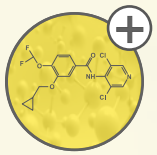
ARCUTIS
BIOTHERAPEUTICS

Arcutis: Innovation in Dermatology

At Arcutis, we are filling the innovation gap in dermatology by developing best-in-class, innovative topical dermatology therapies against validated biological targets and elevating the standard of care. Our goals are to simplify disease management and provide more convenient, safe, and effective options for patients. We are advancing rapidly with an innovative pipeline to improve the lives of patients with serious skin diseases.

Tap here to explore our pipeline

Arcutis Is Building a Robust Dermatology Pipeline



PDE4 Inhibitor

Roflumilast Cream
(ARQ-151)

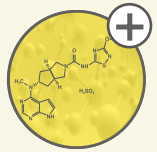
Plaque Psoriasis

Atopic Dermatitis

Roflumilast Foam
(ARQ-154)

Seborrheic Dermatitis

Scalp Psoriasis



JAK1 Inhibitor

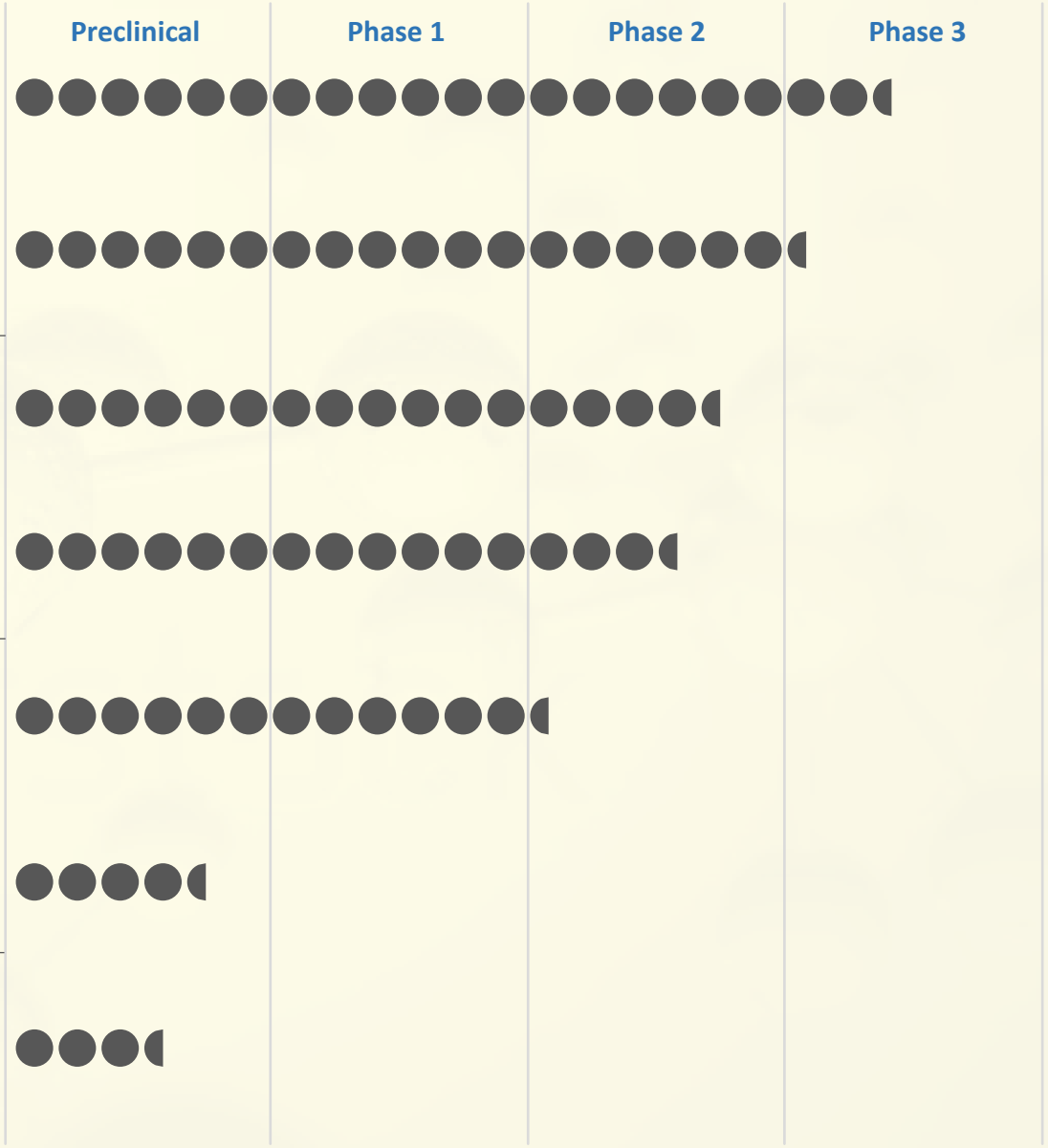
ARQ-252 Cream

Hand Eczema

Vitiligo

ARQ-255 Suspension

Alopecia Areata



Roflumilast is a Highly Selective Topical PDE4 Inhibitor

Topical roflumilast is a selective and highly potent, once-daily, nonsteroidal, *PDE4 inhibitor* under investigation for the treatment of chronic plaque psoriasis, atopic dermatitis, seborrheic dermatitis, and scalp psoriasis

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PDE4 inhibition has been validated for oral psoriasis therapy,[1] but is a novel formulation for topical dermatologic therapy

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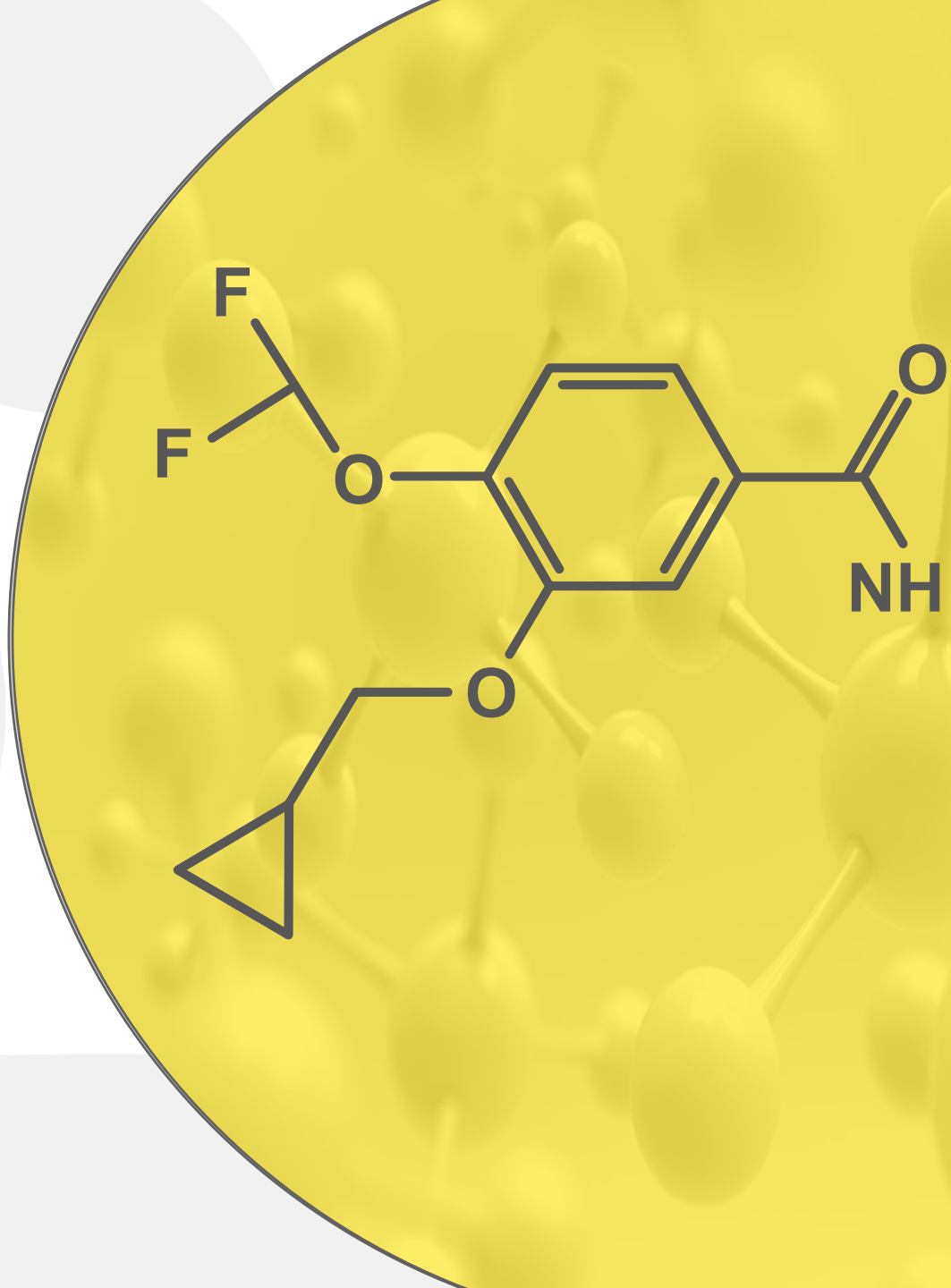
Topical roflumilast is a *cream* or *foam* formulation of the highly potent anti-inflammatory PDE4 inhibitor roflumilast, which was approved by the United States Food and Drug Administration as an oral formulation in 2011 to treat chronic obstructive pulmonary disease[1]



