Rocatinlimab Update
Phase 3 Study: ROCKET ASCEND Topline Data

September 9, 2025.

President and Chief Operating Officer (COO)
Abdul Mullick, Ph.D.

Director of the Board, Executive Vice President & Chief Medical Officer
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協和キリン株式会社

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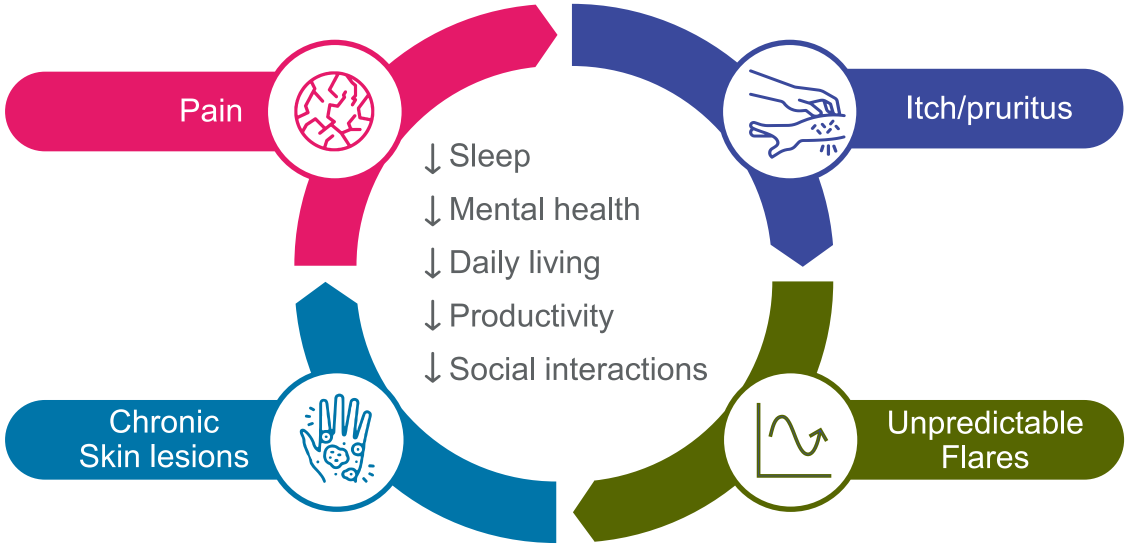
Rocatinlimab is currently under clinical investigation. Its efficacy and safety have not been evaluated by any health authority.

Understanding the complexities and burden of moderate to severe AD

What are the Unmet Medical Needs for the disease?

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



- Globally, up to 10% of adults and 20% of children are living with AD[1]
- Moderate-to-severe AD is characterized by:
  - **Chronic** skin lesions, unpredictable flares, itch/pruritus and pain[1,3-5]
  - Overall decrease in QoL[4,5]
- The many different (**heterogenous**) presentations of AD reflects the complexity of immune pathways[2]

AD, atopic dermatitis; QoL, quality of life.

1. Ständer S. *N Engl J Med*. 2021;384:1136-1143. **2.** Weidinger S, et al. *Nat Rev Dis Primers*. 2018;4:1. **3.** Vakharia PP, et al. *Ann Allergy Asthma Immunol*. 2017;119:548-552.e3. 4. Girolomoni G, et al. *Ther Adv Chronic Dis*. 2022;13:20406223211066728. **5.** Reed B, et al. *Allergy Asthma Proc*. 2018;39:406-410. **6.** Czarnowicki T, et al. *J Allergy Clin Immunol*. 2019;143:1-11.

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]

- **Current treatment options for moderate to severe AD often fail to provide sustained relief or adequately address patient needs, highlighting a significant opportunity for new therapies.**
- **Moreover, some individuals may be ineligible for or unable to tolerate existing treatments.**
- **More than half of patients on systemic therapy today discontinue therapy after just 12 months.**
- **A novel mechanism of action is needed to provide alternative options for patients.**

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.

Immune Memory Plays an Important Role in the pattern of moderate-to-severe AD

AD follows a highly fluctuating, unpredictable, and chronic disease course, with waves of recurrence often occurring in the same area of the body[1,2]

Flare and immune memory development[1,2] | Resolution of flares[1,2] | Immune memory reactivation and disease recurrence[1–3]

