Rocatinlimab Update
Phase 3 Studies: ROCKET Program Summary of Results from 4 Trials in Adults with Moderate to Severe Atopic Dermatitis

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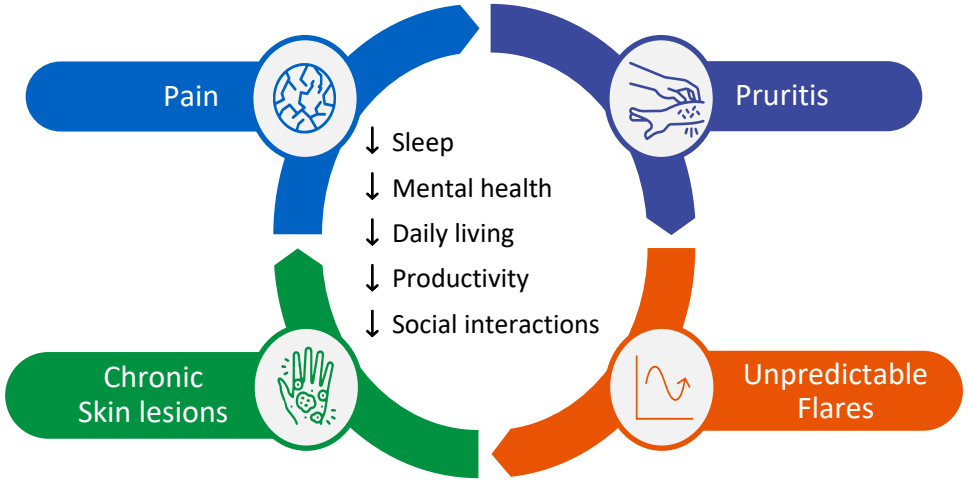
Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

Atopic Dermatitis (AD) is a chronic and heterogeneous inflammatory skin disease that imparts a significant burden on patients and caregivers

- AD causes excessively dry, itchy skin that can be painful
- Repeated scratching can cause the skin to thicken, harden or become vulnerable to infection
- Clinical manifestations of AD are heterogeneous in intensity and distribution, and are driven by complex networks of immune pathways
- Chronic symptoms of moderate-to-severe AD can negatively impact sleep, mental health, daily living, productivity, and social interactions, leading to an overall decrease in quality of life



Despite existing therapies, a high unmet medical need remains as many patients with moderate-to-severe AD continue to experience inadequate disease control[1,2,3]

1. Lio P, et al. *J Drugs Dermatol.* 2023;22:119-131. **2.** Eichenfield LF, et al. *SKIN J Cutaneous Med.* 2024;8(6):s462. **3.** Hongbo Y, et al. *J Invest Dermatol.* 2005;125:659-664.

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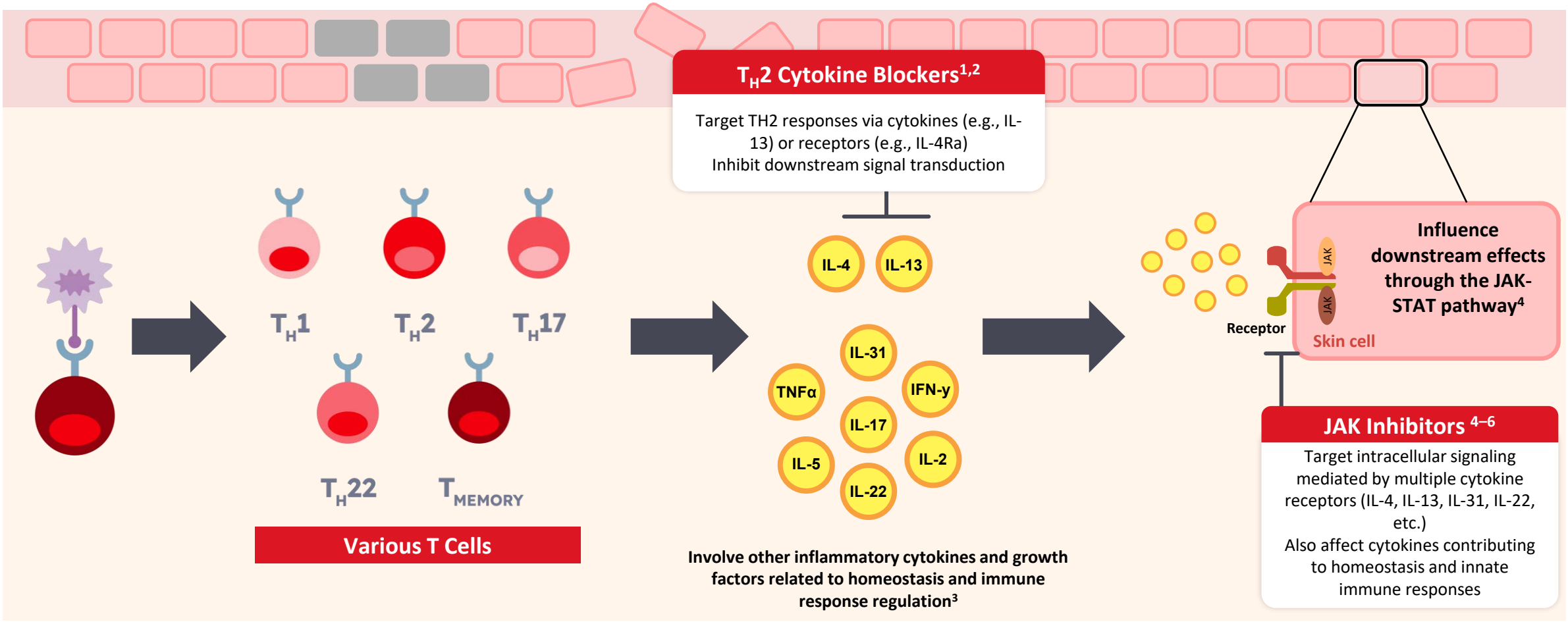
Pathogenesis of Atopic Dermatitis and Existing Drug Targets



Existing systemic therapies for Moderate to Severe AD patients target individual cytokines and their associated signaling pathways

AD, atopic dermatitis; IFN-γ, interferon gamma; IL, interleukin; IL-4Ra, interleukin 4 receptor alpha; JAK, Janus kinase; JAK-STAT, Janus kinase-signal transducer and activator of transcription; TH, T helper cell; TNFα, tumor necrosis factor alpha.

1. Bieber T. *Nat Rev Drug Discov.* 2022;21:21-40. **2.** LEO Pharma. Prescribing information, 2023. [Accessed Jan 2025]. **3.** Huang IH, et al. *Front Immunol.* 2022;13:1068260. **4.** Kamata M, Tada Y. *JID Innov.* 2023;3(3):100195. **5.** Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2020;34:2717-2744. **6.** Pavel AB, et al. *J Allergy Clin Immunol.* 2019;144:1011-1024.

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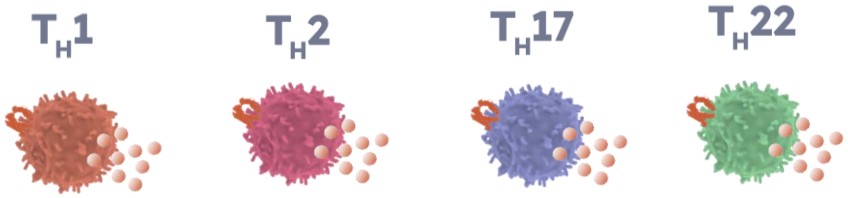
T Cells Play a Central Role in inflammatory disease including AD

Effector T cells[1]

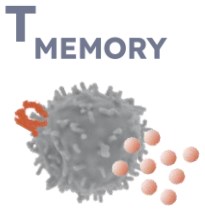
Key contributors to the release of cytokines that drive inflammation and contribute to the heterogeneous clinical symptoms of AD



IFNg, TNFa | IL4, IL13, IL31 | IL17 | IL22

Memory T cells[1,2]

Persist after initial exposure to allergens, rapidly reactivating and releasing cytokines upon re-exposure, contributing to chronicity, recurrence, and severity in AD



Effector T Cells release multiple cytokines (interleukins) that drive immune responses in skin while Memory T Cells confer specific immune memory [1,2]

AD, atopic dermatitis; IFN-γ, interferon gamma; IL, interleukin; T_H, T helper cell; TNF-α, tumor necrosis factor alpha.