1. Li et al. *Front Pharmacol.* 2018;9:1048.

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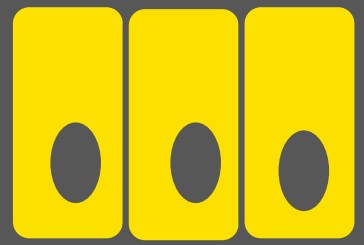
PDE4 plays a key role in immunodermatology

PDE4 is an enzyme that contributes to immunodermatologic conditions

Increases
inflammatory mediators

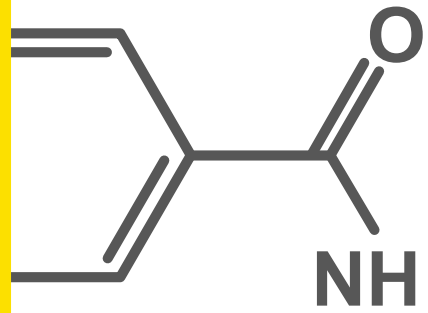


Disrupts skin
barrier balance

Increases
inflammatory response

Click to learn more about how PDE4 inhibition may reduce inflammation

Li et al. *Front Pharmacol.* 2018;9:1048.



1. Li et al. *Front Pharmacol.* 2018;9:1048.

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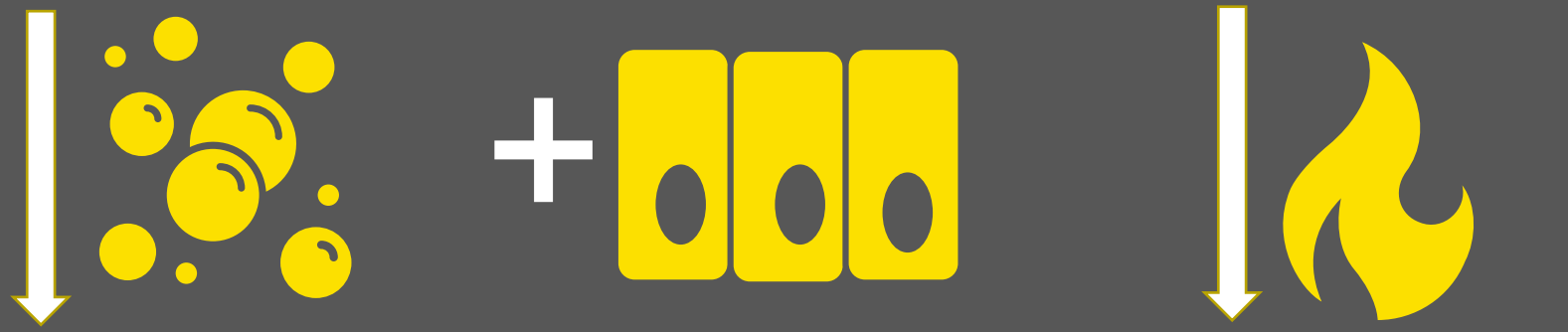
Inhibition of PDE4 modulates the immune response

Inhibition of PDE4 modulates immune responses

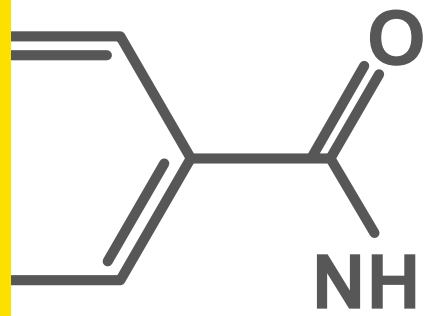


Downregulates inflammatory cytokines

Restores skin barrier balance

Decreases inflammatory response

Li et al. *Front Pharmacol.* 2018;9:1048.



1. Li et al. *Front Pharmacol.* 2018;9:1048.

Roflumilast Cream (ARQ-151)

Roflumilast cream (ARQ-151) is under investigation for the treatment of *psoriasis* and *atopic dermatitis*

Uniquely formulated in an odorless, emollient, water-based moisturizing cream without propylene glycol or alcohols

Cream vehicle incorporates a mild emulsifier, providing smooth delivery of active drug through the stratum corneum

Currently under investigation to address unmet needs, including long-term topical therapy that can be used safely on all regions of the body

Roflumilast Foam (ARQ-154)

Roflumilast foam (ARQ-154) is being investigated for the treatment of *seborrheic dermatitis* and *scalp psoriasis*

Roflumilast foam is identical to roflumilast cream (ARQ-151) and is water based, moisturizing, and formulated without propylene glycol or alcohols

Foam vehicle incorporates an innovative, fast-breaking formulation, promoting easy delivery of active drug

Currently under investigation to address unmet needs for long-term treatment of body surfaces

Additionally, areas where creams are not suitable, such as facial, periocular, and hair-bearing areas, are being studied

Roflumilast Cream (ARQ-151) in Psoriasis

Landscape

- High-potency steroids are limited to short-term use[1]
- Sensitive areas such as the face and intertriginous areas can be challenging to treat and require additional considerations[1]
- Patient adherence to existing topical therapies is generally low[1]
- Patients with psoriasis experience negative impacts to quality of life, reduced work productivity, and sleep disturbances[2,3]

Mechanism

Development

1. Torsekar and Gautam. *Indian Dermatol Online J*. 2017;8:235-245. **2.** Bhosle et al. *Health Qual Life Outcomes*. 2006;4:35. **3.** Henry et al. *PLoS One*. 2016;11:e0157843.
4. Li et al. *Front Pharmacol*. 2018;9:1048. **5.** Papp et al. *J Drugs Dermatol*. 2020;19:734-740. **6.** Lebwohl et al. *N Engl J Med*. 2020;383:229-239.

Roflumilast Cream (ARQ-151) in Psoriasis

Mechanism

- PDE4 activity is elevated in psoriatic skin[4]
- Inhibition of PDE4 results in reduction of proinflammatory factors and restoration of skin barrier[2]
- Roflumilast cream (ARQ-151) is a selective and highly potent PDE4 inhibitor

Landscape

Development

1. Torsekar and Gautam. *Indian Dermatol Online J*. 2017;8:235-245. **2.** Bhosle et al. *Health Qual Life Outcomes*. 2006;4:35. **3.** Henry et al. *PLoS One*. 2016;11:e0157843.
4. Li et al. *Front Pharmacol* 2018;9:1048. **5.** Papp et al. *J Drugs Dermatol*. 2020;19:734-740. **6.** Lebwohl et al. *N Engl J Med*. 2020;383:229-239.

