glands, including the scalp, face (especially on the nose, eyebrows, ears, and eyelids), upper chest, and back.6,[[13]](#endnote-14)

Seb derm is the third most common skin condition for African Americans seen in the dermatology clinic.[[14]](#endnote-15) Diagnosing and treating individuals with darker skin tones and hair textures comes with its own set of unique challenges.6,13,[[15]](#endnote-16)

Traditional topical therapies focused on treating one aspect of this condition caused by a combination of genetic and environmental factors. Antifungal (ketoconazole or ciclopirox) shampoos, applied three-times a week, focused on controlling Malassezia growth while low potency corticosteroids provided symptomatic relief by managing inflammation scaling.6,13,[[16]](#endnote-17) Despite a clear need for new treatment options, there had not been a topical drug approved with a new mechanism of action for seb derm in over two decades, until the approval of ZORYVE® (roflumilast) foam 0.3%.[[17]](#endnote-18) ZORYVE foam was found to control Malassezia growth[[18]](#endnote-19) and managed inflammation by providing the quick relief of itch and reduction of scaling.

Challenges with some current treatments include concerns of safety with long-term use, lack of efficacy, inability to treat both hair- and non-hair-bearing areas, medicated shampoos not respecting cultural hair care practices, and limitations on duration of use in sensitive areas. These often cause individuals living with seb derm to have complicated treatment regimens and application routines.6,13,[[19]](#endnote-20) In fact, according to a study of 300 adults with seb derm conducted by the Harris Poll, on average adults report using six treatments a week, and spend over 30 minutes a day, to treat their seb derm.

Atopic dermatitis is the most common type of eczema, affecting approximately 9.6 million children and 16.5 million adults in the United States alone and may initially develop due to skin barrier dysfunction.4,[[20]](#endnote-21) Atopic dermatitis is a chronic, relapsing inflammatory skin disease that appears as a red, intensely itchy rash, which can occur anywhere on the body, and may present differently in children and adults.[[21]](#endnote-22) People with AD can get rashes anywhere on the body that can ooze, weep fluid, and bleed when scratched, which may make skin vulnerable to infection.20

Living with atopic dermatitis, or being a caregiver, can be difficult and frustrating due to the relentless cycle of treating flares and the chronic nature of the disease.5 Atopic dermatitis negatively affects quality of life, including sleep disturbances and mental health disorders. Management of atopic dermatitis also takes a toll on caregivers and family members due to treatment adherence/complex routines, potential treatment side effects, conflict over scratching, and sleep disturbances.[[22]](#endnote-23)

Typically, people living with atopic dermatitis may use multiple treatments at the same time including moisturizers, topicals, and systemics, which can make for complex treatment routines.[[23]](#endnote-24),[[24]](#endnote-25) Topical steroids are the standard of care for atopic dermatitis, but moderate to high potency steroids are limited by how long they can be used to avoid side effects. In addition to fear of side effects, treatment adherence is also impacted by application difficulty, including multiple applications per day or greasy or irritating formulations, or lack of efficacy.5,[[25]](#endnote-26) However, due to the chronic nature and unpredictable flares of atopic dermatitis, there is a need for more topical treatment options that can be used long-term.

Plaque psoriasis is another common, non-contagious, immune-mediated skin disease that affects approximately 9 million adults in the United States.[[26]](#endnote-27) About 90% of people with psoriasis have plaque psoriasis, which is characterized by “plaques,” or raised, red areas of skin covered with a silver or white layer of dead skin cells. The plaques may have more grayish, purplish, or brownish tones in people with darker skin tones.7,[[27]](#endnote-28)

Psoriatic plaques can appear on any area of the body, but most often appear on the scalp, knees, elbows, trunk, and limbs.7,[[28]](#endnote-29) These plaques are often itchy and sometimes painful.28,[[29]](#endnote-30) Importantly, plaques in certain anatomical areas—including the face, elbows and knees, genitals, and intertriginous areas (areas of skin-to-skin contact)—present particular treatment challenges.[[30]](#endnote-31),[[31]](#endnote-32),[[32]](#endnote-33)