1. Croft M, et al. *Am J Clin Dermatol.* 2024;25(3):447-461. **2.** Chen L, et al. *Cell Mol Immunol.* 2020;17:64-75.

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AD is a chronic condition characterized by repeated cycles of exacerbation and remission, where memory T cells in the skin are responsible for acute flare-ups (flares)[1,2]

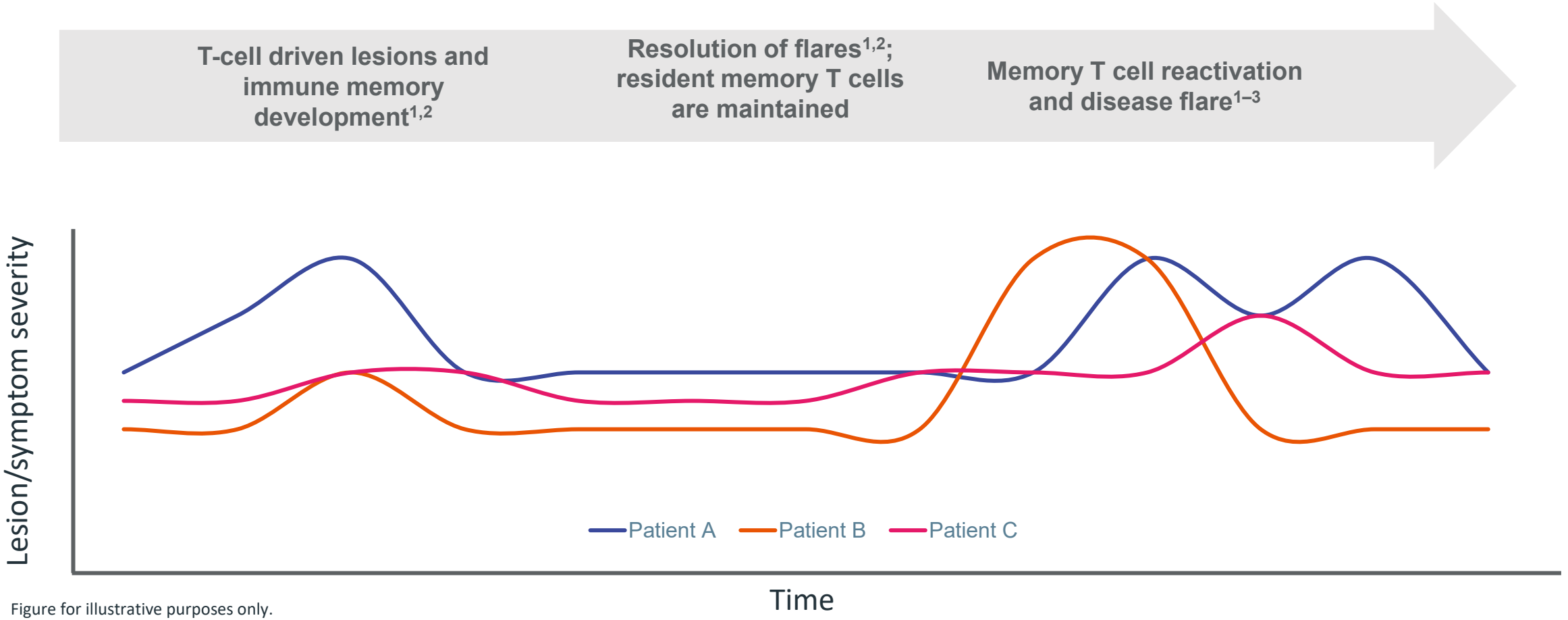

Figure for illustrative purposes only.

AD, atopic dermatitis.

1. Croft M, et al. *Am J Clin Dermatol.* 2024;25(3):447-461. **2.** Chovatiya R, et al. *J Drugs Dermatol.* 2022;21(2):172-176. **3.** Chen L, et al. *Cell Mol Immunol.* 2020;17:64-75. **4.** Carlier TDB, et al. *J Autoimmun.* 2021;120:102634.

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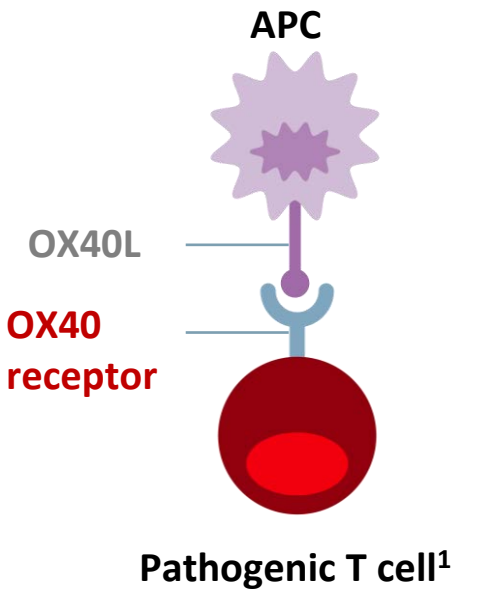
Direct Role for T-Cells and the OX40 Receptor in the Pathogenesis of AD



Pathogenic T cell[1]

What is the OX40 Receptor?

The OX40 receptor is a co-stimulatory molecule with **increased expression on activated effector and memory T cells** at sites of inflammation/disease, but is **not** expressed on naïve T cells[2]

Increased OX40 receptor expression on T cells of patients with AD versus healthy subjects[3]

The number of OX40 receptor+ T cells is **increased and localized to lesional skin** vs non-lesional skin[3,4]

Cytokines enhanced by OX40 receptor signaling may **drive inflammation beyond skin lesions** (e.g., lungs and other mucosal surfaces)[2,5–7]

AD, atopic dermatitis; APC, antigen-presenting cell; OX40L, OX40 ligand.

1. Croft M, et al. *Am J Clin Dermatol*. 2024;25(3):447-461. **2.** Furue M, et al. *J Clin Med*. 2021;10:2578. **3**. Elsner JSH, et al. *Acta Derm Venereol*. 2020;100:adv00099. **4.** Ilves T, Harvima IT. *J Eur Acad Dermatol Venereol.* 2013;27(2):e197-205. **5.** Lebwohl MG, et al. *J Clin Aesthet Dermatol.* 2013;6(7 Suppl):S2-S18. **6.** Ungar B, et al. *J Invest Dermatol*. 2017;137(3):603-613. **7**. Boguniewicz M, et al. *J Allergy Clin Immunol Pract*. 2017;5(6):1519-1531.