Roflumilast Cream (ARQ-151) in Psoriasis

Landscape

Mechanism

Development

- Phase 1/2a results published in *Journal of Drugs in Dermatology*[5]
- Phase 2b results published in *New England Journal of Medicine*[6]
- Two phase 3 studies are ongoing (NCT04211363; NCT04211389)
- A phase 3 open-label extension study is ongoing (NCT04286607)

Click to request:

Phase 1/2a manuscript | Phase 2b manuscript

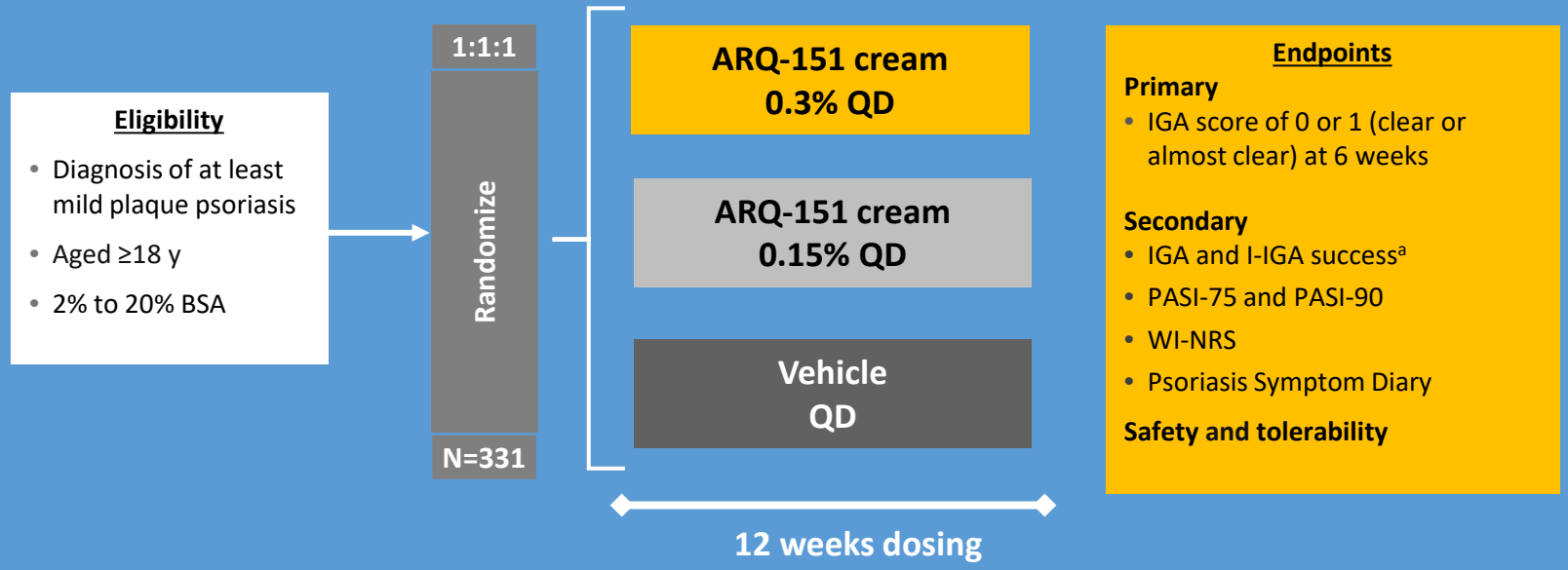
Click to learn more about clinical trials of topical roflumilast:

Learn more

1. Torsekar and Gautam. *Indian Dermatol Online J*. 2017;8:235-245. **2.** Bhosle et al. *Health Qual Life Outcomes*. 2006;4:35. **3.** Henry et al. *PLoS One*. 2016;11:e0157843.
4. Li et al. *Front Pharmacol* 2018;9:1048. **5.** Papp et al. *J Drugs Dermatol*. 2020;19:734-740. **6.** Lebwohl et al. *N Engl J Med*. 2020;383:229-239.

Phase 2b Study of Roflumilast Cream in Psoriasis

Randomized, double-blind, vehicle-controlled multicenter study

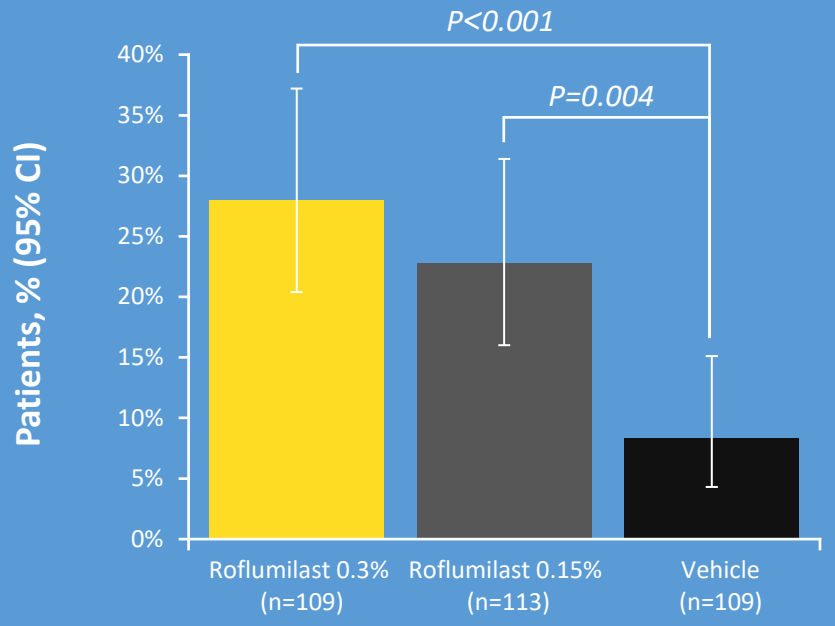


Click here to view data snapshot

[a]IGA success and I-IGA success were defined as scores of 0 or 1 (clear or almost clear) with at least a two-grade improvement from baseline.
BSA, body surface area; IGA, investigator global assessment; I-IGA, intertriginous IGA; PASI, psoriasis area and severity index; QD, once daily; WI-NRS, worst itch numeric rating scale.
NCT03638258. https://clinicaltrials.gov/ct2/show/NCT03638258. Accessed July 20, 2020.

Phase 2b Data for Roflumilast Cream in Psoriasis

Roflumilast met its primary endpoint of statistically significant achievement of IGA 0 or 1 (clear or almost clear) at week 6