Topical treatments are the current standard of care, with over 90% of people with plaque psoriasis being treated with topicals.[[33]](#endnote-34),[[34]](#endnote-35) Topical therapies are often used in conjunction with systemic agents or biologic therapies in patients with moderate to severe disease.31 Individuals living with psoriasis are often prescribed multiple topical medications for different areas of the body due to limitations associated with strength, sensitivity, and the duration of use that a topical can be applied. This need for specific treatments for specific body areas makes for a complicated treatment regimen.6,31

Until recently, there has been a lack of innovation in topicals.Besides wanting treatments that are safe and effective, today’s consumer expects cosmetically-elegant treatments that fit into their lives. Not only does the fear of side effects impact treatment adherence, but treatments that are hard to apply, require multiple applications each day, or are greasy or irritating, have an adverse impact on patients’ use of their therapies.

In Paul Becher’s seminal 1957 book “EMULSIONS: Theory and Practice” cosmetic and pharmaceutical creams were emulsified using one of only three types of emulsifiers: beeswax, polyoxyl esters or sodium alkyl sulfates.[[35]](#endnote-36) Despite the introduction of dozens of cosmetic emulsifiers to the industry since 1957, as of 2021 the FDA Inactive Ingredient Database (IID) of emulsifiers approved for use in pharmaceutical creams approved in the U.S. was still limited to beeswax, polyoxyl esters and sodium alkyl sulfates.11 Arcutis changed this with the development and approval of ZORYVE, which contains an ultra-mild alkyl phosphate blend emulsifying wax (CrodafosTM CES), the first novel emulsifier added to the IID in decades.[[36]](#endnote-37)

In addition, all currently approved topical anti-inflammatory drugs other than those developed by Arcutis contain skin penetration enhancers, to be able to deliver therapeutic concentrations of the drug despite the barrier properties of skin. The skin penetration propylene glycol (PG) elicits an allergenic response in a significant number of patients. When PG is used synergistically with other skin penetration enhancers, such as oleyl alcohol, the otherwise transient compromise of skin barrier function is prolonged and allows environmental irritants and allergens to further inflame the patient’s skin. These enhancers are especially problematic for skin conditions like seb derm and atopic dermatitis that have an inherent skin barrier defect. Additionally, high concentrations of short-chain alcohols like isopropyl alcohol and ethanol that are commonly included in topical medications cause significant drying of the skin and hair. Arcutis has been successful in formulating its topicals without the use of either penetration enhancers or short-chain alcohols.

**Development & Clinical or Preclinical Evidences** (500 words) History of the development of the solution/product

***Word count: 499***

Driven by the belief that people with chronic skin conditions deserve better than the current standard of care, Arcutis developed two formulations of a next-generation, best-in-class topical phosphodiesterase-4 (PDE-4) inhibitor—a foam and a cream. PDE-4 is an established target in dermatology. Roflumilast, a PDE-4 inhibitor, was chosen due to its potency, selectivity, and high binding affinity.[[37]](#endnote-38) The hydrophobicity of roflumilast presented a challenge for developing a moisturizing, water-based formulation.

Arcutis needed to address several challenges when developing its topical formulations to ensure products were highly effective, well tolerated, could be applied anywhere on the skin (including hair-bearing areas), and were cosmetically acceptable to patients.

Arcutis formulated ZORYVE foam and cream to overcome this challenge and ensure medication was delivered without disrupting the skin barrier of patients with chronic skin conditions. In fact, these are the first topical prescription treatments to include Crodafos CES emulsifying wax. Crodafos CES is a mild emulsifier and conditioning agent used in the cosmetic industry,36 but until ZORYVE, it had not been approved by the FDA for use in a prescription product.