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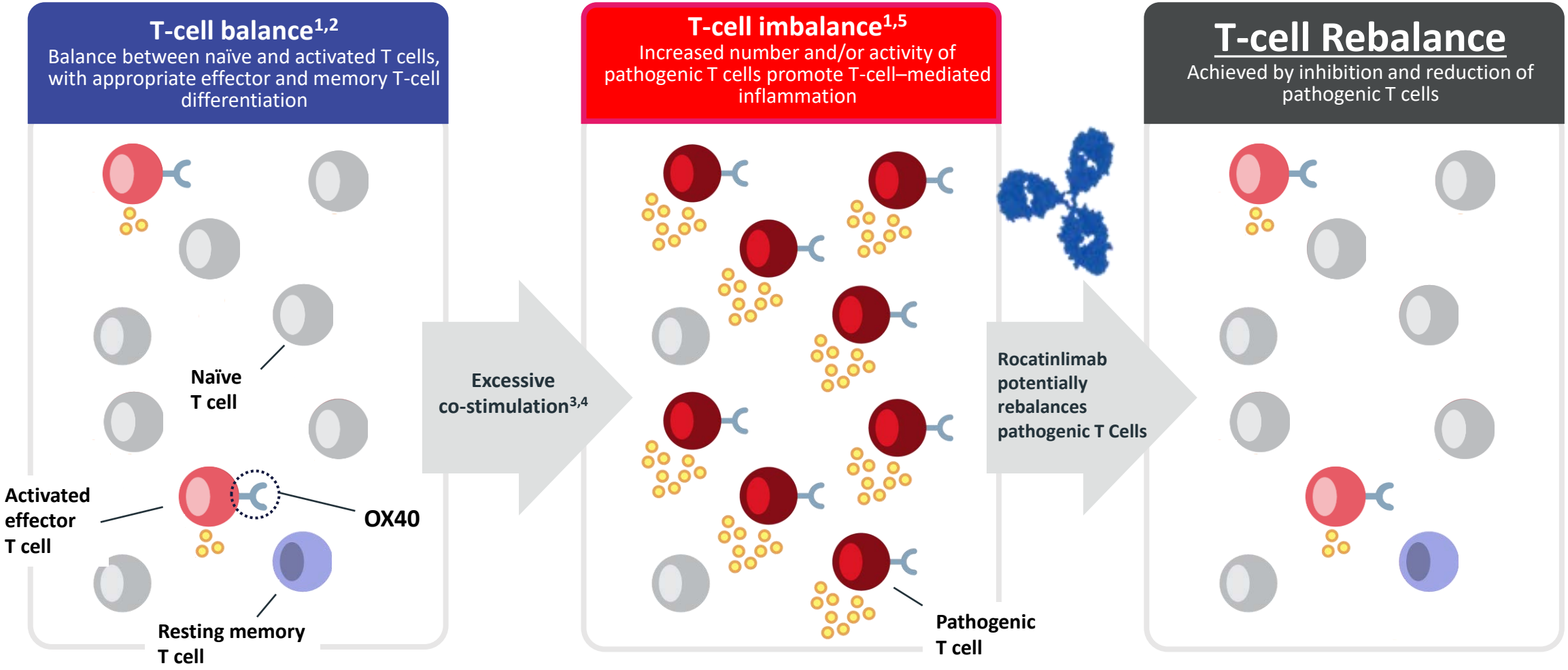
T-cell Rebalance – Aiming for broad and sustained therapeutic effects by addressing a root cause of inflammatory diseases



Novel OX40-mediated mechanism targeting pathogenic T-cells improves T cell imbalance, root cause of inflammatory diseases, aiming for T cell rebalancing. Potential action on memory T cells for sustained symptom control and disease modification

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1. Croft M, et al. *Am J Clin Dermatol.* 2024;25(3):447-461. **2.** Sun L, et al. *Signal Transduct Target Ther.* 2023;8(1):235. **3.** Zhang Q, Vignali DAA. *Immunity.* 2016;44(5):1034-1051. **4.** Zheng C, et al. *Front Immunol.* 2023:14:1081999. **5.** Sadrolashrafi K, et al. *Cells*. 2024;13(7):587.

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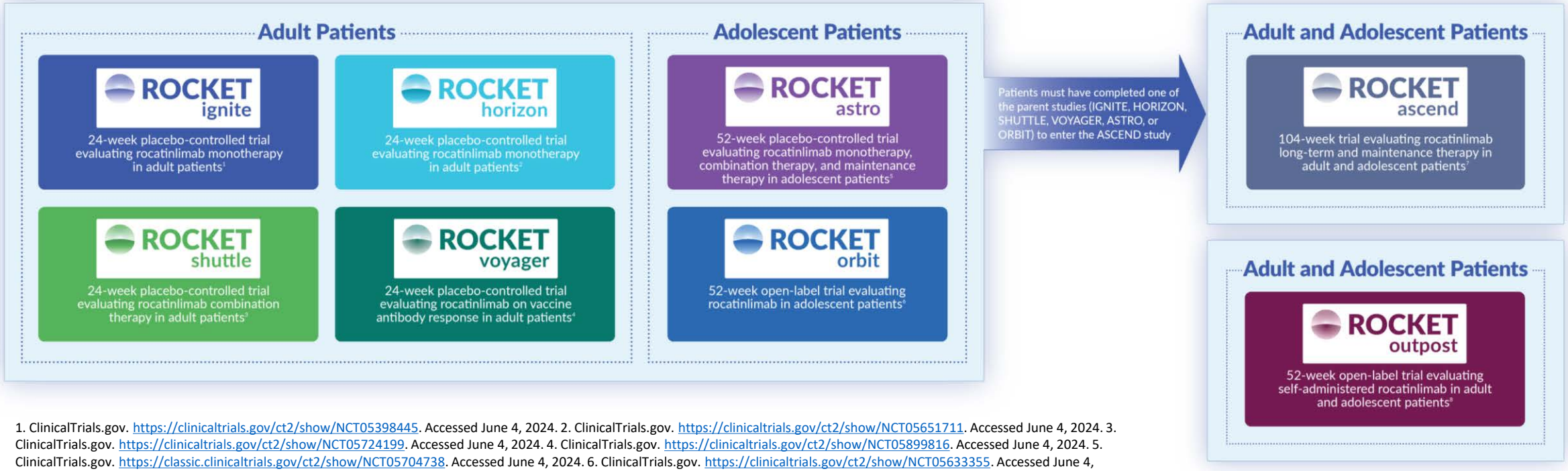
Rocatinlimab – Phase 3 the ROCKET Program

- Composed of eight global studies enrolling adult and adolescent moderate – severe AD patients
- To date, over 3,300 patients have been enrolled with seven studies having completed enrollment
- Studies were designed to examine long-term sustained efficacy and safety



1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05398445. Accessed June 4, 2024. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05651711. Accessed June 4, 2024. 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05724199. Accessed June 4, 2024. 4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05899816. Accessed June 4, 2024. 5. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/NCT05704738. Accessed June 4, 2024. 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05633355. Accessed June 4, 2024. 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05882877. Accessed June 4, 2024. 8. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06224192. Accessed June 4, 2024.

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Rocatinlimab – Today's agenda

Detailed data has been disclosed at the **Late Breaking Abstract** on the afternoon of **March 8, 2025**, US time, at the **American Academy of Dermatology (AAD)**.

Topline data disclosed on March 8, 2025

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ROCKET HORIZON
AAD 2025 Presentation Summary

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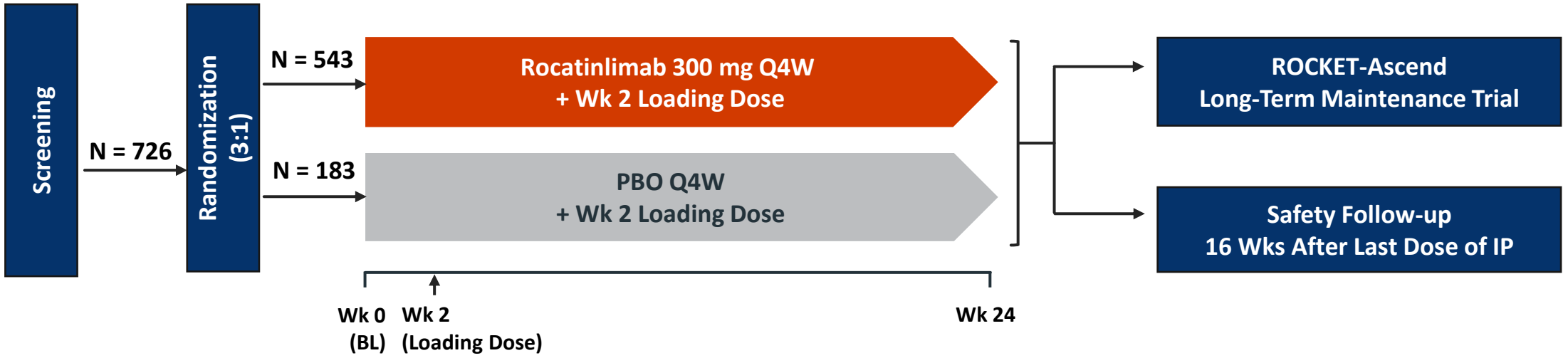
Phase 3 ROCKET-HORIZON Trial Evaluated Rocatinlimab Monotherapy vs PBO in Adults With Moderate-to-Severe AD



Randomization stratified by:

- Baseline disease severity
- Geographic region

Key Inclusion Criteria

- Age ≥ 18 yrs
- AD diagnosis present for ≥ 12 mo
- vIGA-AD™ of 3 or 4
- EASI ≥ 16
- BSA ≥ 10%
- 7-day recall WP-NRS ≥ 4
- Inadequate response to TCS of medium or higher potency (± TCI) or systemic therapy (after appropriate washout period)

Time course of T cell population measured on Day 1 and Wks 8, 16, and 24

AD, atopic dermatitis; baseline, BL; BSA, body surface area; EASI, Eczema Area and Severity Index; IP, investigational product; mo, month; PBO, placebo; Q4W, every 4 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; vIGA-AD, validated Investigator Global Assessment for AD; Wk, Week; WP-NRS, Worst Pruritis Numerical Rating Scale; yr, year.