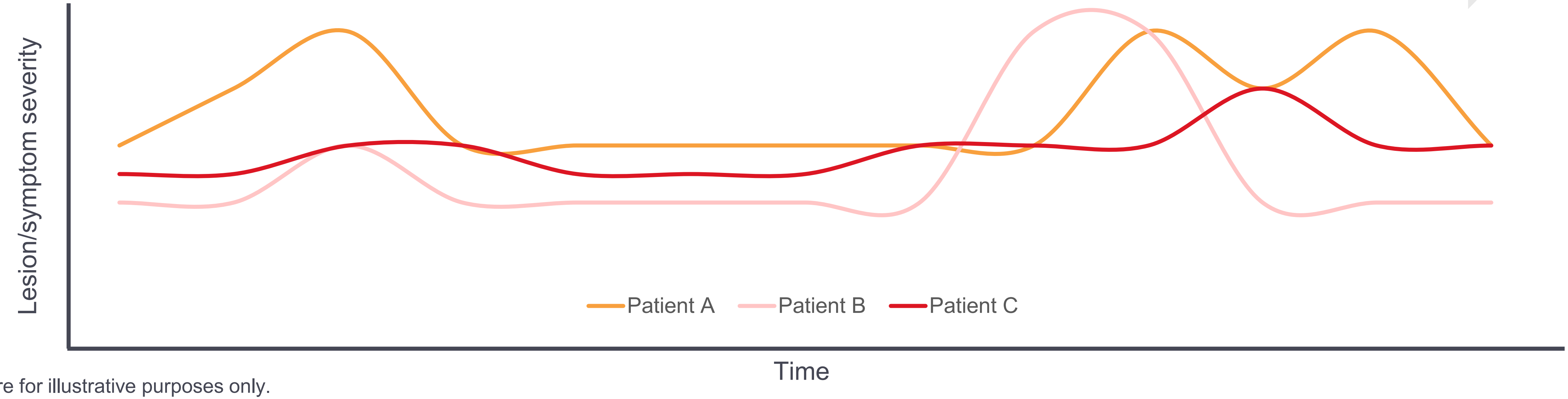


Figure for illustrative purposes only.

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.

T-cell rebalancing therapy with Rocatinlimab: A novel approach for management of moderate to severe atopic dermatitis

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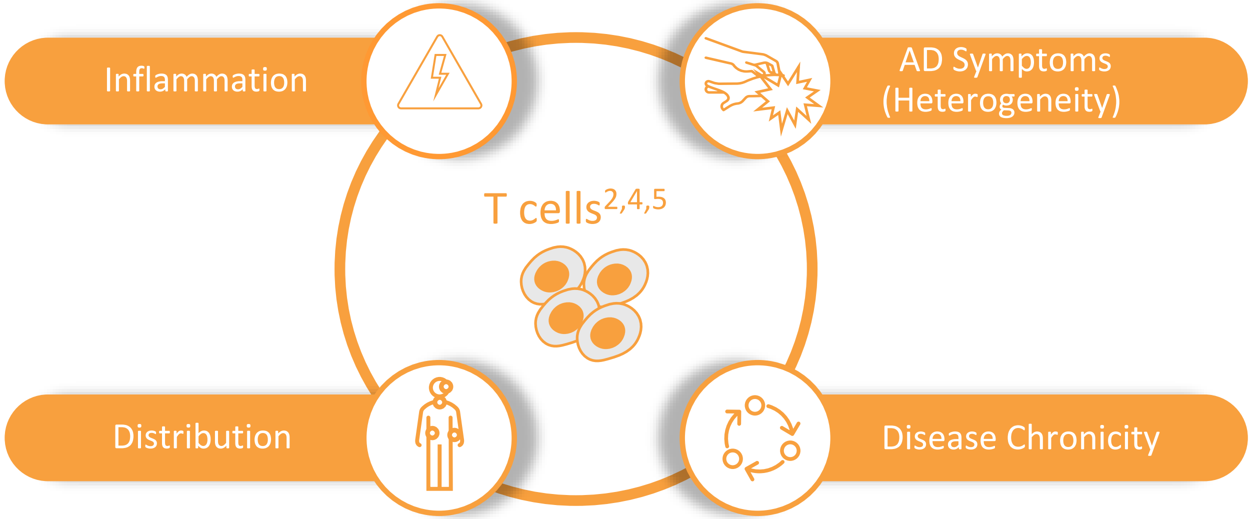
T cells are Central to Inflammation that Drives AD Symptoms

- T cells are a type of white blood cells that protect the body from infection[1]
- Hyperactive T cells play a central role in multiple aspects of AD, including:[2,3]
  - Inflammation
  - Flares and chronic nature of AD
  - Skin thickening
  - Itch and skin pain
- Multiple T cell types, including effector T cells and memory T cells contribute to AD pathogenesis and chronicity through the release of various cytokines[3,4]

