

Roflumilast Cream 0.3% Improved the Severity and Impact of Itch in Patients With Chronic Plaque Psoriasis in the Phase 3 DERMIS-1 and DERMIS-2 Studies

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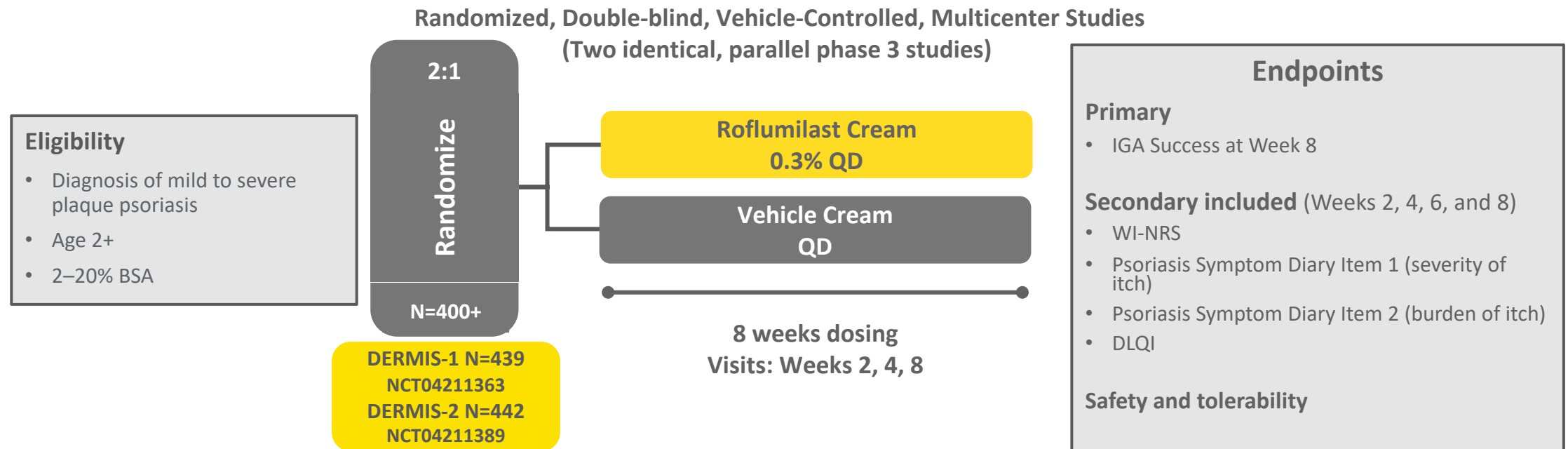
Disclosures: Melinda J. Gooderham, Javier Alonso-Llamazares, Jerry Bagel, John C. Browning, Zoe D. Draelos, Kimberly K. Grande, Adelaide A. Hebert, H. Chih-ho Hong, Mark Lebwohl, Wei Jing Loo, Walter K. Nahm, Kim A. Papp, David M. Pariser, Jennifer Soung, Linda Stein Gold, and Irina Turchin are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; Amy Feng, Patrick Burnett, Robert C. Higham, and David R. Berk are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

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Introduction and Study Design

- Itch is the most burdensome and frequently reported symptom of psoriasis^{1,2}
- Roflumilast is a selective and highly potent phosphodiesterase-4 inhibitor being investigated as a once-daily, nonsteroidal, topical treatment for various dermatologic conditions
 - Roflumilast cream provided significant and rapid improvement of patients with psoriasis, including improving intertriginous plaques and reducing itch, in a phase 2b and two randomized phase 3 randomized, double-blind, vehicle-controlled trials^{3,4}
- Here we report the results of patient-reported outcomes, including itch, from the DERMIS-1 and DERMIS-2 phase 3 trials



1. Elewski et al. *J Eur Acad Dermatol Venereol* 2019;33:1465-76.; 2. Globe et al. *Health Qual Life Outcomes* 2009;7; Lebwohl et al. *N Engl J Med*. 2020;383:229-39; 2. Lebwohl et al. 2021 EADV Spring Symposium.
BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; PSD: Psoriasis Symptom Diary; QD: once daily; WI-NRS: Worst Itch Numeric Rating Scale

Baseline Disease Characteristics (ITT Population)