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Patient Demographics and Disease Characteristics at Baseline

	ROCA	PBO	Total
Full Analysis Set	**N = 543**	**N = 183**	**N = 726**
Age, yrs, mean (SD)	37.8 (14.6)	40.4 (15.6)	38.4 (14.9)
Female, %	45.7	44.3	45.3
Hispanic/Latino, %	11.6	12.0	11.7
Race, %			
White	59.9	58.5	59.5
Asian	29.7	33.3	30.6
Black	3.5	5.5	4.0
Other[a]	7.0	2.7	5.9
BMI, kg/m^2, mean (SD)	26.5 (5.4)	28.0 (6.8)	26.9 (5.8)
vIGA-AD score, %			
Moderate (3)	61.9	61.2	61.7
Severe (4)	38.1	38.8	38.3
EASI total score (0–72), mean (SD)	28.5 (10.9)	28.6 (11.1)	28.5 (11.0)
Moderate (> 16 to ≤ 21), %	27.8	30.6	28.5
Severe/Very Severe (> 21), %	70.7	68.9	70.2
Prior use systemic therapy,[b] %	63.0	63.4	**63.1**
Prior use biologic or systemic JAK inhibitors,[b] %	**23.9**	**16.4**	**22.0**

a. Includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, multiple, and other. b. Prior use to treat AD.
BMI, body mass index; PBO, placebo; ROCA, rocatinlimab; yr, year.

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Need for Rescue Therapy Was Reduced in the rocatinlimab Group vs PBO

	ROCA 300 mg Q4W	PBO
Full Analysis Set	**N = 543**	**N = 183**
	%	**%**
Any use of rescue therapy by Week 24*	**33.5**	**41.5**
Any use of topical rescue therapy only[a]	**28.7**	**29.5**
Low/medium-potency topical therapy	15.5	13.1
High/super-high–potency topical therapy	13.3	16.4
Any use of systemic rescue therapy[a]	**4.8**	**12.0**
Conventional systemic therapy	3.3	11.5
Biologic or systemic JAK inhibitor	1.5	0.5

*Log-rank *P* value = 0.064

Proportion of patients who used systemic rescue therapy was less in the rocatinlimab group vs PBO

[a]Most advanced line of rescue therapy used for AD. Patients in the systemic rescue therapy group could have also used topical rescue therapy, but patients in the topical rescue therapy group could not have used systemic rescue therapy.

AD, atopic dermatitis; JAK, Janus kinase; PBO, placebo; Q4W, every 4 weeks; ROCA, rocatinlimab.

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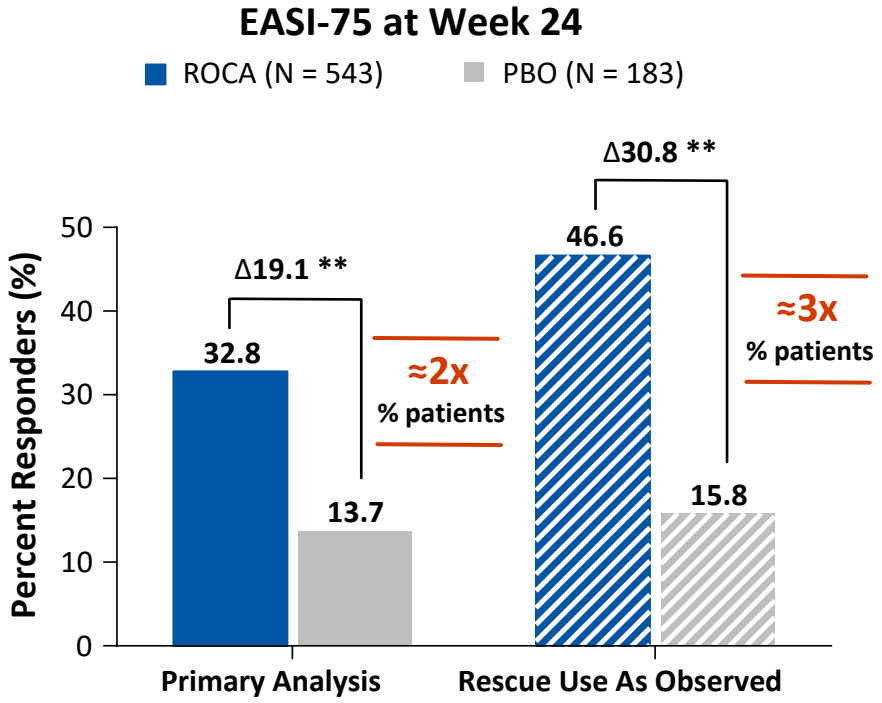
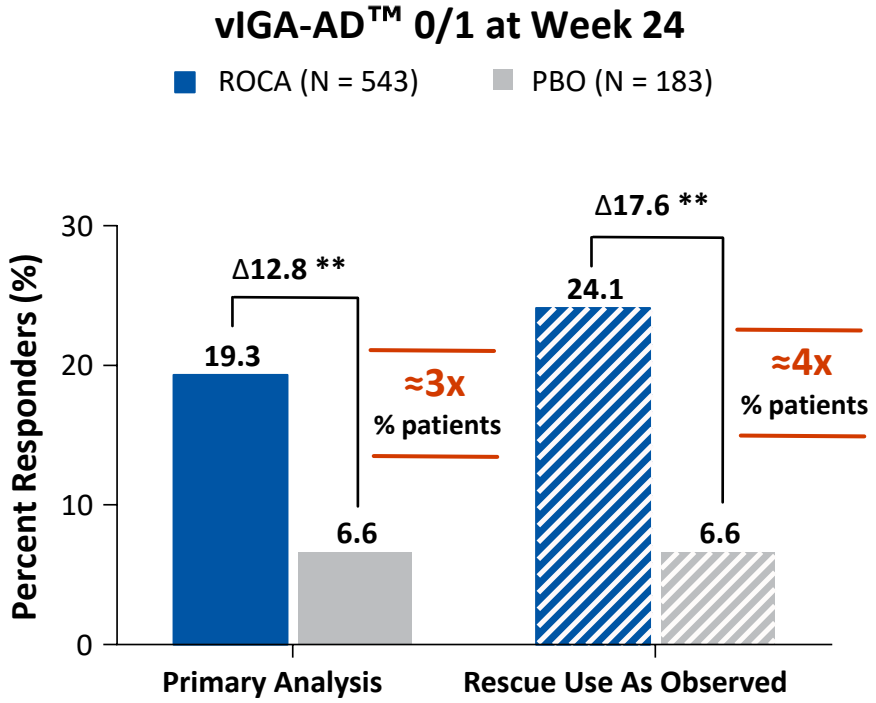
EASI-75 and vIGA-AD 0/1 Responses at Week 24

Primary analysis set (patients with any rescue use classified as nonresponders)
Prespecified analysis (patients with any rescue use classified as observed)





Rocatinlimab met its coprimary endpoints
The prespecified as observed analysis demonstrated greater improvement for rocatinlimab vs PBO

** *P*< 0.001. [a]Values represent the common risk difference. *P* values were obtained from a Cochran-Mantel-Haenszel test and adjusted for the stratification factors of baseline disease severity and geographic region.
EASI-75, ≥ 75% reduction in Eczema Area and Severity Index score from baseline; PBO, placebo; ROCA, rocatinlimab; vIGA, validated Investigator Global Assessment.