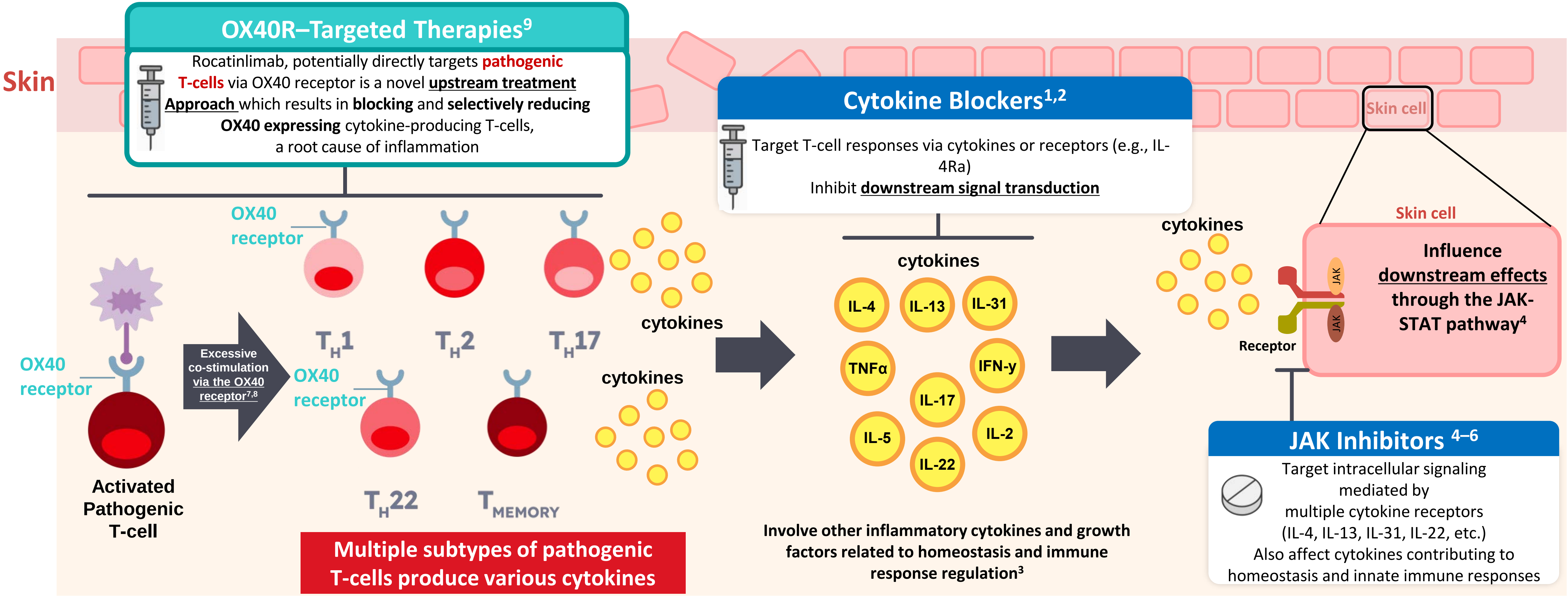


T cells are central to AD pathogenesis, and contribute to severity, flares, and disease chronicity[2,4]

AD, atopic dermatitis.

1. National Cancer Institute. National Cancer Institute. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/t-cell. Accessed June 20, 2025. **2.** De Bruyn Carlier T, et al. *J Autoimmun*. 2021;120:102634. **3.** Kwatra SG, et al. *Clin Transl Immunology*. 2022;11:e1390. **4.** Weidinger S, et al. *Nat Rev Dis Primers*. 2018;4:1. **5.** Weidinger S, et al. *Lancet*. 2016;387:1109-1122.

By directly targeting pathogenic T-cells via the OX40 receptor, rocatinlimab is a potentially novel approach for the management of Moderate-to-Severe AD[10]



AD, atopic dermatitis; IFN-y, 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. 7. Zheng C, et al. Front Immunol. 2023:14:1081999.
8. Zhang Q, Vignali DAA. Immunity. 2016;44(5):1034-51. 9. Bieber T. Nat Rev Drug Discov. 2022;21:21-40, 10. Croft M, et al. Am J Clin Dermatol. 2024;25(3):447-461.