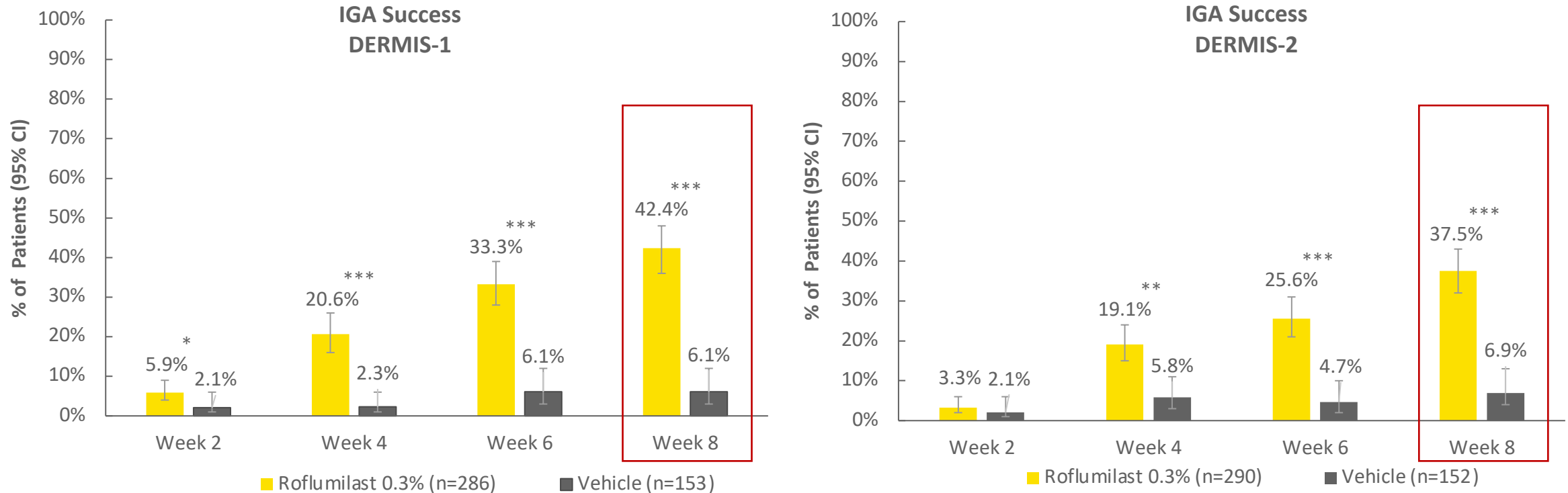
	DERMIS-1		DERMIS-2	
	Roflumilast Cream 0.3% (n=286)	Vehicle (n=153)	Roflumilast Cream 0.3% (n=290)	Vehicle (n=152)
Psoriasis-affected BSA, mean % (SD)	6.3 (4.38)	7.4 (4.76)	7.1 (4.84)	7.7 (5.05)
IGA score, n (%)				
2 (mild)	51 (17.8)	20 (13.1)	50 (17.2)	24 (15.8)
3 (moderate)	206 (72.0)	122 (79.7)	220 (75.9)	118 (77.6)
4 (severe)	29 (10.1)	11 (7.2)	20 (6.9)	10 (6.6)
PASI, mean score (SD)	6.3 (3.15)	6.8 (3.70)	6.5 (3.22)	7.0 (3.52)
WI-NRS, mean score (SD)	5.7 (2.75)	5.7 (2.84)	5.8 (2.61)	6.1 (2.75)
WI-NRS score ≥4, n (%)	218 (76.2)	115 (75.2)	229 (79.0)	116 (76.3)
PSD total score, mean (SD)	72.1 (42.75)	73.4 (41.29)	69.3 (40.66)	77.4 (41.24)
PSD Item 1: severity of itch, mean (SD)	5.5 (2.89)	5.6 (2.88)	5.6 (2.74)	6.0 (2.88)
PSD Item 2: burden of itch, mean (SD)	5.4 (2.97)	5.3 (2.98)	5.4 (2.89)	6.0 (3.02)
DLQI, mean score (SD)	7.4 (5.69)	7.0 (5.04)	6.9 (5.51)	7.8 (5.74)

BSA: body surface area; DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; ITT: intent-to-treat; PASI: Psoriasis Area Severity Index; PSD: Psoriasis Symptoms Diary; WI-NRS: Worst Itch-Numeric Rating Scale; SD: standard deviation

Roflumilast Cream Demonstrated Statistical Superiority in IGA Success Over Vehicle in Both Phase 3 Studies