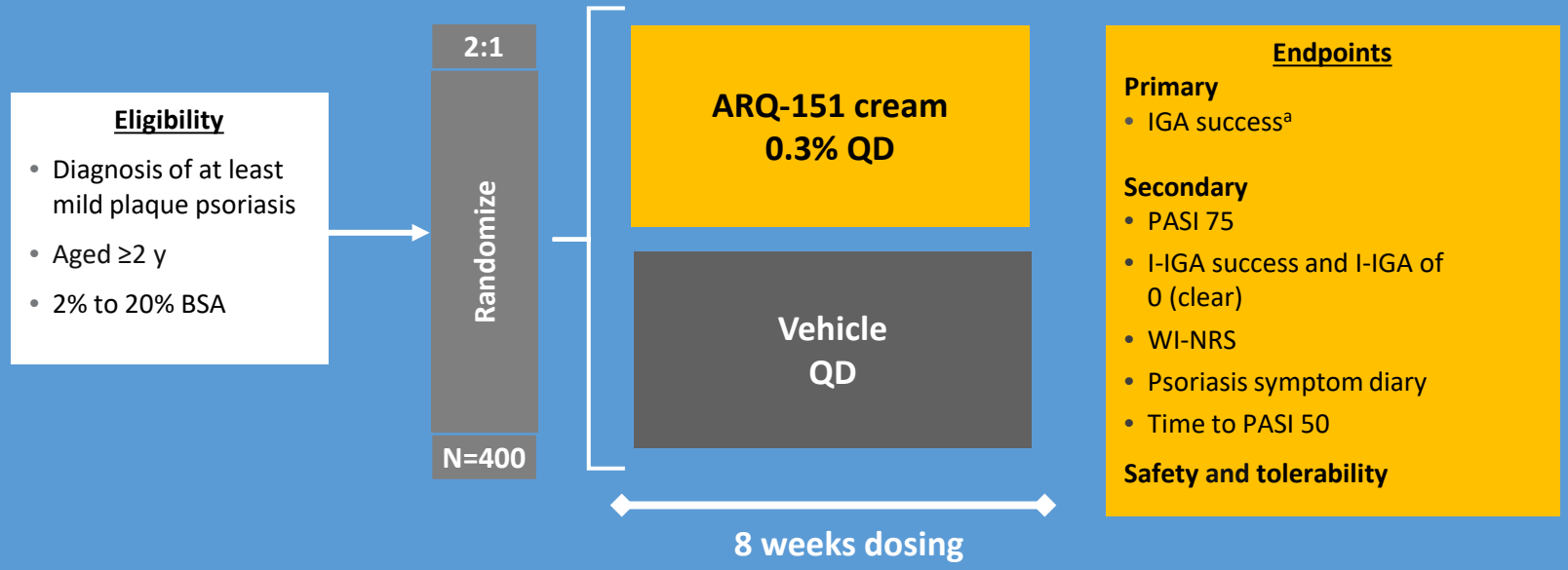


- Most patients with baseline intertriginous psoriasis of at least mild severity achieved I-IGA status of "clear" at week 12 (93%)
- Rapid improvement in patient-reported itch and burden of disease as early as week 2[a]
- Most TEAEs were mild or moderate, and the incidence of application-site reactions was similar between groups

Click here to request the publication in New England Journal of Medicine

[a]The first time point after the start of roflumilast treatment was week 2.
CI, confidence interval; IGA, investigator global assessment; I-IGA, intertriginous investigator global assessment.
Lebwohl et al. *N Engl J Med.* 2020;383:229-239.

Two Phase 3 Studies (DERMIS-1/-2) Are Ongoing for Roflumilast Cream in Psoriasis[1,2]



A phase 3 open-label extension study (DERMIS-OLE) evaluating long-term safety of topical 0.3% roflumilast is also ongoing[3]

[a]IGA success and I-IGA success were defined as scores of 0 or 1 (clear or almost clear) with at least a two-grade improvement from baseline.
BSA, body surface area; IGA, investigator global assessment; I-IGA, intertriginous IGA; PASI, psoriasis area and severity index; QD, once daily; WI-NRS, worst itch numeric rating scale.
1. NCT04211389. https://clinicaltrials.gov/ct2/show/NCT04211389. Accessed July 20, 2020. **2.** NCT04211363. https://clinicaltrials.gov/ct2/show/NCT04211363. Accessed July 20, 2020. **3.** NCT04286607. https://clinicaltrials.gov/ct2/show/NCT04286607. Accessed July 20, 2020.

Roflumilast Cream (ARQ-151) in Atopic Dermatitis

Landscape

- Atopic dermatitis is a common chronic inflammatory skin disease that affects both children and adults[1]
- Itch is the most burdensome symptom, causing patients to experience substantially reduced quality of life and sleep disturbances[2]
- The skin barrier is typically compromised in atopic dermatitis[3]
- Topical corticosteroids and emollients are the standard of care[3]
- Steroids are not suitable for long-term use, and children are at risk for greater systemic absorption[3]

Mechanism

Development

1. Bieber. *Ann Dermatol.* 2010;2:125-137. **2.** Silverberg et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347. **3.** Nygaard et al. *Dermatology.* 2017;233:333-343. **4.** Baumer et al. *Inflamm Allergy Drug Targets.* 2006;6:17-26.

Roflumilast Cream (ARQ-151) in Atopic Dermatitis

Mechanism

- Elevated PDE4 levels are found in the keratinocytes of individuals with atopic dermatitis[3]
- PDE4 inhibition decreases inflammatory response and pruritus[3,4]
- Roflumilast cream (ARQ-151) is a selective and highly potent PDE4 inhibitor that may reduce inflammatory response in atopic dermatitis

Landscape

Development

1. Data on file, Arcutis BioSciences. **2.** Silverberg et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347. **3.** Nygaard et al. *Dermatology.* 2017;233:333-343. **4.** Baumer et al. *Inflamm Allergy Drug Targets.* 2006;6:17-26.

Roflumilast Cream (ARQ-151) in Atopic Dermatitis

Landscape

Mechanism

Development

- Phase 2 study completed (NCT03916081)
- Phase 3 study planned

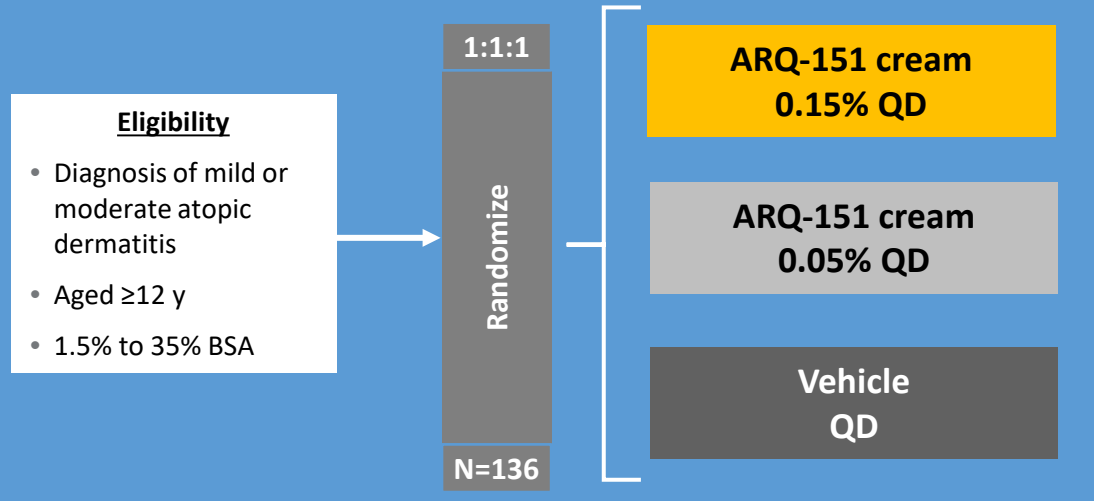
Click to learn more about clinical trials of topical roflumilast:

Learn more

1. Data on file, Arcutis BioSciences. **2.** Silverberg et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347. **3.** Nygaard et al. *Dermatology.* 2017;233:333-343. **4.** Baumer et al. *Inflamm Allergy Drug Targets.* 2006;6:17-26.

Phase 2 Study of Roflumilast Cream in Atopic Dermatitis

Randomized, double-blind, vehicle-controlled multicenter study



Endpoints

Primary
- EASI change from baseline

Secondary
- EASI percentage change from baseline
- Percentage of EASI 50 and EASI 75 responders
- Change from baseline in BSA
- WI-NRS

Exploratory
- Validated Investigator's Global Assessment – Atopic Dermatitis

Safety and tolerability

Click here to view data

BSA, body surface area; EASI, eczema area and severity index; QD, once daily; WI-NRS, worst itch numeric rating scale.
NCT03916081. https://clinicaltrials.gov/ct2/show/NCT03916081. Accessed July 20, 2020.

Clinical Development of Roflumilast Cream in Atopic Dermatitis

- A phase 2 proof-of-concept study showed consistent evidence of symptomatic improvement across endpoints and favorable tolerability
- Both 0.05% and 0.15% doses showed statistically significant improvements compared with vehicle on key secondary endpoints
- Roflumilast cream 0.15% trended toward significance for the primary endpoint (EASI change from baseline)
- Pivotal phase 3 clinical trials are planned to begin in late 2020 or early 2021

Data on file, Arcutis Biosciences.

