Demonstration of Early Proof-of-Concept for STAR-0310, a Long-Acting OX40 Receptor Antagonist: Initial Safety, PK, and PD Results from a Phase 1a Trial

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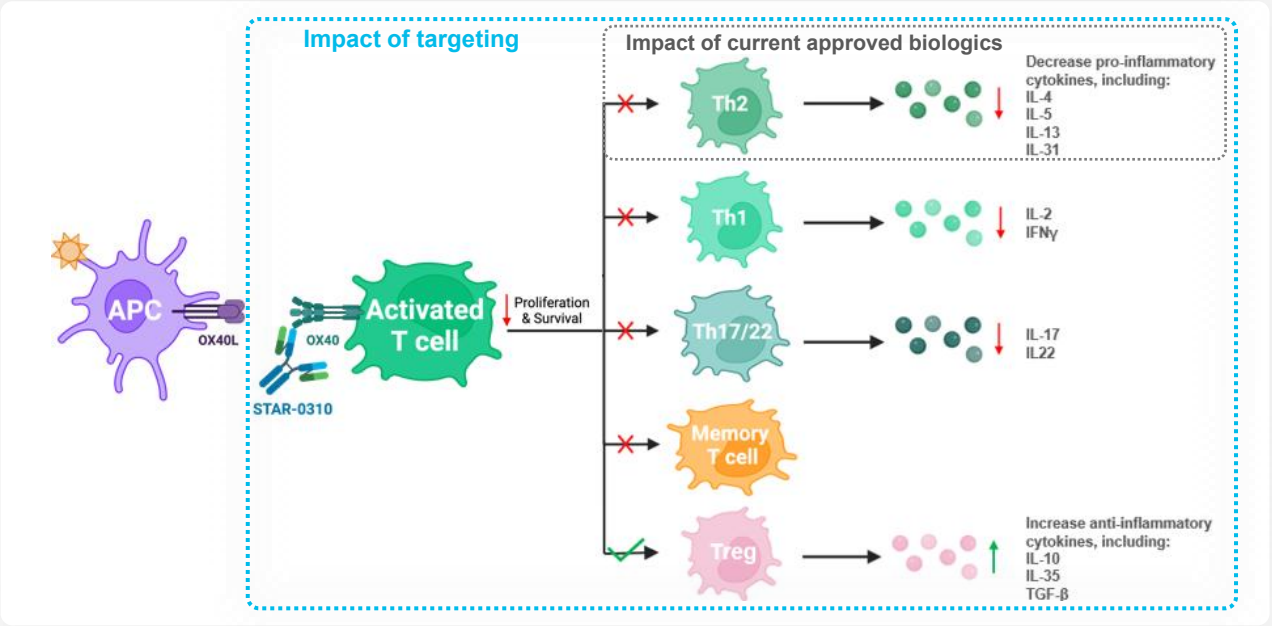
Presented by: Stephan Weidinger, MD, PhD

Disclosure

Stephan Weidinger has received institutional research grants from LEO Pharma A/S, Pfizer, and Sanofi; consulting and advisory board fees from AbbVie, Almirall, Apogee, Astria, Boehringer, Eli Lilly, GSK, LEO Pharma A/S, Pfizer, Regeneron, and Sanofi; and honoraria for lectures from AbbVie, Almirall, Eli Lilly, LEO Pharma A/S, Pfizer, Regeneron, and Sanofi.

Immunomodulating T Cells by Targeting the OX40 Pathway Has the Potential for Deep Disease Modification