IGA Success = Clear or Almost Clear plus ≥ 2 -grade improvement from baseline

**The primary endpoint was achieved in both
DERMIS-1 and DERMIS-2 (Week 8)**



* $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$

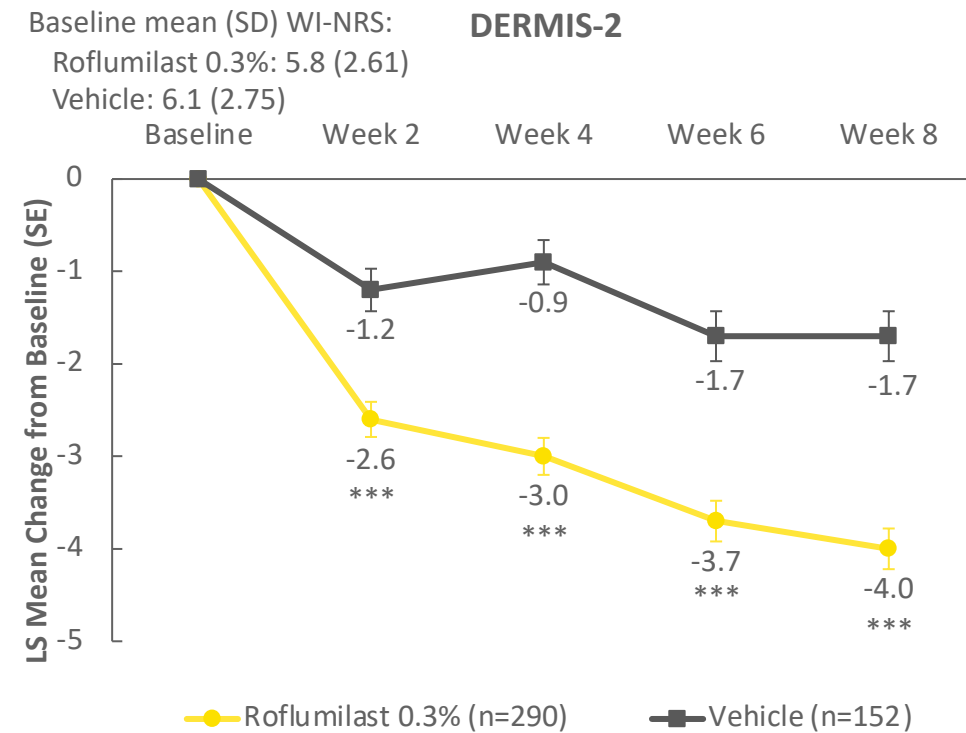
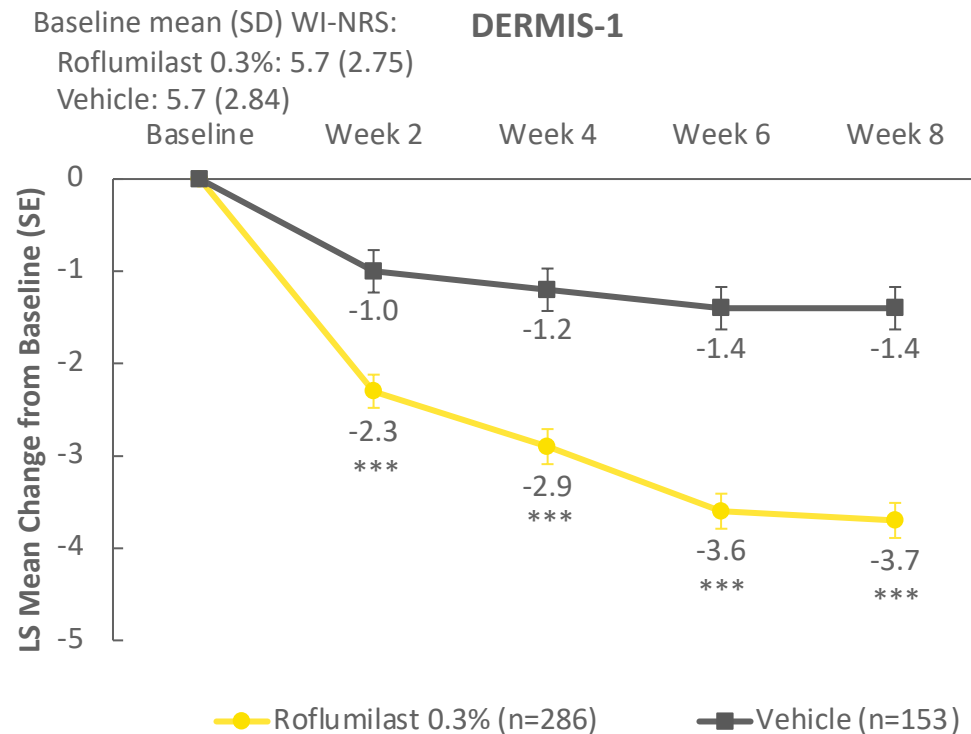
Analyzed using a Cochran-Mantel-Haenszel test stratified by site, baseline IGA, and baseline intertriginous involvement; 95% CI obtained using the Wilson method; missing scores imputed using multiple imputations. Intent-to-treat population.