Roflumilast Foam (ARQ-154) in Seborrheic Dermatitis

Landscape

- Seborrheic dermatitis typically appears as erythematous patches on the scalp and face[1]
- Seborrheic dermatitis is associated with itch and reduced quality of life[1,2]
- Current treatments include topical antifungals and corticosteroids for the face and body, and medicated shampoos for the scalp[1]
- Treatment may require alternative formulation (eg, foam) suitable for hair-bearing areas

Mechanism

Development

1. Clark et al. *Am Fam Physician*. 2015;91:185-190. **2.** Araya et al. *Indian J Dermatol*. 2015;60:519.

Roflumilast Foam (ARQ-154) in Seborrheic Dermatitis

Mechanism

- Roflumilast is a selective and highly potent anti-inflammatory PDE4 inhibitor that may reduce itch and flaking of the skin
- Foam formulation allows for use on all parts of the body, including hair-bearing areas

Landscape

Development

1. Clark et al. *Am Fam Physician*. 2015;91:185-190. **2.** Araya et al. *Indian J Dermatol*. 2015;60:519.

Roflumilast Foam (ARQ-154) in Seborrheic Dermatitis

Landscape

Mechanism

Development

- Phase 2b study is ongoing (NCT04091646)
- Open-label long-term study is ongoing (NCT04445987)

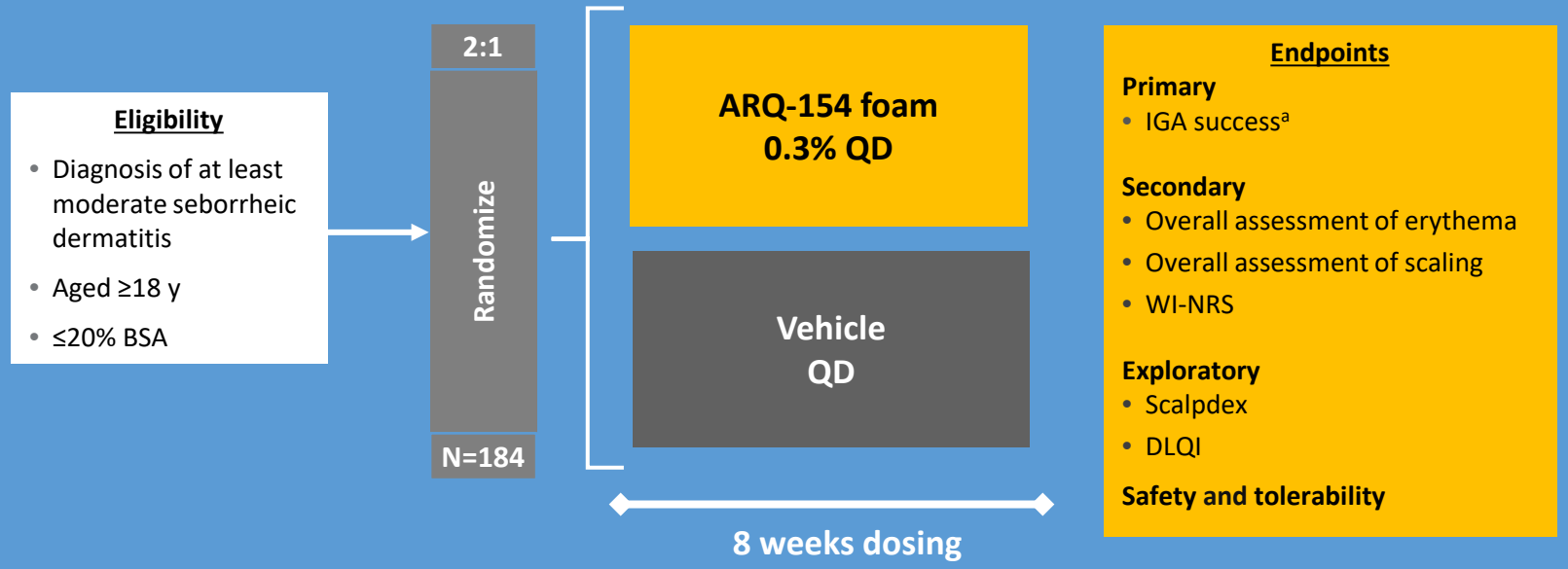
Click to learn more about clinical trials of topical roflumilast:

Learn more

1. Clark et al. *Am Fam Physician*. 2015;91:185-190. **2.** Araya et al. *Indian J Dermatol*. 2015;60:519.

Phase 2 Proof-of-Concept Study of Roflumilast Foam in Seborrheic Dermatitis

Randomized, double-blind, vehicle-controlled multicenter study



[a]IGA success was defined as IGA score of 0 or 1 (clear or almost clear) with at least a two-grade improvement from baseline.
BSA, body surface area; DLQI, dermatology life quality index; IGA, investigator global assessment; QD, once daily; WI-NRS, worst itch numeric rating scale.
NCT04091646. https://clinicaltrials.gov/ct2/show/NCT04091646. Accessed July 20, 2020.

Roflumilast Foam (ARQ-154) in Scalp Psoriasis

Landscape

- Scalp psoriasis is characterized by silvery-white scales and is often the first manifestation of psoriasis on the body[1]
- Patient with scalp psoriasis experience reduced quality of life due to itch and embarrassment[1]
- Many topical formulations may be difficult to apply directly to hair-bearing areas or may make the appearance of hair unacceptable[1]
- Requires formulation (eg, foam) suitable for hair-bearing areas

Mechanism

Development

1. Merola et al. *Dermatol Ther*. 018;31:e12589. **2.** Li et al. *Front Pharmacol.* 2018;9:1048.

Roflumilast Foam (ARQ-154) in Scalp Psoriasis

Mechanism

- PDE4 activity is elevated in psoriatic skin[2]
- Roflumilast is a highly potent anti-inflammatory, antipruritic PDE4 inhibitor
- Foam formulation allows for use on all parts of the body, including hair-bearing areas

Landscape

Development

1. Merola et al. *Dermatol Ther*. 018;31:e12589. **2.** Li et al. *Front Pharmacol.* 2018;9:1048.

Roflumilast Foam (ARQ-154) in Scalp Psoriasis

Landscape

Mechanism

Development

- Phase 2b trial is ongoing (NCT04128007)