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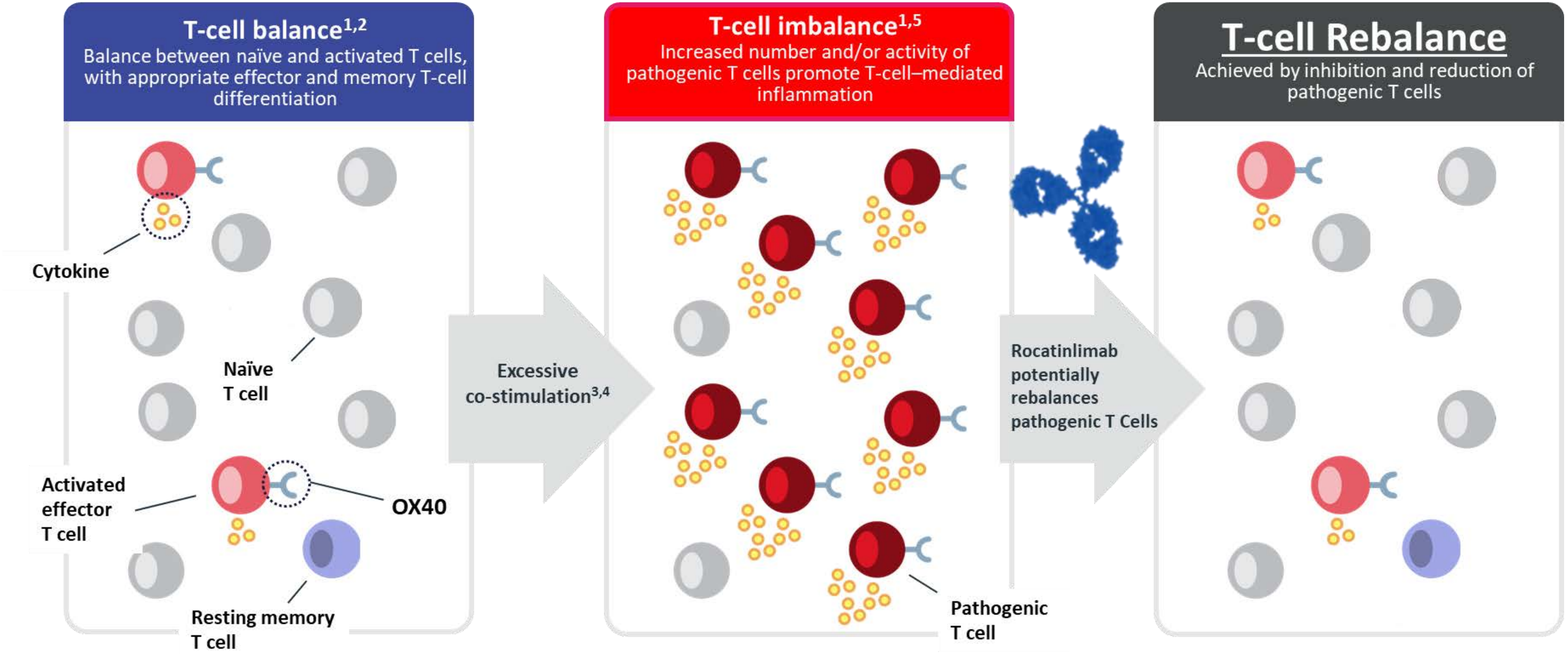
T-cell Rebalance – Aiming for broad and sustained therapeutic effects by addressing a root cause of inflammatory diseases



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 supports sustained symptom control and disease modification.

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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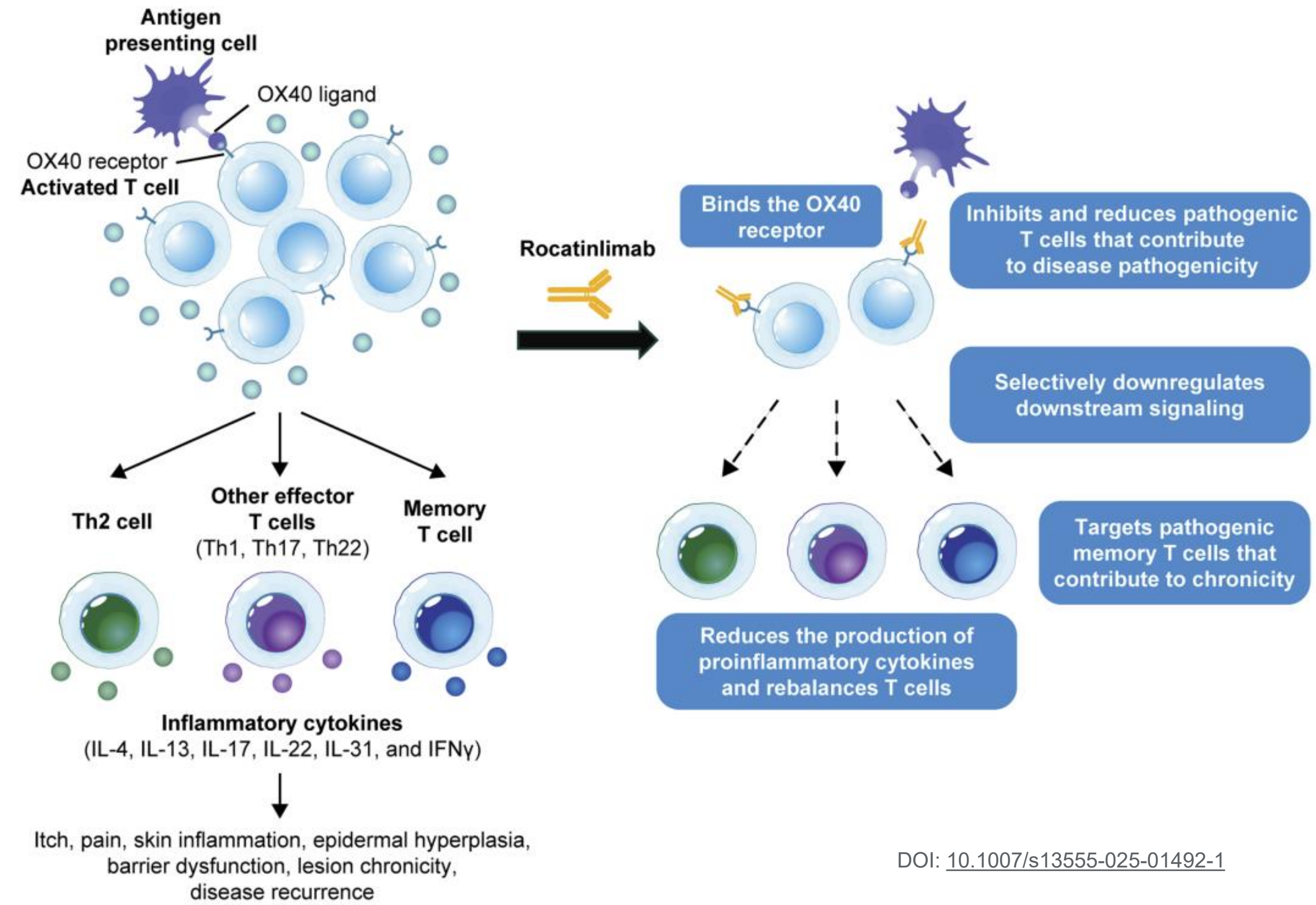
Peer-Reviewed article just published:
Rocatinlimab as a novel T-cell rebalancing therapy