CI: confidence interval; IGA: Investigator Global Assessment.

LS Mean Change From Baseline in WI-NRS Was Significantly Greater with Roflumilast Cream

Improvements in LS mean change from baseline with roflumilast cream occurred as early as Week 2 (first timepoint evaluated)

LS mean change from baseline in WI-NRS:
Patient's assessment of worst itch over the past 24 hours



*** p<0.0001

WI-NRS scale: 0 (No Itch) to 10 (Worst Imaginable Itch); evaluated in the intent-to-treat population of patients; analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline WI-NRS score as independent variables.

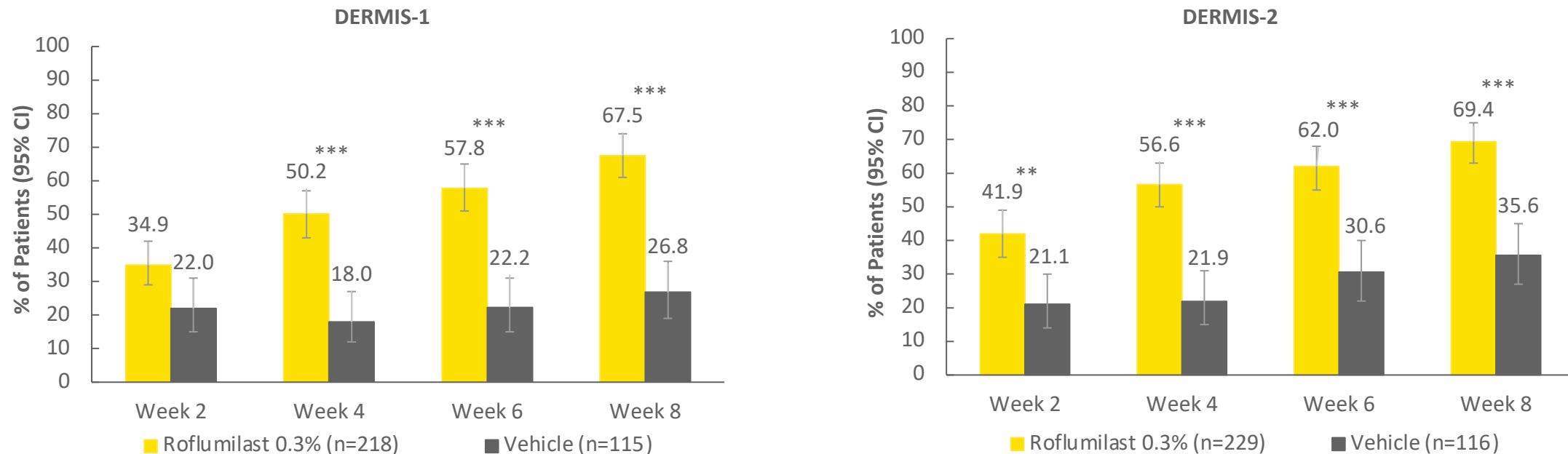
IGA: Investigator Global Assessment; LS: least square; SE: standard error; WI-NRS: Worst Itch Numeric Rating Scale

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Significantly Greater Percentages of Roflumilast-Treated Patients Achieved ≥ 4 -Point Reduction in WI-NRS at Week 8

Among patients with baseline WI-NRS score ≥ 4 , more than two-thirds of roflumilast-treated patients achieved ≥ 4 -point reduction in WI-NRS

Proportion of patients who achieved a ≥ 4 -point improvement in WI-NRS from baseline score of ≥ 4 :
Patient's assessment of worst itch over the past 24 hours