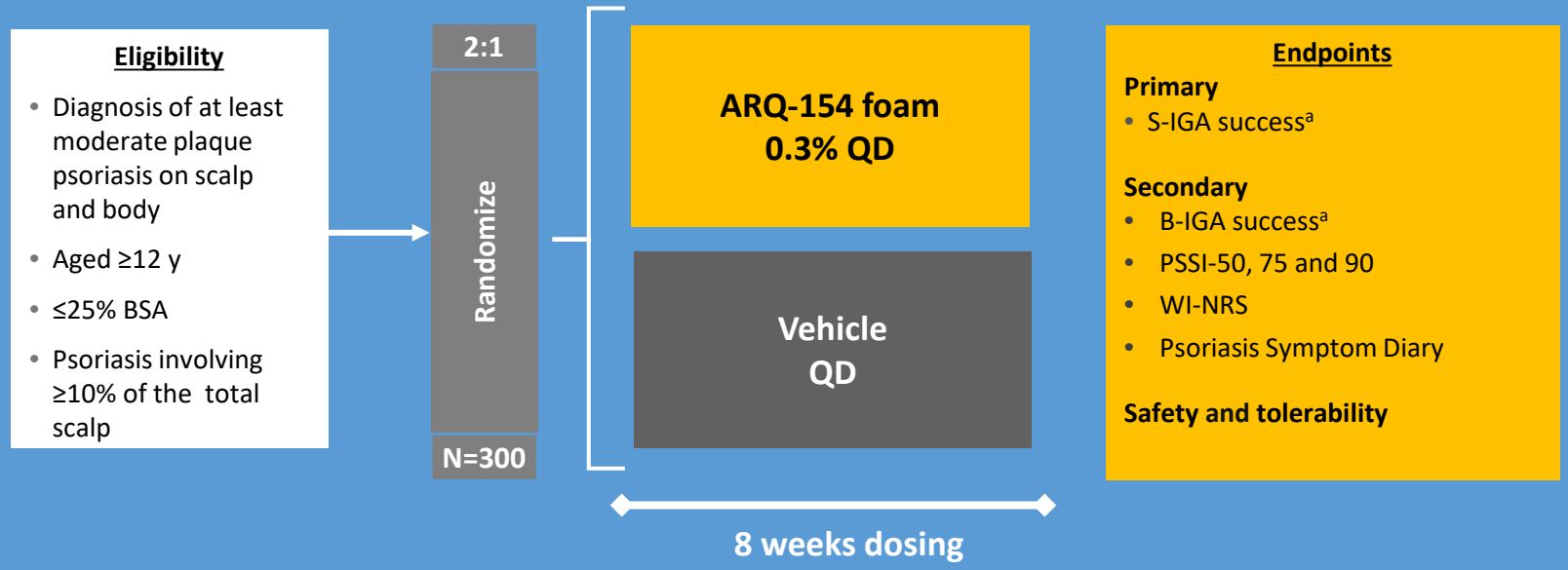
Click to learn more about clinical trials of topical roflumilast:

Learn more

1. Merola et al. *Dermatol Ther*. 018;31:e12589. **2.** Li et al. *Front Pharmacol.* 2018;9:1048.

Phase 2b Study of Roflumilast Foam in Scalp Psoriasis

Randomized, double-blind, vehicle-controlled multicenter study



[a]S-IGA success and B-IGA success were defined as scores of 0 or 1 (clear or almost clear) with at least a two-grade improvement from baseline.
B-IGA, body investigator global assessment; BSA, body surface area; PSSI, psoriasis scalp severity index; QD, once daily; S-IGA, scalp investigator global assessment; WI-NRS, worst itch numeric rating scale.
NCT04128007. https://clinicaltrials.gov/ct2/show/NCT04128007. Accessed July 20, 2020.

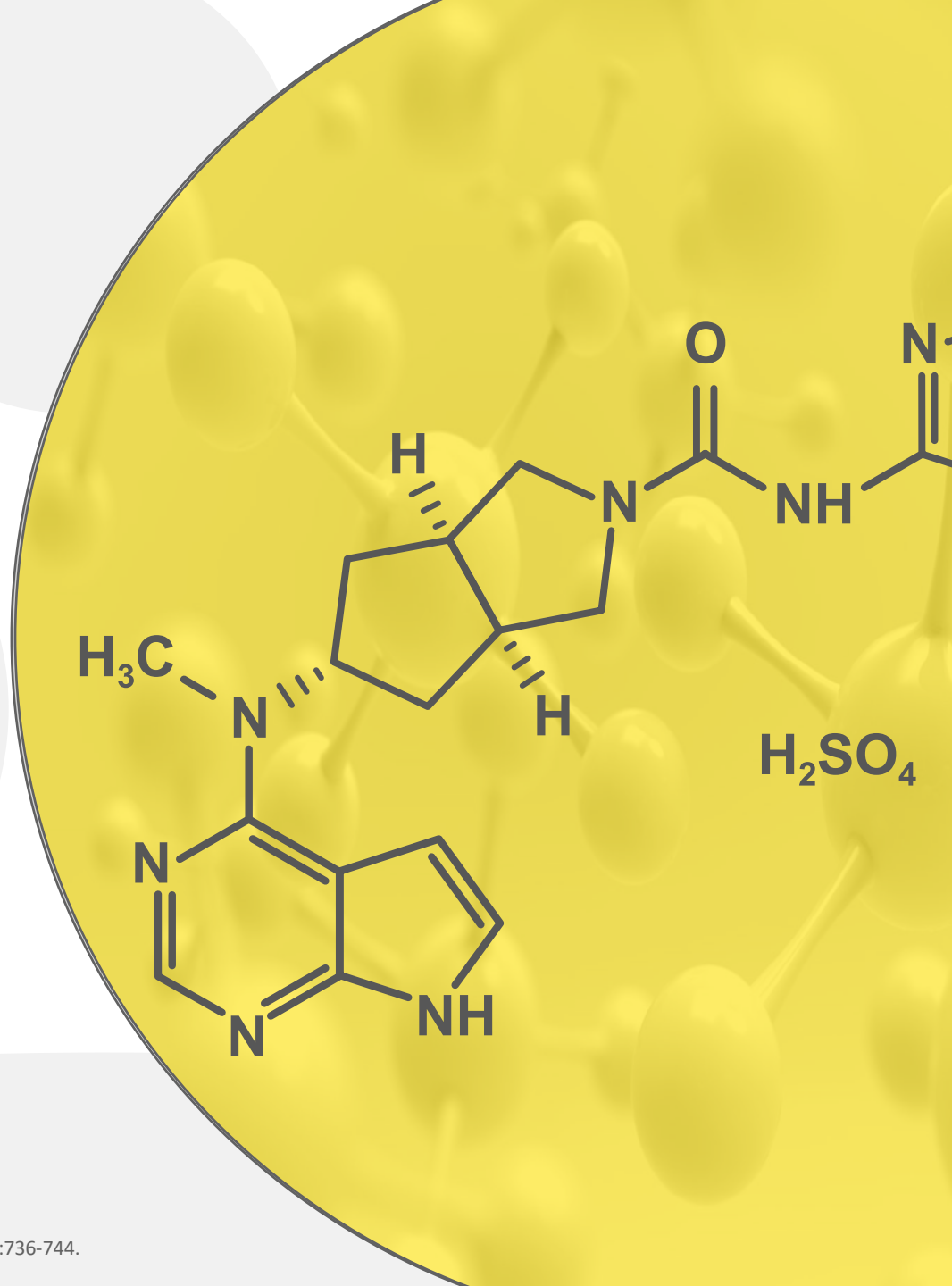
JAK1 Inhibitors
ARQ-252 and ARQ-255

ARQ-252 is a selective and highly potent topical JAK1 inhibitor under investigation as a cream for the treatment of *hand eczema* and *vitiligo*

ARQ-252 demonstrates greater potency for JAK1 than JAK2,[1] which may avoid hematological adverse effects typically associated with JAK2 inhibition[2]

Selective inhibition of JAK1 has demonstrated efficacy for treatment of inflammatory conditions including rheumatoid arthritis, Crohn's disease, psoriasis, and atopic dermatitis[3]

ARQ-255 is a formulation of ARQ-252 modified to deliver the drug deep into the dermis for the treatment of *alopecia areata*



Click here to learn more about JAK1 inhibition

1. Data on file, Arcutis Biosciences. **2.** Biggioggero et al. *Drugs Context.* 2019;8:212595. **3.** Damsky and King. *J Am Acad Dermatol.* 2017;76:736-744.