- *Journal: Dermatology and Therapy* (September 2025)
- *Title: **Rocatinlimab: A Novel T-Cell Rebalancing Therapy Targeting the OX40 Receptor in Atopic Dermatitis***
- **Authors:** Emma Guttman-Yassky, Eric Simpson, Ehsanollah Esfandiari, Hirotaka Mano, Jillian Bauer, Prista Charuworn, Kenji Kabashima
- **Key Summary points:**
  - *There is an unmet need for novel treatments for moderate-to-severe atopic dermatitis that offer **longer dosing intervals and provide durable responses off therapy**.*
  - ***T-cell imbalance** is a root cause of atopic dermatitis.*
  - *Rocatinlimab (AMG 451/KHK4083) is a **first-in-class T-cell rebalancing therapy** that inhibits and reduces pathogenic T cells by targeting the OX40 receptor.*
  - *To date, rocatinlimab demonstrated strong efficacy, favorable safety, and durable response on and off therapy in treating moderate-to-severe atopic dermatitis.*

Rocatinlimab Mechanism of Action



DOI: 10.1007/s13555-025-01492-1

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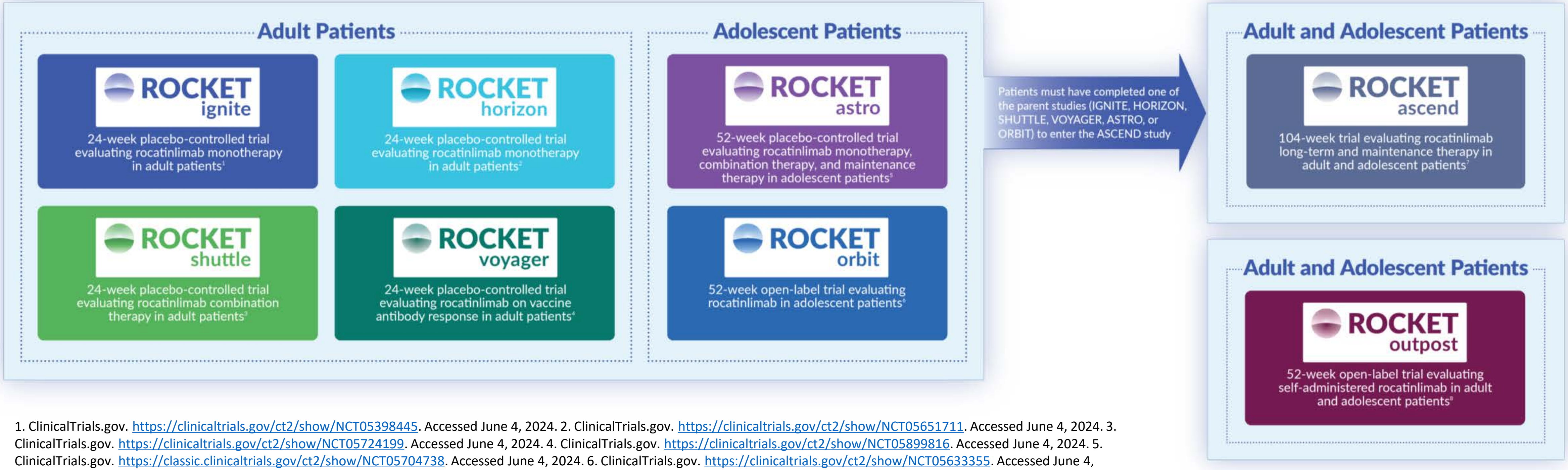
Phase 3 ROCKET Program
Results to date and new study results

Rocatinlimab – Phase 3 the ROCKET Program

- Composed of eight global studies enrolling adult and adolescent moderate to 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.