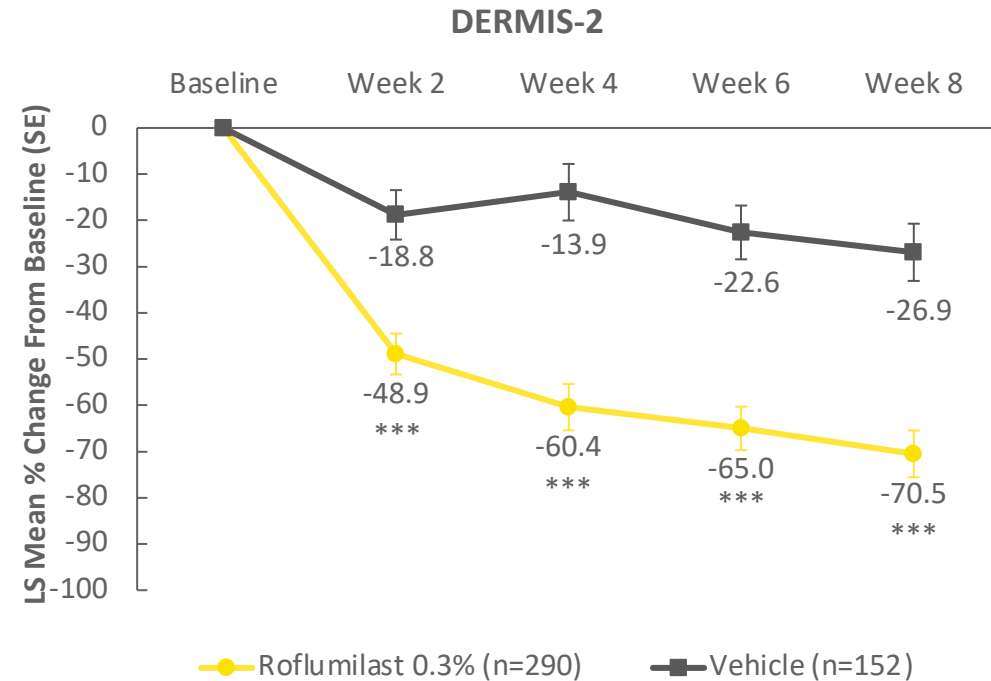
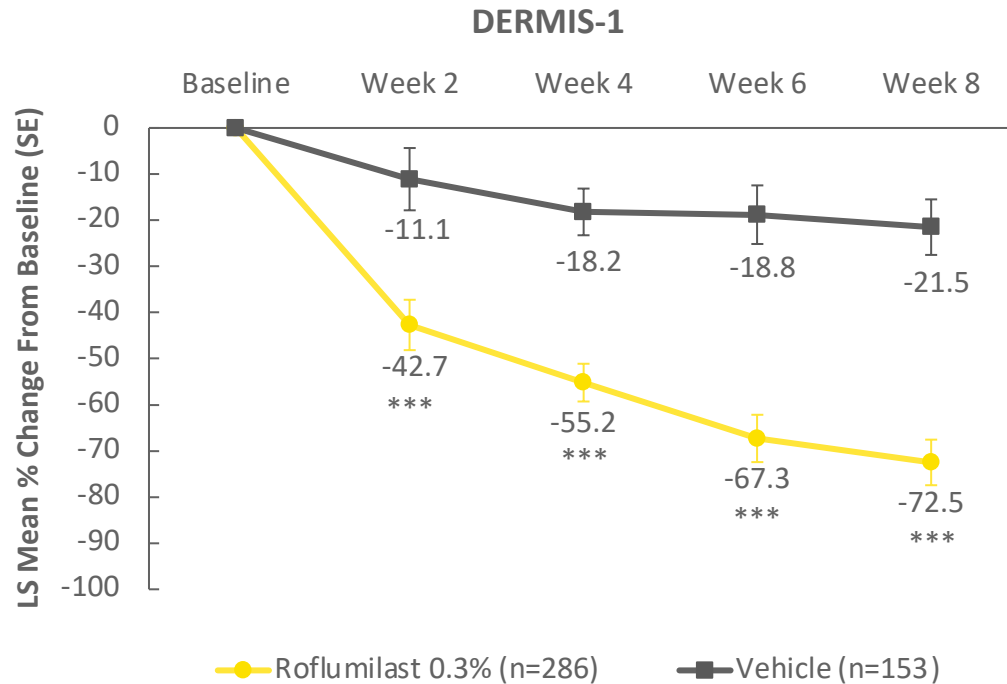


** p<0.01; *** p<0.0001

WI-NRS scale: 0 (No Itch) to 10 (Worst Imaginable Itch); evaluated in a subset of the intent-to-treat population of patients with WI-NRS pruritus score ≥ 4 at baseline using a Cochran-Mantel-Haenszel test stratified by site, baseline IGA, and baseline intertriginous involvement; missing scores imputed using multiple imputations; 95% CI obtained using the Wilson method
CI: confidence interval; WI-NRS: Worst Itch Numeric Rating Scale

Roflumilast Cream Reduced the Patient-Reported Severity of Itch

LS mean percentage change from baseline in Psoriasis Symptom Diary item 1:
How severe was your psoriasis-related itching over the past 24 hours?