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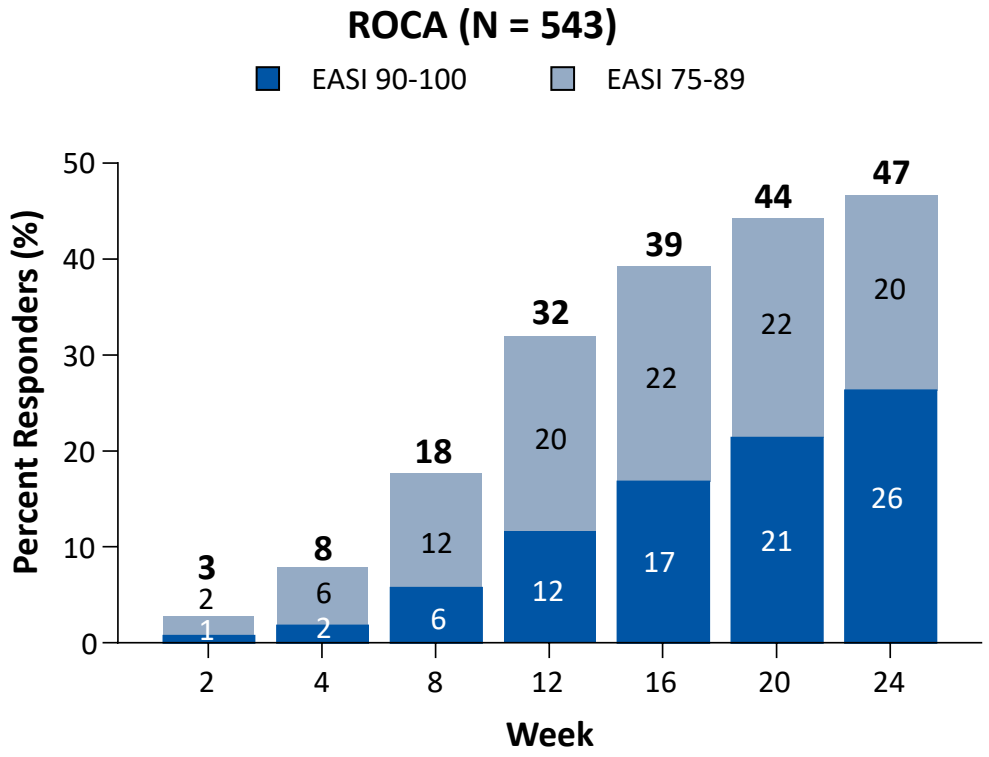
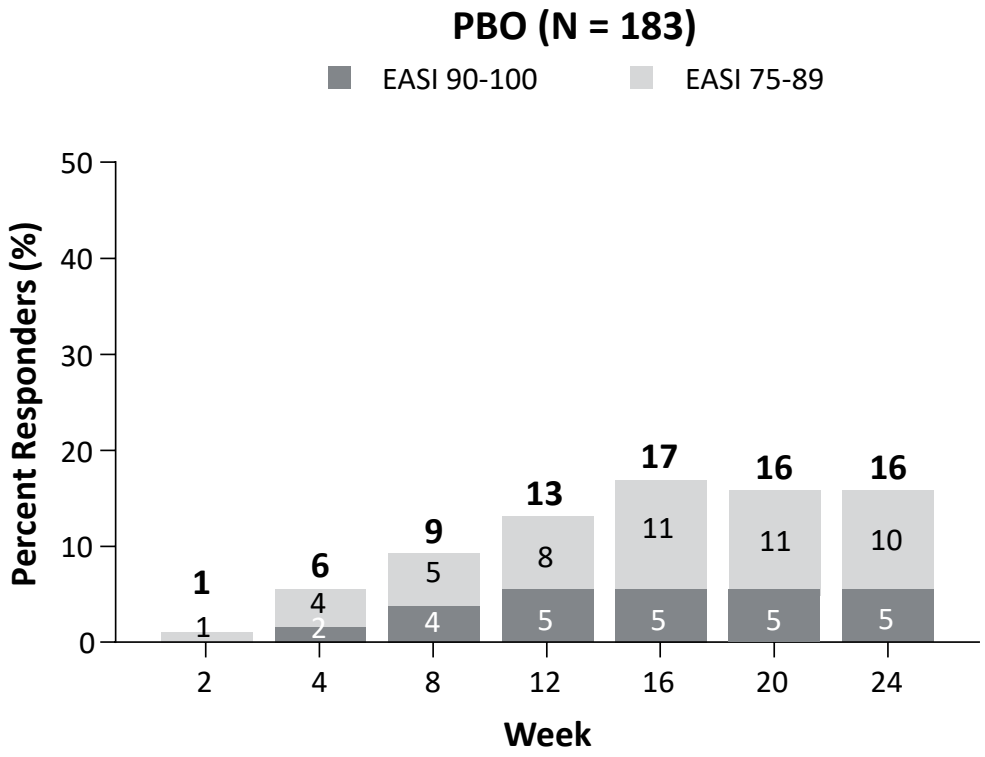
EASI 75-89 and EASI 90-100 at Week 24

Prespecified analysis (patients with any rescue use classified as observed)





Depth of skin response for patients treated with rocatinlimab vs PBO continued to increase through Week 24

Values above bars indicate the percent of patients that were EASI-75 responders.
EASI, Eczema Area and Severity Index; EASI-75, ≥ 75% reduction in Eczema Area and Severity Index score from baseline; EASI 75-89, ≥ 75% to ≤ 89% reduction in EASI score from baseline; EASI 90-100, ≥ 90% to ≤ 100% reduction in EASI score from baseline; PBO, placebo; ROCA, rocatinlimab.