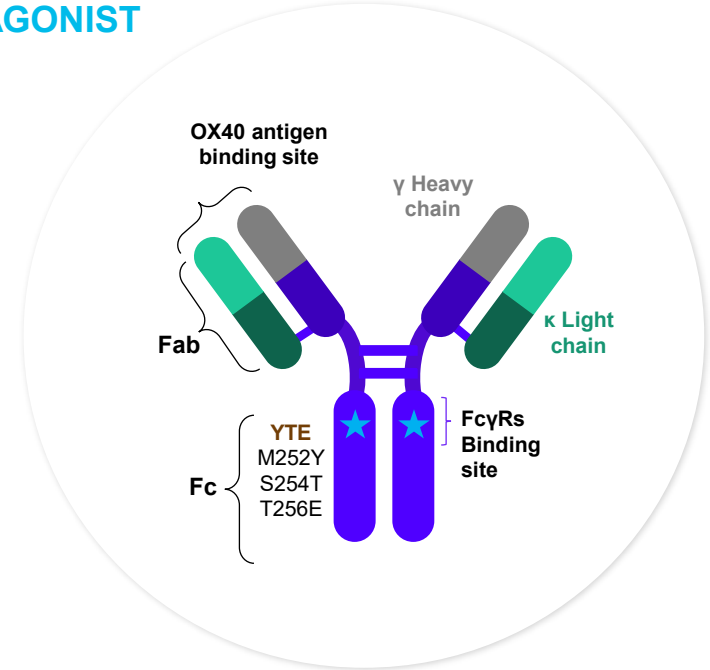
- AD is driven by a diversity of T cells
- Current approved biologics target only the Th2 pathway
- **OX40 inhibition broadly immunomodulates T cells in disease, creating potential for deep, broad and sustained responses**

AD, atopic dermatitis; Th2, T helper Type 2 cells, IL, Interleukin; IFNγ, Interferon-gamma; TGF-β,Transforming growth factor-beta

STAR-0310: Novel, Potential Best-in-Class OX40 Receptor Antagonist

POTENT OX40 RECEPTOR ANTAGONIST

- Pure antagonist and may disrupt preformed OX40/OX40L complexes
- Designed to block receptor signaling without inducing T-cell activation, which may offer potential for disease modification



LOW TREATMENT BURDEN

- YTE engineered to extend half-life and enable longer dosing intervals

WIDE THERAPEUTIC WINDOW

- Reduced Fc-mediated effector activity
- Decreased likelihood of ADCC-driven adverse events (e.g., fever and chills)
- May allow for improved tolerability and higher dosing to drive more efficacy

AD, atopic dermatitis; ADCC, antibody-dependent cellular cytotoxicity; YTE, M252Y/S254T/T256E.

References: Zhao et al., AAAAI 2025; 2. Zhao et al., SID 2024; 3. Biris et al., EAACI 2024. Preclinical data; further clinical evaluation is ongoing

Ongoing Burden of Atopic Dermatitis Highlights the Need for An Innovative Approach

Gaps with Current AD Treatment	Opportunity for a novel OX40 Pathway Antagonist
Incomplete responses, with relapses	OX40 is an immuno-regulatory target pathway, providing patients the potential for disease modification
Lack of long-term disease control	OX40/ OX40L antagonists have demonstrated durable clinical activity
Safety and tolerability	Potential for efficacy without special safety warnings
Frequent medication use	Potential for less-frequent dosing than the standard of care

AD, atopic dermatitis; SOC, EASI, Eczema Area and Severity Index; Th, T helper cell.

References: Guttman-Yassky E, et al. Lancet. 2023;402(10393):1905-1917. Weidinger S et al. J Allergy Clin Immunol. 2024;153(6):1569-1581. Lobefaro et al. *Biomedicines*. 2022;10:2927. Croft et al. *Am J Clin Dermatol.* 2024;25:447-461. Ratchataswan et al. *J Allergy Clin Immunol Pract*. 2021;9:1053-1065. Ferrucci et al. *Dermatol Ther (Heidelb)*. 2023;13:1071-1081. Silverberg et al. *J Eur Acad Dermatol Venereol.* 2021;35:1797-1810. Martora et al. *J Dermatolog Treat.* 2024;35:1. Tang et al. *J Allergy Clin Immunol.* 2014;133:1615-25.e1. RINVOQ (upadacitinib) Prescribing Information. AbbVie Inc; 2025. CIBINQO (abrocitinib) Prescribing Information. Pfizer Inc., 2023. OLUMIANT (baricitinib) Prescribing Information. Eli Lilly and Co, 2022. RINVOQ SmPC. European Medicines Agency. Updated 2024. CIBINQO SmPC. European Medicines Agency. Updated 2024. OLUMIANT SmPC. European Medicines Agency. Updated 2024. DUPIXENT (dupilumab) Prescribing Information. Sanofi/Regeneron, 2025. Dupixent SmPC. EMA; 2024