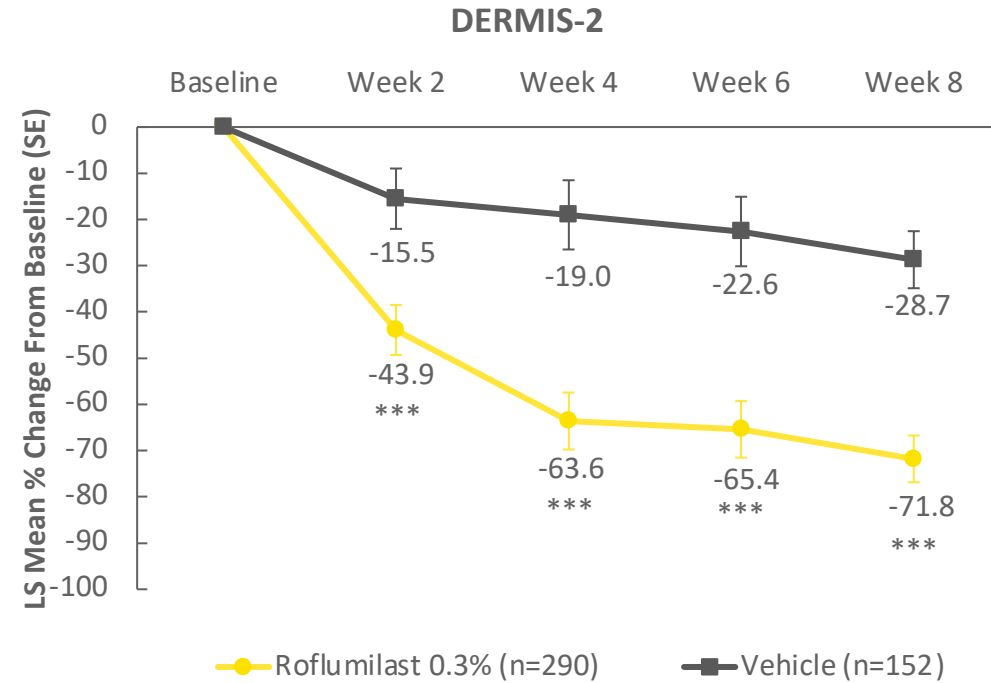
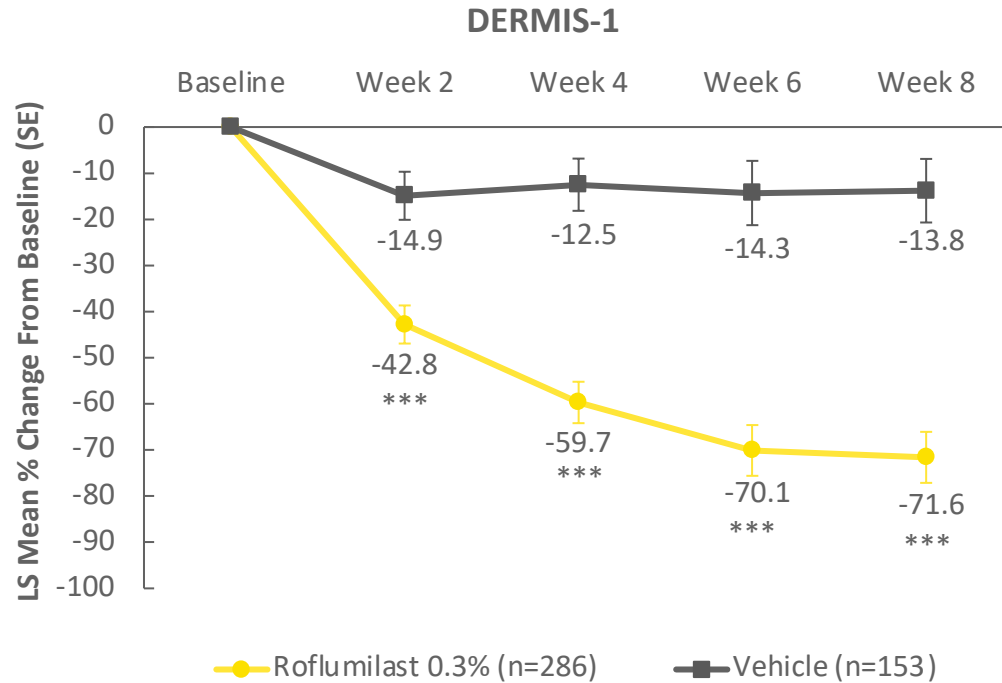
*** p<0.0001

Significantly greater improvements in itch severity were observed with roflumilast cream in both studies

Evaluated in the intent-to-treat population; analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline PSD score as independent variables.
IGA: Investigator Global Assessment; LS: Least squares; SE: standard error; WI-NRS: Worst Itch Numeric Rating Scale

Roflumilast Cream Significantly Reduced Patient-Reported Burden of Itch at All Timepoints

LS mean percentage change from baseline in Psoriasis Symptom Diary item 2:
How bothered were you by your psoriasis-related itching over the past 24 hours?