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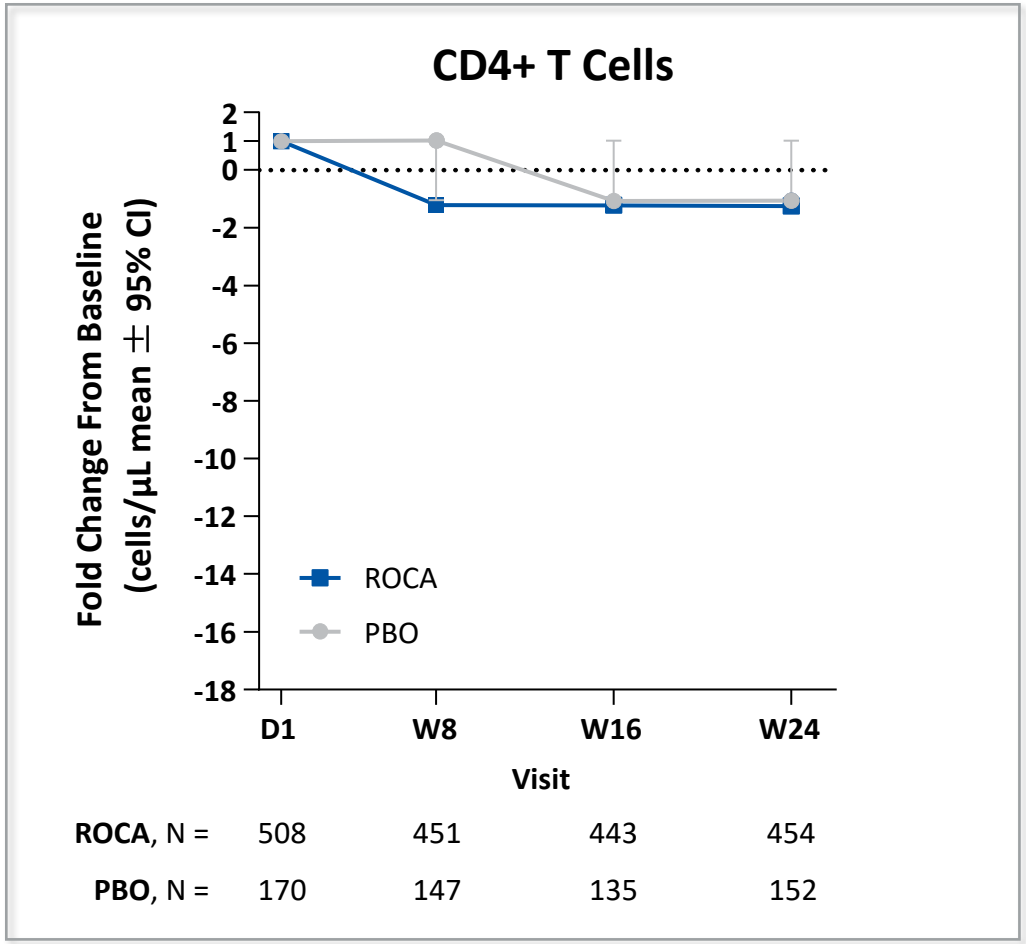
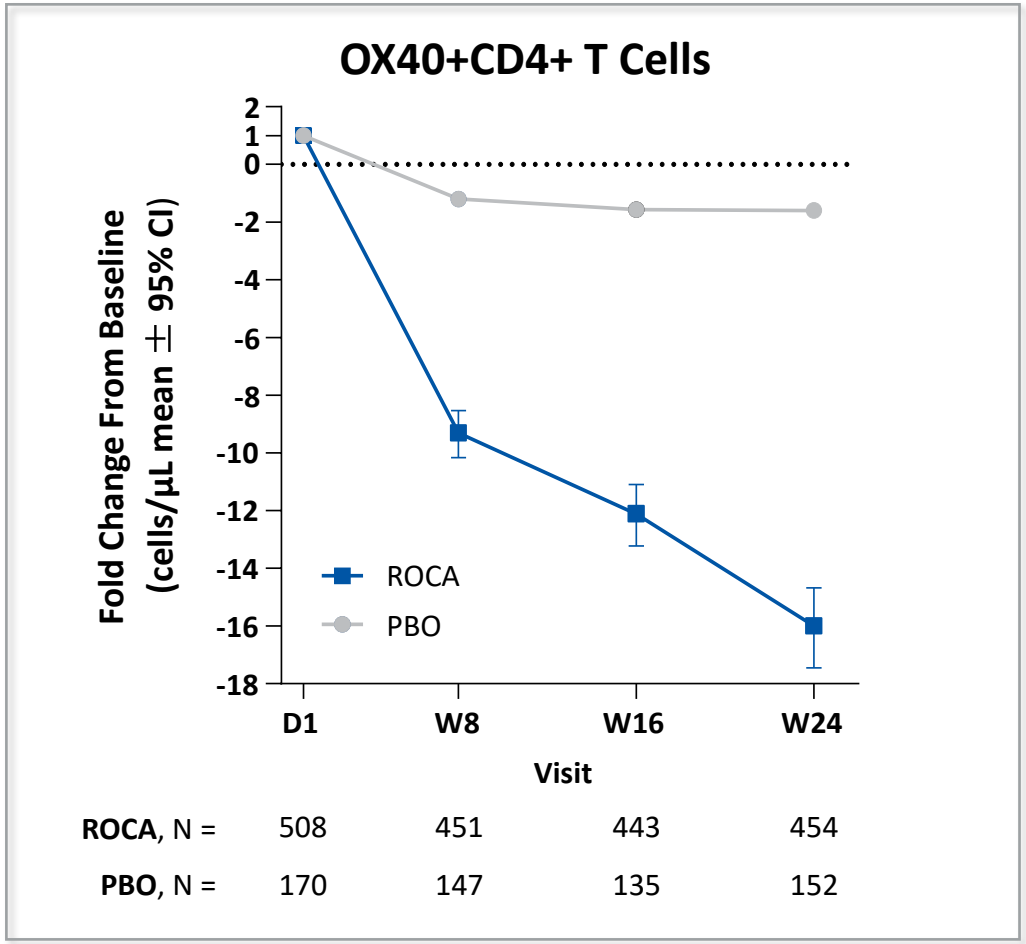
Longitudinal change of T cell number after rocatinlimab treatment





Rocatinlimab Specifically Reduced OX40+ T Cells but Not Conventional T Cells* Over 24 Weeks

*Conventional T cells defined as CD4+ T cell that is not a T regulatory cell; conventional T cells include effector and memory cells.
CD, cluster of differentiation; D, Day; PBO, placebo; ROCA, rocatinlimab; W, Week.

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Safety Analysis

Safety Analysis Set	ROCA 300 mg Q4W N = 544[a] %	PBO N = 180[b] %
TEAEs[c]	**68.4**	**63.3**
Mild	28.1	16.1
Moderate	36.8	38.9
Severe	3.5	8.3
Serious adverse events	**1.8**	**4.4**
Fatal adverse events	**0**	**0**
TEAEs leading to discontinuation of IP	**2.6**	**2.8**
Serious	0.2	1.1
Nonserious	2.4	1.7
TEAEs ≥ 4% in Any Treatment Group		
Dermatitis atopic	19.1	26.7
Pyrexia	10.3	1.1
Nasopharyngitis	8.8	11.7
Headache	7.2	3.9
Upper respiratory tract infection	6.3	3.3
Chills	6.1	1.1
COVID-19	4.0	1.1
Aphthous ulcer	4.0	0.6

Pyrexia and chills were predominantly reported and resolved within 48 hours after first dose of IP

[a]Coded using Medical Dictionary for Regulatory Activities version 27.0. [b]One patient in the PBO group received one dose of ROCA at Week 8 in error and thus was included in the ROCA group for safety analyses. [c]Two patients in the PBO group did not receive any IP and were excluded from the safety analyses.
PBO, placebo; Q4W, every 4 weeks; ROCA, rocatinlimab; TEAE, treatment-emergent adverse event.

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Topline Data of ROCKET IGNITE, SHUTTLE, and VOYAGER

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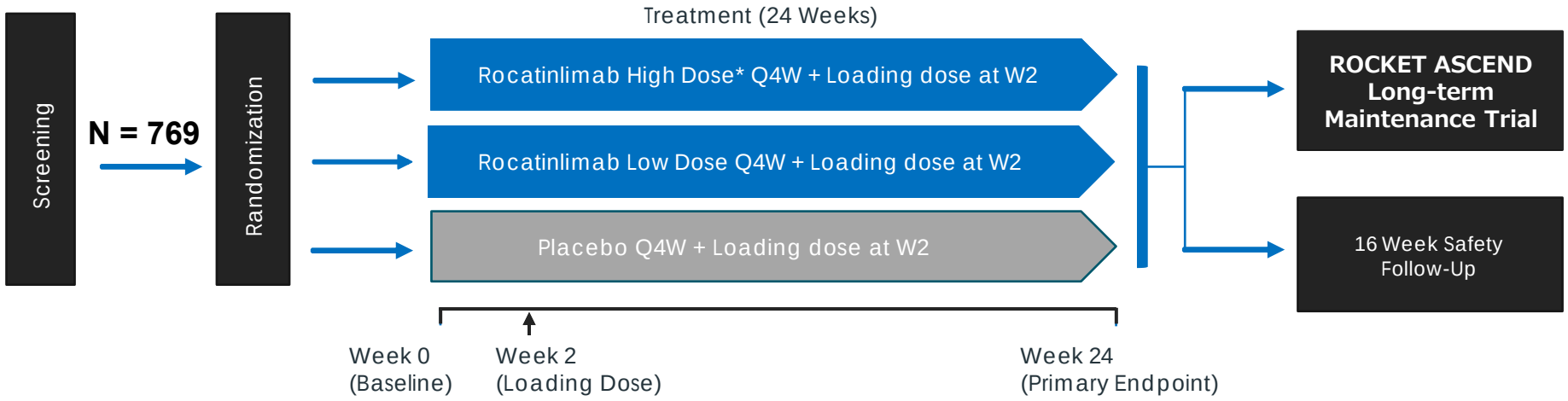
ROCKET-IGNITE Topline Efficacy



Primary Endpoints	ROCA Higher Dose		ROCA Lower Dose	
	%	Difference from PBO (p-value)	%	Difference from PBO (p-value)
EASI-75	42.3	29.5 (p<0.001)	36.3	23.4 (p<0.001)
vIGA-AD 0/1	23.6	14.9 (p<0.001)	19.1	10.3 (p=0.002)
rIGA-0/1	22.7	14.4 (p<0.001)	16.3	8.0 (p=0.01)

ROCKET-Ignite met its co-primary endpoints and all key secondary endpoints, achieving statistical significance for both rocatinlimab doses versus placebo.