JAK1 Inhibitors
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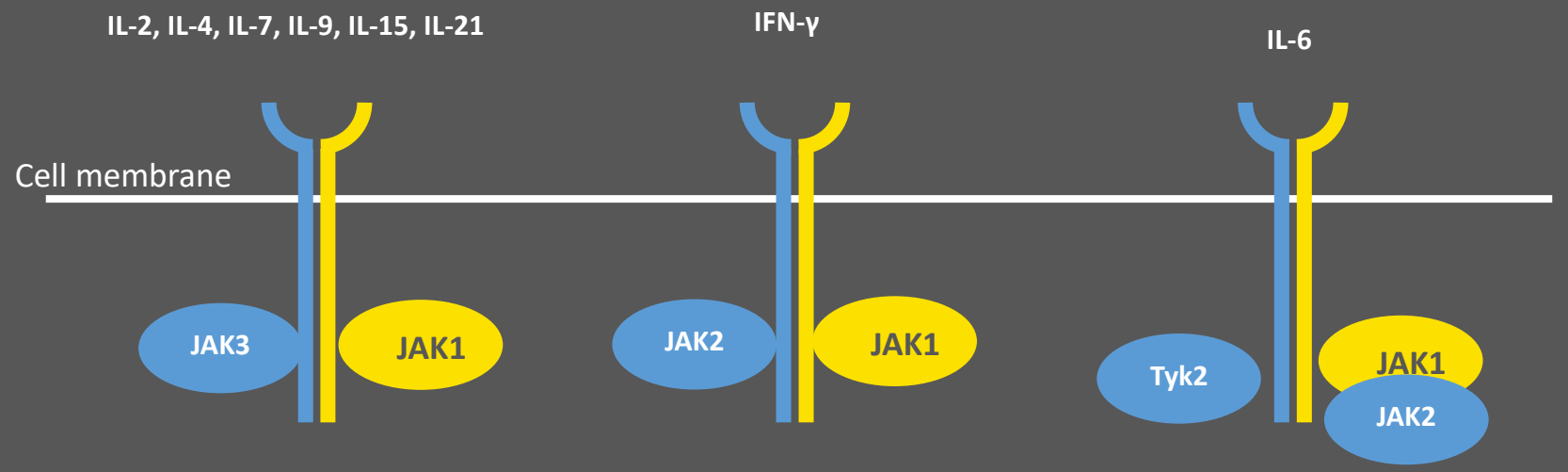
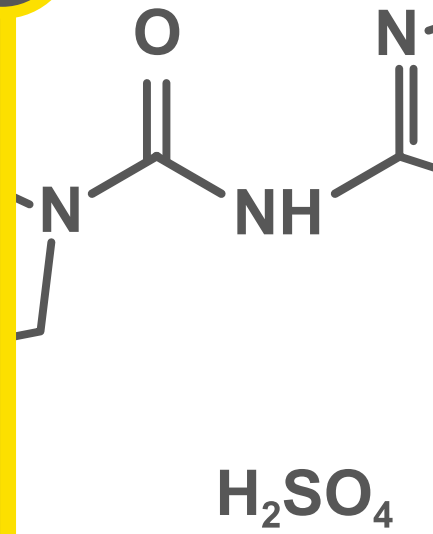
Role of JAK1 in immunomodulation

JAK-dependent cytokines contribute to immunodermatologic conditions[1,2]



Click to learn more about how JAK1 inhibition may reduce inflammation

IL, interleukin; IFN, interferon.
1. Schwartz et al. *Nat Rev Drug Discov*. 2017;17:78. **2.** Fragoulis et al. *Rheumatology*. 2019;58:i43-i54.



H_2SO_4

1. Data on file, Arcutis Biosciences. **2.** Biggioggero et al. *Drugs Context.* 2019;8:212595. **3.** Damsky and King. *J Am Acad Dermatol.* 2017;76:736-744.

JAK1 Inhibitors
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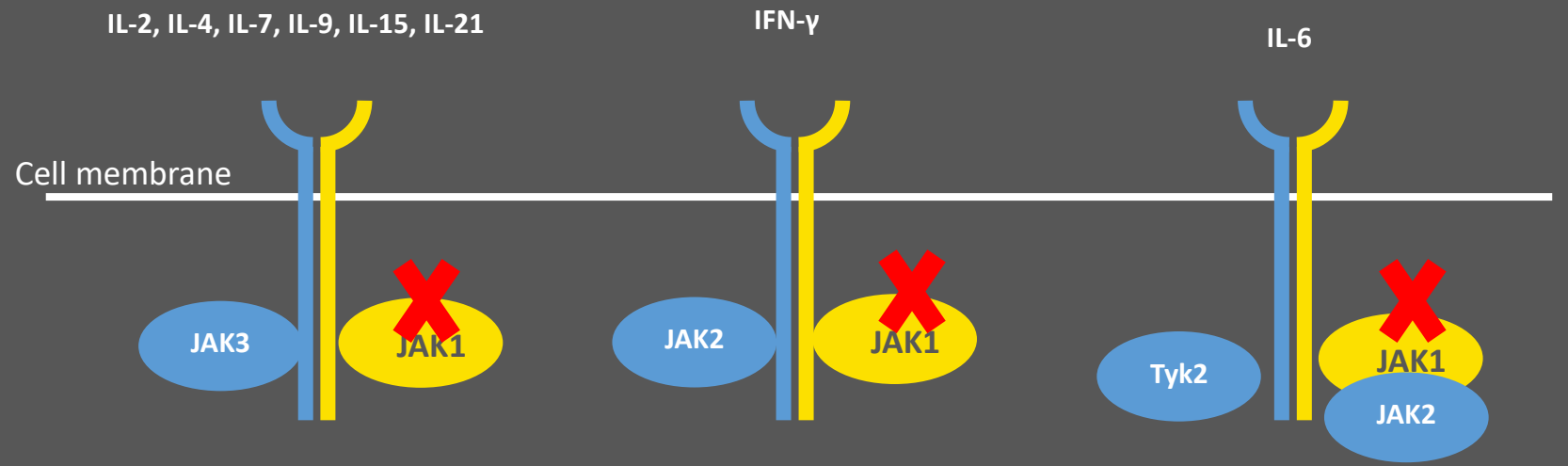
Selective JAK1 inhibition modulates immunodermatology pathways

Selective JAK1 inhibition modulates or reduces the activity of specific cytokines while maintaining other JAK-dependent immunomodulatory pathways, with the potential for fewer adverse events than pan-JAK inhibitors

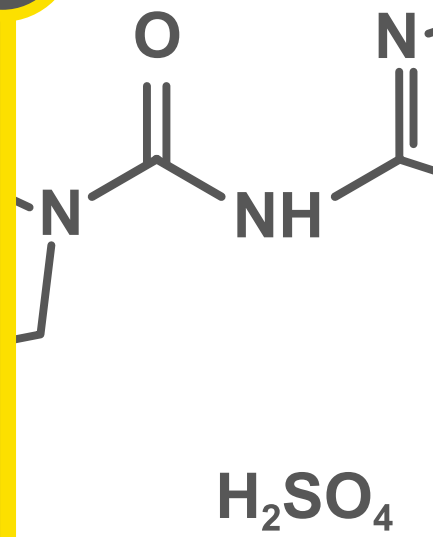


May be a mechanism to treat
- Atopic dermatitis/eczema
- Vitiligo

May be a mechanism to treat
- Alopecia areata

May be a mechanism to treat
- Atopic dermatitis/eczema

Schwartz et al. *Nat Rev Drug Discov*. 2017;17:78.



H_2SO_4

1. Data on file, Arcutis Biosciences. **2.** Biggioggero et al. *Drugs Context.* 2019;8:212595. **3.** Damsky and King. *J Am Acad Dermatol.* 2017;76:736-744.

Topical JAK Inhibitor Cream (ARQ-252) in Hand Eczema

Mechanism

Development

Landscape

- Chronic hand eczema is a common condition that occurs in different forms[1]
- Chronic hand eczema negatively affects quality of life and incurs a substantial economic burden (eg, reduced work productivity)[2,3]
- There is a considerable unmet need for new therapies for hand eczema, since few therapies are approved, and most patients and physicians are not satisfied with current treatment options[3]

1. Diepgen et al. *Br J Dermatol*. 2009;160:353-358. **2.** Bingefors et al. *Acta Derm Venereol.* 2011;91:452-458. **3.** Dibenedetti et al. *J Clin Aesthet Dermatol.* 2015;8:19-27. **4.** Howell et al. *Front Immunol*. 2019;10:2342.