Topline Data: ROCKET IGNITE, SHUTTLE, VOYAGER

https://ir.kyowakirin.com/en/news/news-3032964777820161808/main/00/link/e20250308.pdf

ROCKET ignite

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

Monotherapy

Primary Endpoint*	rocatinlimab Higher Dose (Week 24)		rocatinlimab Lower Dose (Week 24)	
	%	**Difference from placebo** (p-value)	%	**Difference from placebo** (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 shuttle

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

Combination with TCS/TCI

Primary Endpoint*	rocatinlimab Higher Dose (Week 24)		rocatinlimab Lower Dose (Week 24)	
	%	**Difference from placebo** (p-value)	%	**Difference from placebo** (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 voyager

24-week placebo-controlled trial evaluating rocatinlimab on vaccine antibody response in adult patients

Responses to vaccinations

Demonstrated that rocatinlimab does not interfere with responses to tetanus and meningococcal vaccinations.

*In the US, revised Investigator Global Assessment (rIGA) replaces vIGA as co-primary endpoint

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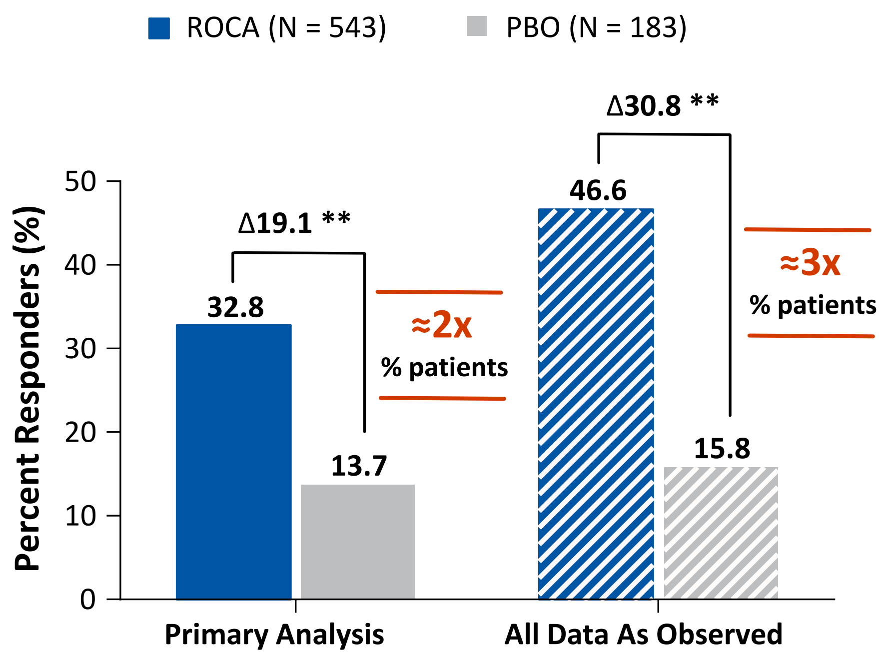
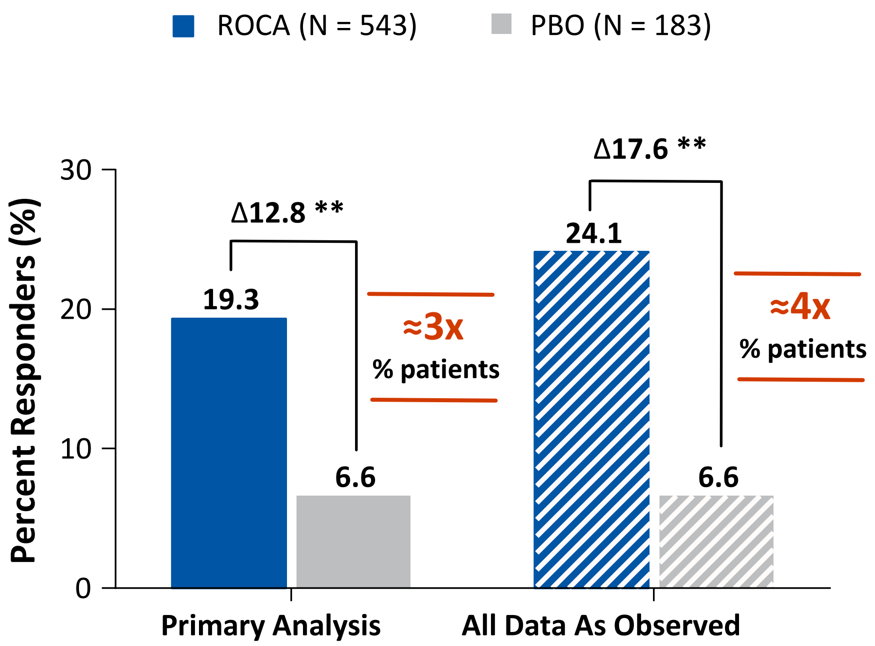
ROCKET HORIZON: EASI-75 and vIGA-AD™ 0/1 Responses at Week 24