Clinical Results

STAR-0310 Phase 1a Trial to Assess Safety and Pharmacokinetics in Healthy Participants

Study Design

- 3:1 randomized, sponsor open, placebo-controlled trial

Objectives

Primary objectives:

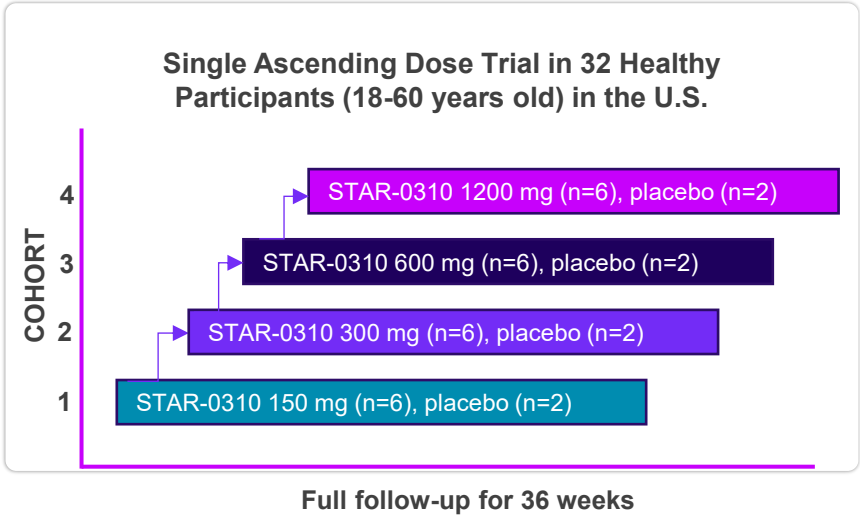
- Assess safety/tolerability of escalating single dose SC administrations

Secondary objectives:

- To characterize pharmacokinetics (extended half-life)
- To assess immunogenicity

***Exploratory Objective*:**

- Evaluate the impact of STAR-0310 on biomarkers related to the mechanism of action



SC, subcutaneous

NCT# 06782477.This interim analysis includes available safety, PK and PD (ex vivo cytokine) data from all cohorts through the following follow-up windows: Day 168 for Cohort 1 (150 mg), Day 140 for Cohort 2 (300 mg), Day 112 for Cohort 3 (600mg), and Day 84 for Cohort 4 (1200 mg). Data Cut-off: 16-July-2025.

Baseline Demographics Are Generally Similar Across Cohorts

	STAR-0310					Pooled Placebo
	Cohort 1 150 mg	Cohort 2 300 mg	Cohort 3 600 mg	Cohort 4 1200 mg	Pooled STAR-0310	
Total Randomized, n	6	6	6	6	24	8
Age, years						
Mean (SD)	35.5 (11.38)	33.2 (14.44)	31.5 (9.40)	36.2 (9.68)	34.1 (10.80)	49.4 (8.60)
Weight, kg						
Mean (SD)	83.5 (19.29)	82.4 (18.44)	70.0 (9.80)	83.4 (16.88)	79.8 (16.47)	75.1 (12.60)
Sex, n (%)						
Female	4 (66.7)	3 (50.0)	2 (33.3)	3 (50.0)	12 (50.0)	4 (50.0)
Race, n						
White	4	3	5	3	15	7
Black	2	1	1	3	7	-
Multi-Racial	-	2	-	-	2	-

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STAR-0310 Demonstrates a Favorable Safety Profile, Without ADCC-Related Adverse Events

	Cohort 1 150 mg (N=6) n (%)	Cohort 2 300 mg (N=6) n (%)	Cohort 3 600 mg (N=6) n (%)	Cohort 4 1200 mg (N=6) n (%)	Pooled STAR-0310 (N=24) n (%)	Pooled Placebo (N=8) n (%)
Incidence of Treatment Emergent Adverse Events (TEAEs)						
Any TEAE	2 (33.3)	3 (50.0)	3 (50.0)	4 (66.7)	12 (50.0)	2 (25.0)
Mild TEAE	2 (33.3)	3 (50.0)	2 (33.3)	4 (66.7)	11 (45.8)	2 (25.0)
Moderate TEAE	-	1 (16.7)	2 (33.3)	-	3 (12.5)	-
Incidence of TEAEs in ≥ 2 participants						
Procedure site bruising	-	1 (16.7)	1 (16.7)	3 (50.0)	5 (20.8)	1 (12.5)
Injection site reaction	1 (16.7)	2 (33.3)	-	1 (16.7)	4 (16.7)	0
Headache	1 (16.7)	-	-	1 (16.7)	2 (8.3)	0
Diarrhea	-	1 (16.7)	-	1 (16.7)	2 (8.3)	0
Incidence of ADCC-Related Adverse Events						
Fevers	-	-	-	-	-	-
Chills	-	-	-	-	-	-