*The higher rocatinlimab dose used in IGNITE and SHUTTLE was identical to the dose used in HORIZON.

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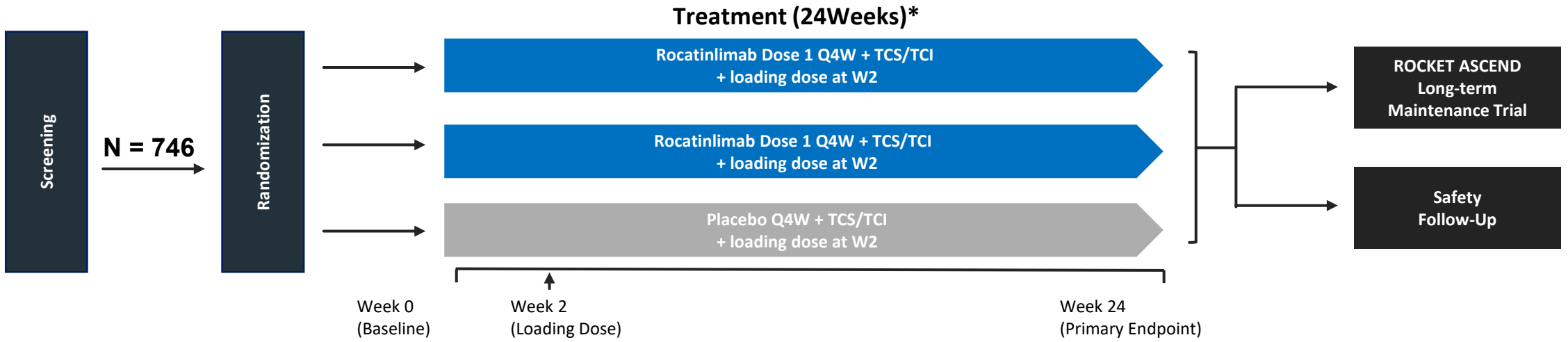
ROCKET-SHUTTLE Topline Efficacy



Primary Endpoints	ROCA Higher Dose		ROCA Lower Dose	
	%	Difference from PBO (p-value)	%	Difference from PBO (p-value)
EASI-75	52.3	28.7 (p<0.001)	54.1	30.4 (p<0.001)
vIGA-AD 0/1	26.1	13.8 (p<0.001)	25.8	13.5 (p<0.001)
rIGA-0/1	23.3	11.5 (p<0.001)	22.7	10.9 (p=0.002)

ROCKET-Shuttle met its co-primary endpoints and all key secondary endpoints, achieving statistical significance for both rocatinlimab doses versus placebo.

*The higher rocatinlimab dose used in IGNITE and SHUTTLE was identical to the dose used in HORIZON.

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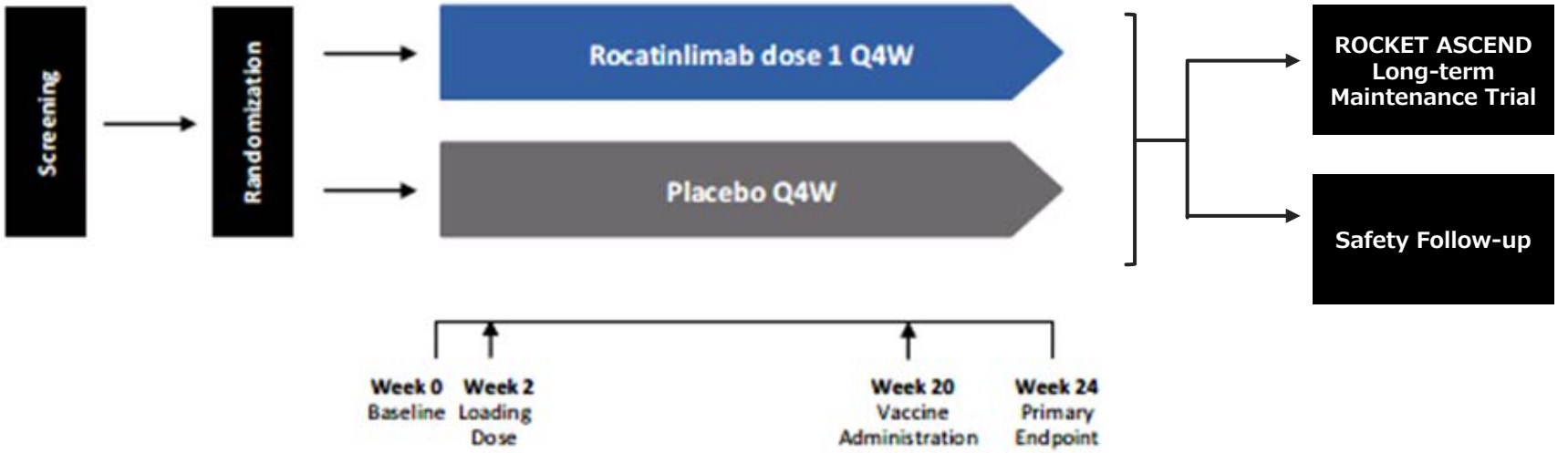
ROCKET-VOYAGER Topline Results



- Tetanus and meningococcal vaccination occurred at week 20 prior to IP
- IgG Abs were assessed at W20, pre vaccination, and at W24

The VOYAGER study successfully demonstrated that rocatinlimab does not interfere with responses to tetanus and meningococcal vaccinations.

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ROCKET Program: Summary of four Phase 3 studies

HORIZON Study Detailed Results @ 2025 AAD Late-breaking Abstract

- Patient background: Over 60% had previous experience with systemic therapy, and more than 20% had prior use of Biologics and JAK inhibitors
- Achieved co-primary endpoints and key secondary endpoints with monotherapy 300mg once every 4 weeks dosing (with a loading dose at week 2)
- Deep efficacy on skin, percentage of patients achieving EASI 90-100 increased with each treatment, not yet reaching plateau at week 24
- Adverse effects were similar to Phase 2 study

IGNITE Study, SHUTTLE Study, VOYAGER Study Topline Data

- IGNITE (monotherapy two-dose study): Both doses achieved co- primary and key secondary endpoints. Higher efficacy scores confirmed compared to HORIZON, and efficacy not yet plateaued at week 24
- SHUTTLE (combination therapy with topical agents): Both doses achieved co-primary and key secondary endpoints
- VOYAGER (vaccine response study): rocatinlimab does not interfere with responses to tetanus and meningococcal vaccinations

Overall

- All 4 studies (total of over 2,400 adult AD patients) achieved co- primary endpoints and key secondary endpoints
- Across ROCKET program results to date, safety findings were generally consistent with the safety profile of rocatinlimab previously observed. The most frequent treatment-emergent adverse events (≥5%) with higher observed proportion in rocatinlimab groups were pyrexia, chills and headache. Fever and chills were mainly reported after the initial dose and resolved within 48 hours.
- A higher number of patients receiving rocatinlimab vs. placebo experienced gastrointestinal ulceration events, with an overall incidence of less than 1%

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ROCKET Program – Future Plan

ROCKET horizon
24-week placebo-controlled trial evaluating rocatinlimab monotherapy in adult patients