Primary analysis set (patients with any rescue use classified as non-responders)
All Data as observed (patient population analyzed based on observed data regardless of rescue therapy use)

EASI-75 at Week 24



vIGA-AD™ 0/1 at Week 24



- **Rocatinlimab met its coprimary endpoints**
- **All Data as observed analysis : higher EASI-75 and vIGA-AD™ 0/1 achievement rates in rocatinlimab group**

** *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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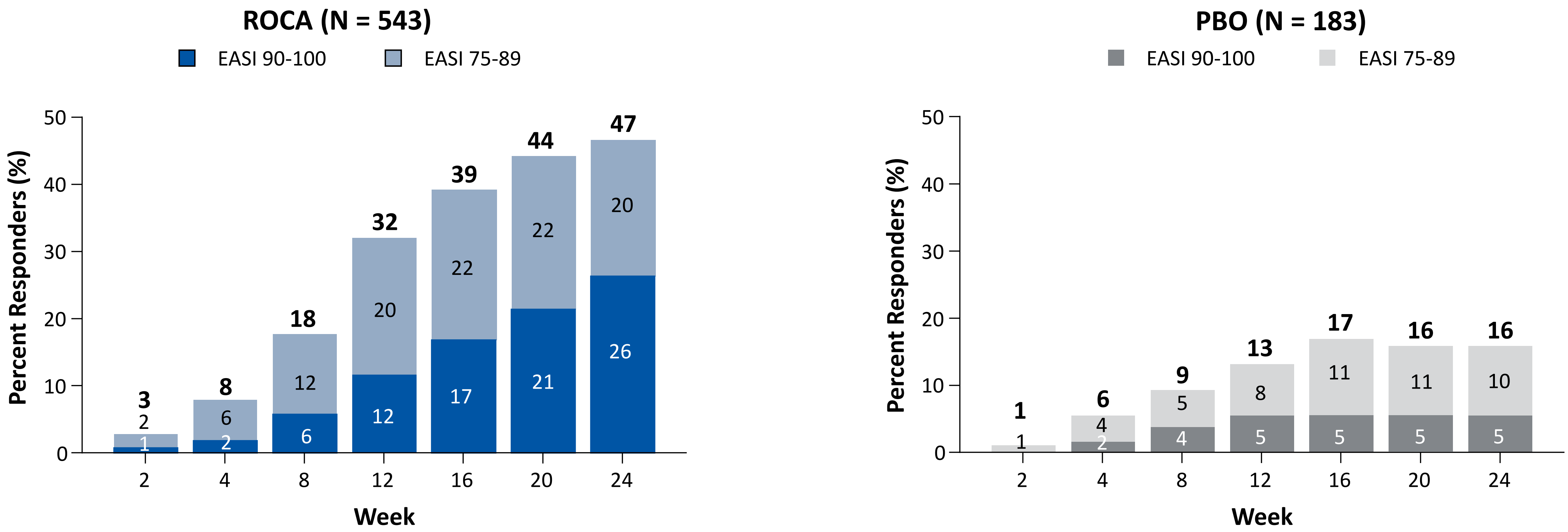
ROCKET HORIZON: EASI 75-89 and EASI 90-100 at Week 24

All Data as observed (patient population analyzed based on observed data regardless of rescue therapy use)



Rocatinlimab-treated patients showed a continuous increase in deep remission (EASI 90–100) rates

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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ROCKET-ASCEND TRIAL DESIGN: ADULT COHORTS[1]

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Study Subjects (at 24 wks)	ROCKET-ASCEND Cohort (104 wks)
Adult Monotherapy Responders† IGNITE/HORIZON*	**Adult Randomized Treatment Withdrawal** 150mg or 300mg, Q4W, Q8W or PBO (withdrawal) monotherapy
Adult Responders† Combo and vaccine studies SHUTTLE/VOYAGER	**Adult Maintenance Treatment** 150mg or 300mg, Q4W, Q8W + TCS/TCI
	Relapse‡ → **Open-label re-treatment** 300mg Q4W
Adult Nonresponders† IGNITE/HORIZON/ SHUTTLE/ VOYAGER†	**Open-label 300mg Q4W**

32-Week Interim Analysis Endpoints

Primary Endpoint:
Safety: Treatment-emergent adverse events in all adult cohorts

Secondary Endpoints:
Maintenance of skin clearance and itch response in adult randomized treatment withdrawal cohort evaluated at W32 of ASCEND study (56 weeks in total including the parent studies)

*Additional data will be generated in adolescents including Q4W maintenance, Q8W extension (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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ROCKET ASCEND Topline: Primary Endpoint
1-year Safety Profile in adult population

ROCKET ascend

104-week trial evaluating rocatinlimab long-term and maintenance therapy in adult and adolescent patients[7]

- The most frequent TEAE in adults (≥ 5 per 100 patient-years in any of the rocatinlimab groups and greater than placebo) included upper respiratory infections (including nasopharyngitis and pharyngitis), aphthous ulcers, headache, influenza, cough and rhinitis, which were observed in previous ROCKET trials.
- The discontinuation rate due to AEs was low across the adult rocatinlimab treated cohorts.
- Across the Phase 3 ROCKET program including ASCEND, the incidence of gastrointestinal ulceration events with rocatinlimab to date is less than 1 per 100 patient-years.