*** p<0.0001

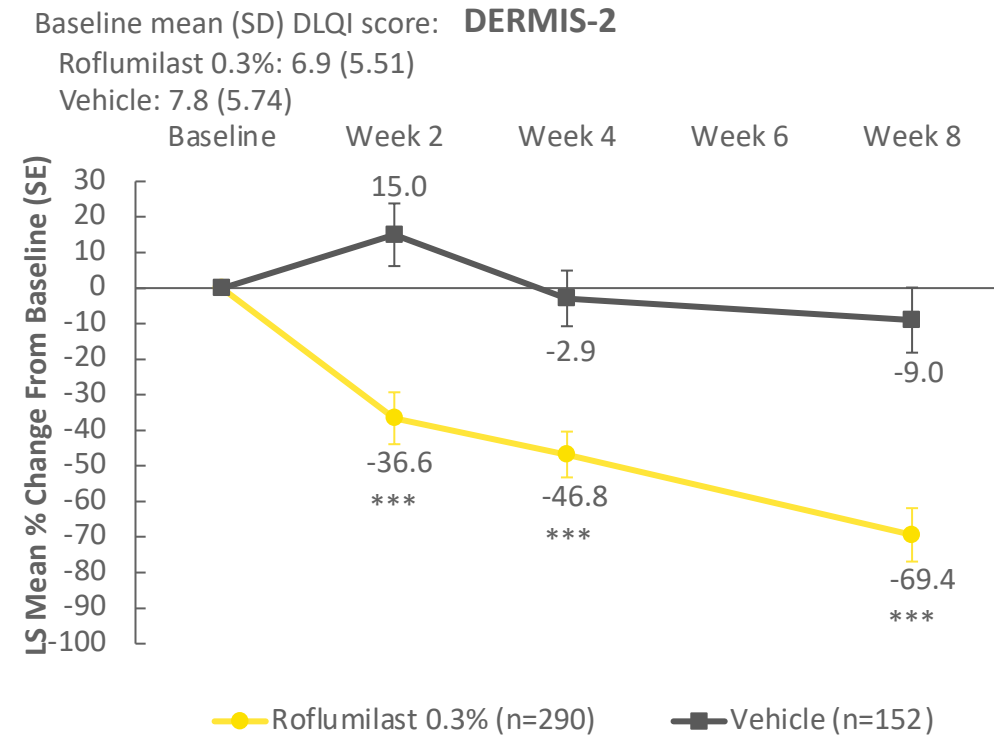
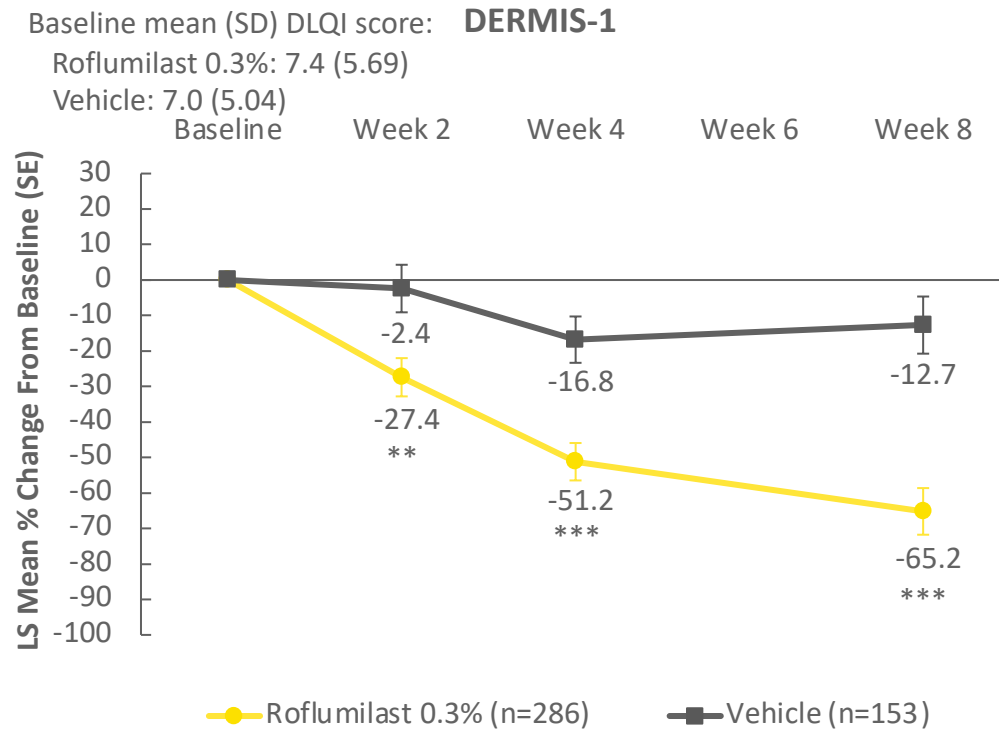
Significantly greater improvements in burden of itch were observed with roflumilast cream in both studies