AD, atopic dermatitis; ADCC, antibody-dependent cellular cytotoxicity

No fevers/chills, no severe TEAEs or serious adverse events were reported, and no discontinuations occurred due to TEAEs

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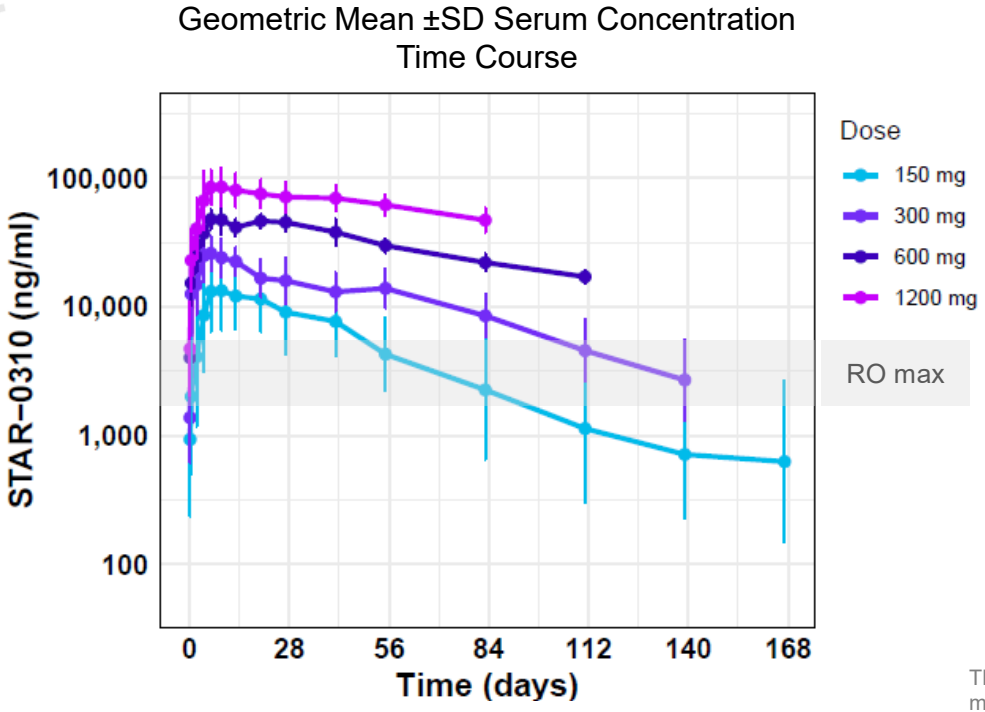
STAR-0310 Exhibits Dose-Dependent Pharmacokinetics with Extended Half-Life



- Demonstrates a **dose-dependent increase** in concentrations across 150 mg, 300 mg, 600 mg, and 1200 mg cohorts
- T_{max} observed between **6 to 9 days**
- Preliminary **mean half-life** of **68 days** (range: 59 to 78 days**,** ~10 weeks) at 600 and 1200 mg dose levels
- Observed concentrations at clinically relevant doses are above the concentration predicted to achieve maximum OX40 receptor occupancy within the skin for **~112-140 days** (~3-4 months) after single doses

The **grey RO max*** on the plot indicate the predicted range of serum concentrations at which maximum receptor occupancy (RO) is expected to be achieved within the skin.