Landscape

Development

Topical JAK Inhibitor Cream (ARQ-252) in Hand Eczema

Mechanism

- JAK inhibition, including JAK1, has been shown to reduce pruritus[4]
- ARQ-252 is a selective and highly potent topical, small molecule JAK1 inhibitor

1. Diepgen et al. *Br J Dermatol*. 2009;160:353-358. **2.** Bingefors et al. *Acta Derm Venereol.* 2011;91:452-458. **3.** Dibenedetti et al. *J Clin Aesthet Dermatol.* 2015;8:19-27. **4.** Howell et al. *Front Immunol*. 2019;10:2342.

Landscape

Mechanism

Topical JAK Inhibitor Cream (ARQ-252) in Hand Eczema

Development

- Phase 1/2b study is ongoing (NCT04378569)

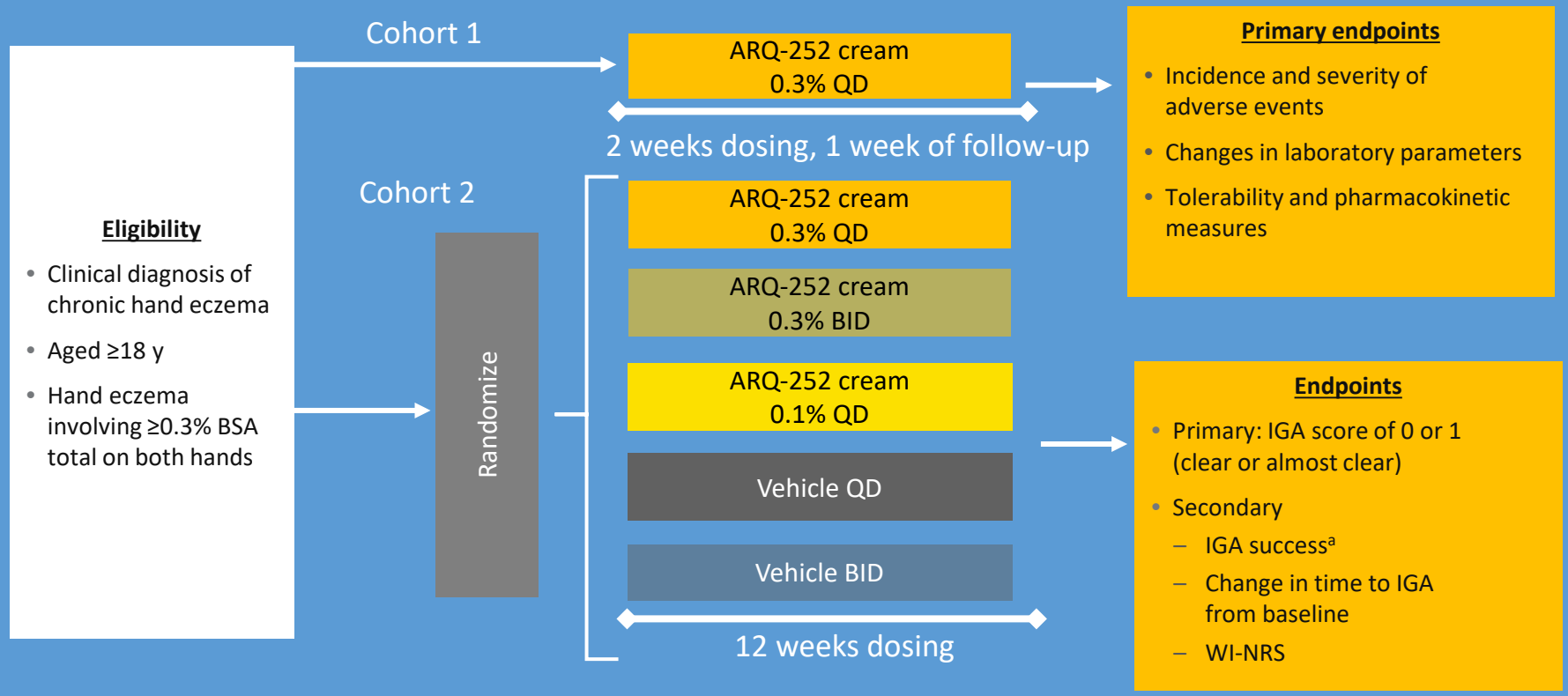
Click to learn more about clinical trials of topical JAK inhibition:

Learn more

1. Diepgen et al. *Br J Dermatol*. 2009;160:353-358. **2.** Bingefors et al. *Acta Derm Venereol.* 2011;91:452-458. **3.** Dibenedetti et al. *J Clin Aesthet Dermatol.* 2015;8:19-27. **4.** Howell et al. *Front Immunol*. 2019;10:2342.

Phase 1/2b Study Design of Topical JAK Inhibitor Cream in Hand Eczema

Randomized, Double-blind, Vehicle-controlled Multicenter Study



[a]IGA success was defined as scores of 0 or 1 (clear or almost clear) with at least a two-grade improvement from baseline.
BID, twice daily; BSA, body surface area; IGA, investigator global assessment; QD, once daily; WI-NRS, worst itch numeric rating scale.
NCT04378569. https://clinicaltrials.gov/ct2/show/NCT04378569. Accessed July 20, 2020.

Topical JAK Inhibitor Cream (ARQ-252) in Vitiligo

Mechanism

Development

Landscape[1]

- Recommended therapies include narrow band ultraviolet B, tacrolimus, and topical steroids
- As there are limited treatment options available to treat vitiligo, there is a critical need for safe and effective drug therapies for this condition

1. Ezzedine et al. *Lancet*. 2015; 386:74-84. **2.** Liu et al. *Am Acad Dermatol.* 2017;77:675-682.

Landscape

Development

Topical JAK Inhibitor Cream (ARQ-252) in Vitiligo

Mechanism

- Inhibition of the JAK-STAT pathway induces successful repigmentation in vitiligo[2]
- ARQ-252 is a selective and highly potent topical, small molecule JAK1 inhibitor

1. Ezzedine et al. *Lancet*. 2015; 386:74-84. **2.** Liu et al. *Am Acad Dermatol.* 2017;77:675-682.

Landscape

Mechanism

Topical JAK Inhibitor Cream (ARQ-252) in Vitiligo

Development

- Phase 2a planned

1. Ezzedine et al. *Lancet*. 2015; 386:74-84. **2.** Liu et al. *Am Acad Dermatol.* 2017;77:675-682.

Topical Roflumilast Suspension (ARQ-255) in Alopecia Areata

Mechanism

Development

Landscape[1,2]

- There are currently no approved therapies for alopecia areata
- Because of unpredictable and spontaneous remission, optimal duration of therapy and therapeutic dosing regimens have not been well characterized

1. Wagner. *J Invest Derm Symp P.* 2015;17:67-69. **2.** Fricke and Miteva. *Clin Cosmet Investig Dermatol.* 2015;8:397-403. **3.** Triyangkulsri and Suchonwanit. *Drug Des Devel Ther.* 2018:12.

Landscape

Development

Topical Roflumilast Suspension (ARQ-255) in Alopecia Areata

Mechanism

- JAK-STAT inhibition is a promising target for the treatment of alopecia areata[3]
- ARQ-255 is a selective and highly potent topical, small molecule JAK1 inhibitor formulated to deliver drug deep into the dermis

1. Wagner. *J Invest Derm Symp P.* 2015;17:67-69. **2.** Fricke and Miteva. *Clin Cosmet Investig Dermatol.* 2015;8:397-403. **3.** Triyangkulsri and Suchonwanit. *Drug Des Devel Ther.* 2018:12.

Landscape

Mechanism

Topical Roflumilast Suspension (ARQ-255) in Alopecia Areata

Development

- Preclinical

1. Wagner. *J Invest Derm Symp P.* 2015;17:67-69. **2.** Fricke and Miteva. *Clin Cosmet Investig Dermatol.* 2015;8:397-403. **3.** Triyangkulsri and Suchonwanit. *Drug Des Devel Ther.* 2018:12.