Evaluated in the intent-to-treat population; analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline PSD score as independent variables.
IGA: Investigator Global Assessment; LS: least squares; SE: standard error; WI-NRS: Worst Itch Numeric Rating Scale

Roflumilast Cream Improved Patient Quality of Life

LS mean change from baseline in DLQI total scores favored roflumilast over vehicle across both studies

LS mean percentage change from baseline in DLQI



** p<0.01; *** p<0.0001

Evaluated in the intent-to-treat population; analysis of covariance with treatment, site, baseline IGA, baseline intertriginous involvement, and baseline DLQI score as independent variables.
DLQI: Dermatology Life Quality Index; IGA: Investigator Global Assessment; LS: least squares; SD: standard deviation; SE: standard error; WI-NRS: Worst Itch Numeric Rating Scale

Patient Disposition: Few Patients Discontinued Due to Adverse Events

Patients, n (%)	DERMIS-1		DERMIS-2	
	Roflumilast Cream 0.3% (n=286)	Vehicle (n=153)	Roflumilast Cream 0.3% (n=290)	Vehicle (n=152)
Completed	255 (89.2)	133 (86.9)	264 (91.0)	131 (86.2)
Prematurely discontinued	31 (10.8)	20 (13.1)	26 (9.0)	21 (13.8)
Reason for discontinuation				
Withdrawal by patient	11 (3.8)	11 (7.2)	10 (3.4)	11 (7.2)
Physician decision	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
Noncompliance	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
Protocol violation	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Lost to follow-up	12 (4.2)	4 (2.6)	15 (5.2)	7 (4.6)
Adverse event	5 (1.7)	2 (1.3)	1 (0.3)	2 (1.3)
Pregnancy	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (0.3)	2 (1.3)	0 (0.0)	0 (0.0)

Safety and Tolerability of Roflumilast Cream Were Similar to Vehicle

- Roflumilast cream demonstrated low rates of application site AEs, treatment-related AEs, and discontinuations due to AEs
 - Rates were comparable to vehicle
- There were no treatment-related SAEs
- Application site reactions were low
- Over 96% of patients in each group had no evidence of irritation at Week 4 or Week 8 as assessed by the investigators

n (%)	DERMIS-1		DERMIS-2	
	Roflumilast cream 0.3% (n=286)	Vehicle (n=153)	Roflumilast cream 0.3% (n=290)	Vehicle (n=152)
Patients with any TEAE	72 (25.2)	36 (23.5)	75 (25.9)	28 (18.4)
Patients with any treatment-related TEAE	7 (2.4)	3 (2.0)	16 (5.5)	8 (5.3)
Patients with any SAE	2 (0.7)	1 (0.7)	0 (0.0)	1 (0.7)
Patients who discontinued study due to AE	5 (1.7)	2 (1.3)	1 (0.3)	2 (1.3)
Most common TEAE (>2% in any group), preferred term				
Hypertension ^a	5 (1.7)	6 (3.9)	4 (1.4)	0 (0.0)
Headache	3 (1.0)	2 (1.3)	11 (3.8)	1 (0.7)
Diarrhea	10 (3.5)	0 (0.0)	8 (2.8)	0 (0.0)
Psoriasis	0 (0.0)	3 (2.0)	1 (0.3)	0 (0.0)
Nasopharyngitis	5 (1.7)	3 (2.0)	1 (0.3)	1 (0.7)

^aHypertension includes synonymous terms (eg, blood pressure increased)

Data are presented for safety population. AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event

Conclusions

- Once-daily treatment with roflumilast cream 0.3% provided significant, consistent, and sustained improvements in the severity and burden of itch and QoL in patients with chronic plaque psoriasis
 - Onset of action of patient-reported improvements were observed as early as the first timepoint measured (2 weeks) and improvement continued through Week 8
 - Results were reproducible across both phase 3 studies
- Roflumilast cream was associated with low rates of application site AEs, treatment-related AEs, and discontinuations due to AEs
- DERMIS-1 and DERMIS-2 support the potential use of investigational roflumilast cream as an effective and well-tolerated non-steroidal topical therapy in patients with chronic plaque psoriasis

These two phase 3 studies demonstrate **roflumilast cream**, an investigational once-daily, non-steroidal topical PDE-4 inhibitor, was effective in reducing itch, which decreased disease burden and improved QoL in patients with chronic plaque psoriasis