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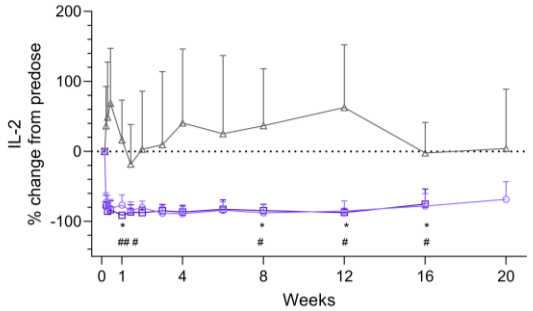
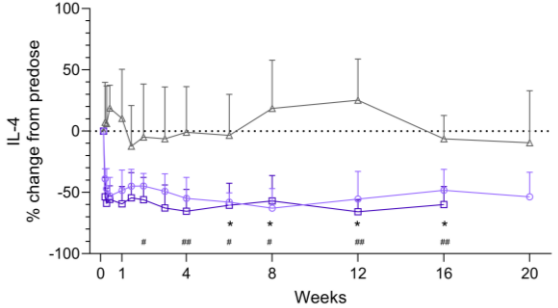
RO based on in vitro data. Concentration of STAR-0310 within the skin was assumed to be 5 to 15% of the serum concentrations.
References: Drug Metab Pharmacokinet. 2019 Feb;34(1):3-13. J Pharmacokinet Pharmacodyn. 2012 Feb;39(1):67-86.

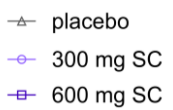
STAR-0310 Durably Inhibits Multiple Inflammatory Pathways Beyond Th2 in *ex vivo* Cytokine Assays

IL-2

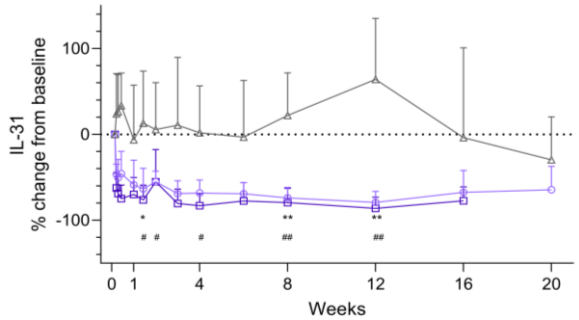


IL-4

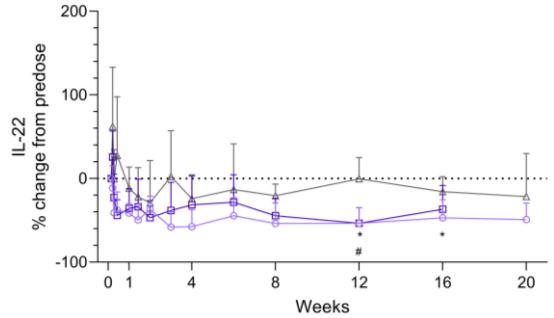




IL-31



IL-22



Mean±SD.
One-way ANOVA with Dunnett's test
300 mg: * p<0.05,
**p<0.01 vs. placebo
600 mg: # p<0.05,
p<0.01 vs. placebo

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Key Takeaways

STAR-0310 Is a Differentiated OX40 Antagonist

- **In these interim Phase 1a results:**
  - **STAR-0310 was well tolerated with no ADCC-related TEAEs, e.g. fevers or chills, and no serious adverse events.**
  - **STAR-0310 achieved an extended half-life (68 days) with dose-proportional exposures and a median T_{max} of 6–9 days.**
  - **STAR-0310 achieved deep (50–90%) and durable (>16 week) inhibition of IL-2, IL-4, IL-31, and IL-22 cytokines suggesting immune modulation beyond Type 2 helper T cells.**

These results demonstrate early proof of concept for STAR-0310's potential as a long-acting, differentiated OX40 receptor antagonist.

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ADCC, antibody-dependent cellular cytotoxicity; T_{max}, time to maximum plasma concentration; IL, interleukin
Interim analysis. Data Cut-off: 16-July-2025.

STAR-0310 – Next Steps in OX40 Pathway Modulation in Immune-Mediated Diseases

These results support advancing STAR-0310 into patients. Next steps include:

- **Identifying induction and maintenance** dosing strategies that could enhance efficacy and extend the durability of treatment outcomes.
- **Understanding Population-Specific Responses:** Opportunity remains to better characterize how different patient populations respond to OX40 modulation.
- **Combination Opportunities:** Evaluating rationale combination regimens to amplify clinical benefits and broaden therapeutic reach.


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