The study is ongoing and continues to evaluate the long-term safety and efficacy of rocatinlimab up to 104 weeks in adult and adolescent patients with moderate to severe AD.

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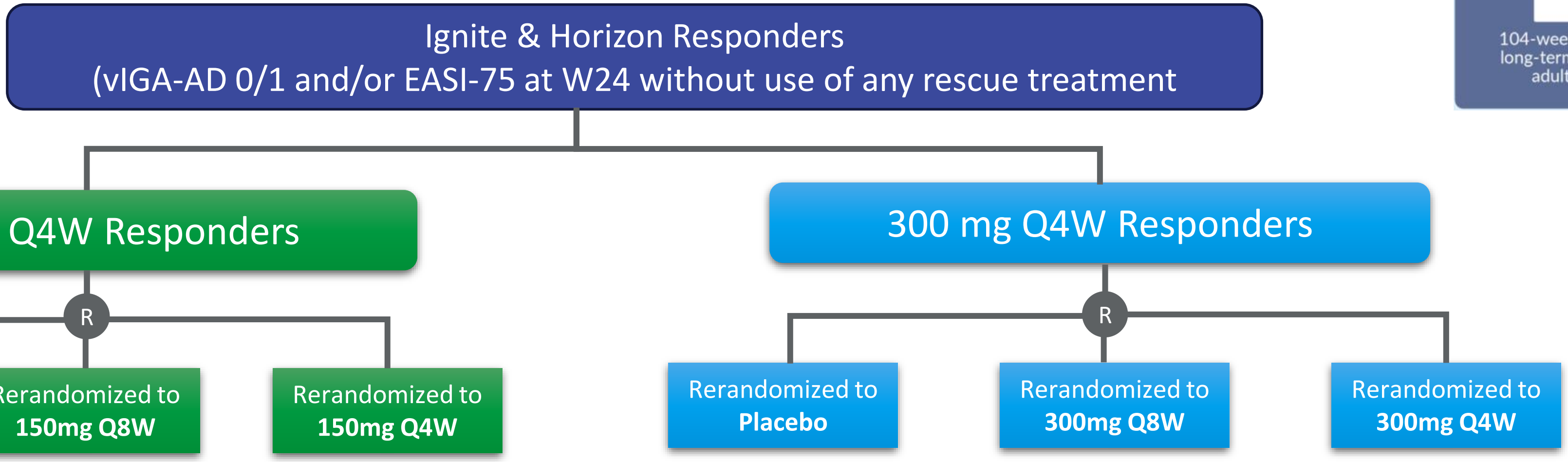
ROCKET ASCEND Topline: Secondary Endpoints

ROCKET ascend

104-week trial evaluating rocatinlimab long-term and maintenance therapy in adult and adolescent patients[7]



Key Questions

- **Long-term maintenance on efficacy with Q4W?**
- **Ability to extend dosing frequency?**

Topline Outcomes

- **Maintenance of response was evaluated at W56 (W32 of ASCEND Study)**
- **Majority of subjects rerandomized to Q4W and Q8W were able to maintain the response across measures of skin response and itch without use of any rescue therapy, including TCS/TCI**

Use of **ANY rescue therapy including TCS[1]/TCI[2] was considered **a relapse** and handled **as a non-responder***

1. Topical corticosteroids, 2. topical calcineurin inhibitors

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Summary

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]

- Current treatment options for moderate to severe AD often fail to provide sustained relief or adequately address patient needs, highlighting a significant opportunity for new therapies.
- Moreover, some individuals may be ineligible for or unable to tolerate existing treatments.
- More than half of patients on systemic therapy today discontinue therapy after just 12 months.
- A novel mechanism of action is needed to provide alternative options for patients.

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ROCKET ASCEND topline data: Executive Summary

- The most frequent treatment emergent adverse events in adults in any of the rocatinlimab groups, and greater than placebo, were observed in the previous ROCKET studies. The discontinuation rate due to AEs was low across the adult rocatinlimab treated cohorts.
- Majority of subjects rerandomized to Q4W and Q8W were able to maintain the response at W56 across measures of skin response and itch, suggesting the potential for extended dosing intervals after patients achieve clinical response
- These results mark an important milestone in furthering our understanding of rocatinlimab. The findings from ASCEND characterize rocatinlimab's ongoing therapeutic benefit at one-year of treatment in adult patients with moderate to severe AD, with possible maintenance dosing as infrequently as every eight weeks, following initial 24-week dosing, an approach that may lessen the ongoing burden of treatment.

We will continue our efforts toward the 2025/2026 submission to deliver life-changing value to more patients.

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