Detailed data will be disclosed at the **Late Breaking Session** on the afternoon of **March 8, 2025**, local time, at the **American Academy of Dermatology (AAD)**. (Follow-up at this meeting)

ROCKET ignite
24-week placebo-controlled trial evaluating rocatinlimab monotherapy in adult patients

ROCKET shuttle
24-week placebo-controlled trial evaluating rocatinlimab combination therapy in adult patients

ROCKET voyager
24-week placebo-controlled trial evaluating rocatinlimab on vaccine antibody response in adult patients[4]

Topline data disclosed on **March 8 Detailed data to be disclosed in 2025/2026**

ROCKET ascend
※中間解析

ROCKET astro

Data readout is anticipated in 2H 2025

Current plan for regulatory submission is 2025/2026

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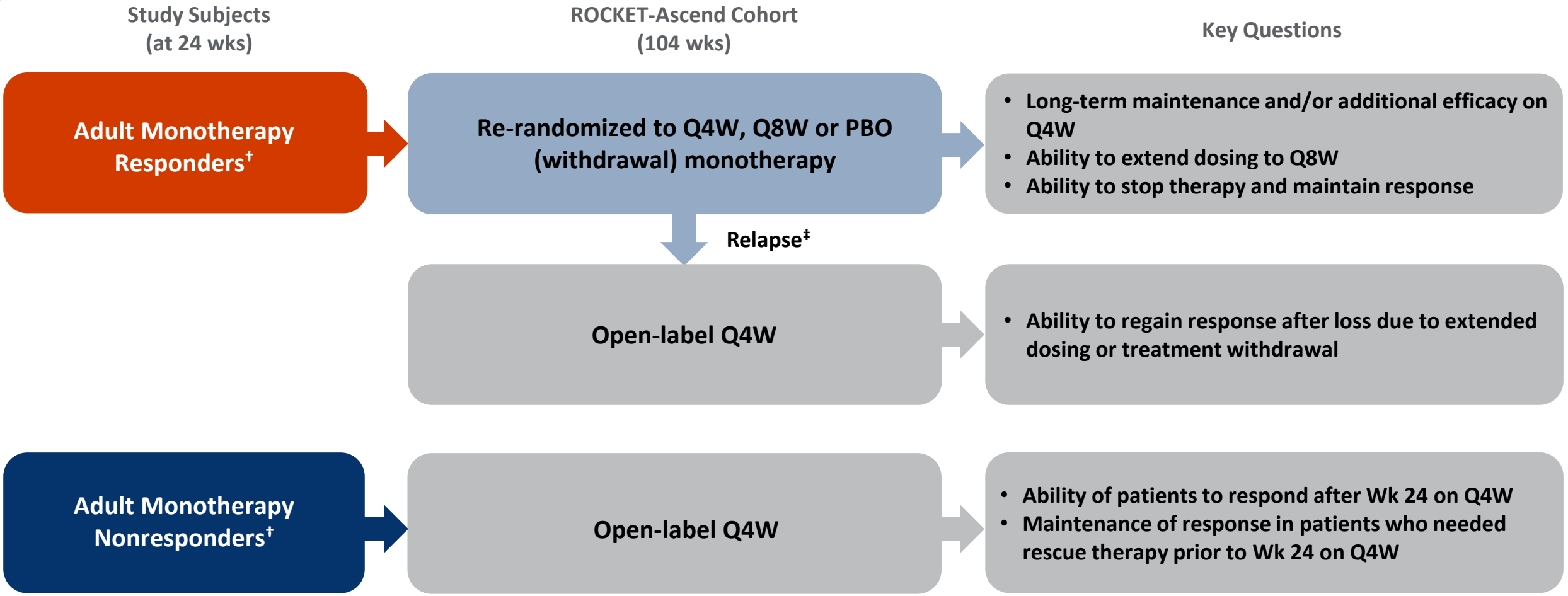
Future Looking: ROCKET ASCEND Design – Adult Cohorts[1,*]



*Additional data will be generated in adolescents including Q4W maintenance, Q8W extension and treatment withdrawal (not shown). †Responders are defined as achieving EASI-75 and/or vIGA 0/1 at Wk 24 without the use of rescue therapy. ‡Relapse defined as loss of at least 50% of improvement in EASI response at Wk 24 of parent study from parent study baseline, or initiation of rescue therapy for AD.
AD, atopic dermatitis; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid; Wk, Week

1. Guttman-Yassky E, et al. [Published online ahead of print February 26, 2025]. *Immunotherapy*.

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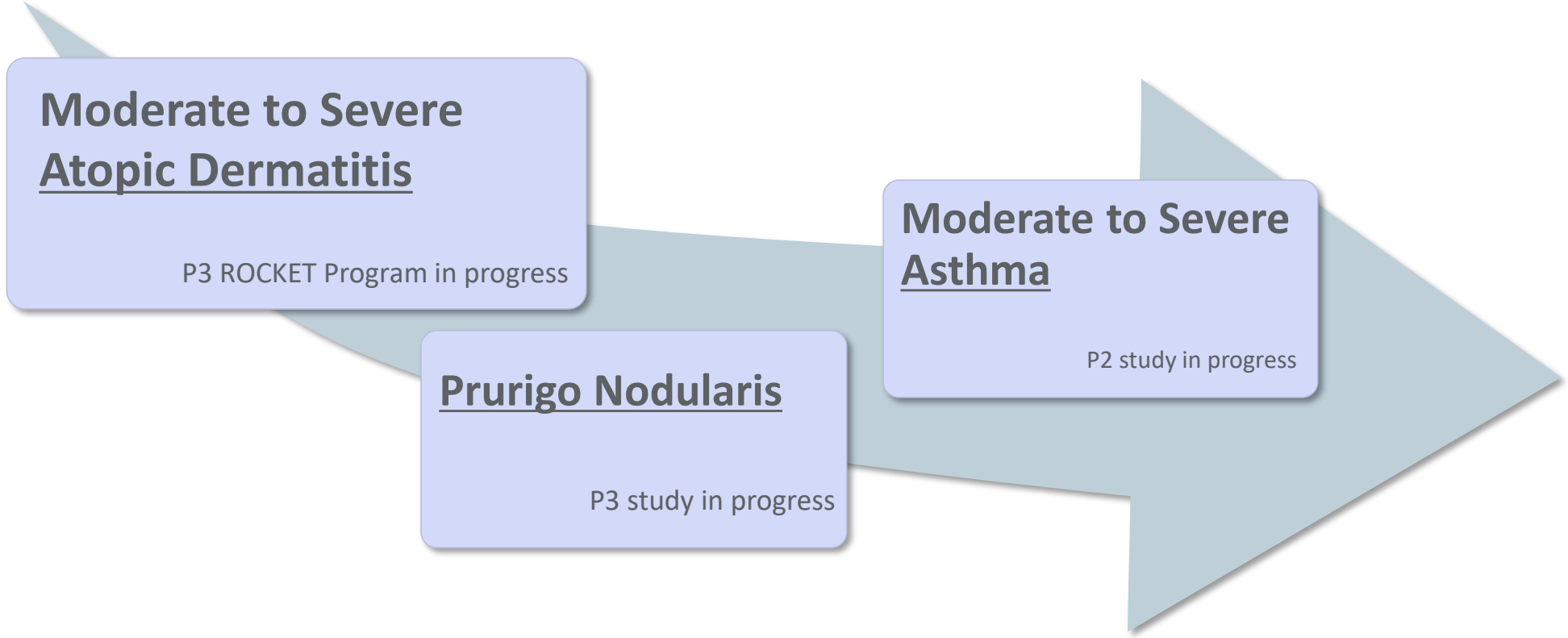
Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

Anti-OX40* antibody – Potential new treatment option for multiple inflammatory diseases

Future expansion into indications where "T-cell rebalancing" is expected to lead to reduced disease activity



We will continue our efforts to deliver Life-changing value to more patients in the future

*OX40 is expressed transiently on T cells when these become activated, and is distinct from its ligand, OX40L.

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