ZORYVE is uniquely formulated as an emollient, water-based product without fragrances or penetration enhancers, which are commonly used in prescription topicals and are known to irritate the skin, causing local tolerability issues.36,[[38]](#endnote-39),[[39]](#endnote-40),[[40]](#endnote-41) Arcutis’ formulations are also pH balanced to the skin and contain moisturizing properties.26,38,[[41]](#endnote-42)

In July 2022 ZORYVE cream 0.3% was approved by the FDA as the first and only topical PDE-4 inhibitor for the treatment of plaque psoriasis in individuals ages 12 and older and later in October 2023 the indication was expanded to include children between the ages of 6 to 11.[[42]](#endnote-43)

The FDA approved ZORYVE foam, 0.3% as the first topical drug with a new mechanism of action for seb derm in over two decades in December 2023.17,[[43]](#endnote-44) In clinical trials, treatment with ZORYVE foam resulted in rapid improvement in disease clearance and reduction in symptoms including itch, one of the most bothersome symptoms of seb derm.17 Nearly 80% of individuals achieved the primary efficacy endpoint and just over 50% of individuals reached complete clearance at Week 8.

In May 2025, the FDA approved ZORYVE (roflumilast) topical foam, 0.3%, as treatment for plaque psoriasis of the scalp and body in individuals 12 years of age and older. [[44]](#endnote-45) In clinical trials, ZORYVE foam demonstrated significant improvements in signs and symptoms of psoriasis on both the body and scalp.[[45]](#endnote-46),[[46]](#endnote-47) ZORYVEfoam, which can be used on all skin and hair types,fills a critical unmet need as it was intentionally formulated to meet the total need of individuals with psoriasis, including hard-to-treat areas of the body.[[47]](#endnote-48)

In July 2024, ZORYVE® cream 0.15% was approved by the FDA for the treatment of mild-to-moderate atopic dermatitis in individuals ages 6 and older. 9 out of 10 people saw symptom improvement with ZORYVE cream.[[48]](#endnote-49)

Lastly, the FDA has accepted a sNDA for ZORYVEcream 0.05% for the treatment of mild-to-moderate atopic dermatitis in children aged 2 to 5 years old.[[49]](#endnote-50)

**Innovation** (500 words) Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

***Word count: 377***

Following decades without significant innovation in topical treatment options for chronic immune-mediated skin conditions, ZORYVE offers those living with these conditions, and their healthcare providers, new hope. ZORYVE possesses several unique qualities that address unmet needs of patients and is uniquely designed to simplify disease management for millions of people living with chronic, immune-mediated inflammatory skin diseases.

Notably, ZORYVE offers a convenient, once-daily, steroid-free, water-based topical treatment option that can be used anywhere on the body as well as across all skin and hair types and the full spectrum of disease severity. The unique topical formulations of ZORYVE allow the product to spread easily and absorb quickly.26,41-44 This combination of a novel formulation and the properties of roflumilast contribute to ZORYVE’s ability to be used once a day, on all affected areas of the body, with no limitations on duration of use.42-44

Given that seb derm and psoriasis can affect individuals across all demographics, ZORYVE foam was optimally designed for use on the scalp and other hair-bearing areas. To ensure its suitability for a wide variety of skin and hair types, Arcutis confirmed with industry experts that the formulation of ZORYVE foam does not include any ingredients that may adversely affect hair and skin health, affirming its status as a safe and effective treatment option for all hair types.41

Additionally, the National Psoriasis Foundation recently awarded ZORYVE its Seal of Recognition, which highlights and recognizes products created or intended to be non-irritating and safe for those living with psoriatic disease.

ZORYVE is the first and only topical PDE-4 inhibitor approved for the treatment of plaque psoriasis and the only topical for which efficacy has been specifically demonstrated in the treatment of intertriginous psoriasis, highlighting its novelty.43 For seb derm, ZORYVE is the first topical drug with a new mechanism of action in over two decades.17 As a steroid-free option that can be used anywhere on the body, especially in difficult-to-treat areas, with no limitations on duration, ZORYVE is a meaningful innovation to simplify disease management for topical treatment of immune-mediated skin conditions.

Arcutis remains committed to solving today’s biggest medical dermatology challenges and is has initiated trials for roflumilast cream 0.05% for the treatment of mild to moderate atopic dermatitis in infants ages three to 24 months.

**Please provide appropriate references** (PubMed, Abstract, Website)

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