# EVERLAST-A: A Phase 2a Study Design of ORKA-001, a Novel Half-Life Extended IL-23p19 Monoclonal Antibody for Plaque Psoriasis

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## Introduction

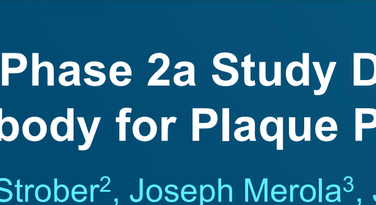
- Oruka Therapeutics is advancing a portfolio of potentially best-in-class antibodies that target the core mechanisms underlying plaque psoriasis and other dermatologic and inflammatory diseases
- ORKA-001 is a novel, highly specific, humanized IgG1 monoclonal antibody that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor, with an Fc region designed to ablate effector function and extend half-life
- A Phase 1 first-in-human trial evaluating ORKA-001 in healthy participants (NCT06698939) showed favorable safety and tolerability across all dose levels, with PK and PD supporting the potential for once-yearly dosing and exposures that may enable higher rates of skin clearance than the current standard of care
- The Phase 2a EVERLAST-A study (NCT07090330) is a multicenter, randomized, double-blinded, placebo-controlled, proof-of-concept study in patients with moderate-to-severe plaque psoriasis and is **currently enrolling subjects** across sites in the United States and Canada

**Disclosures:**

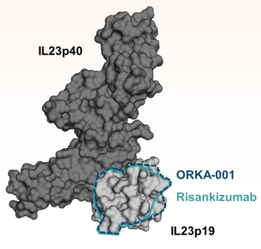
- Eugenia Levi and Joana Goncalves are employees of Oruka Therapeutics
- Andrew Blauvelt, Eugenia Levi and Joana Goncalves are stockholders of Oruka Therapeutics

## Figure 1: ORKA-001 is a novel IL-23p19 inhibitor with binding similar to risankizumab

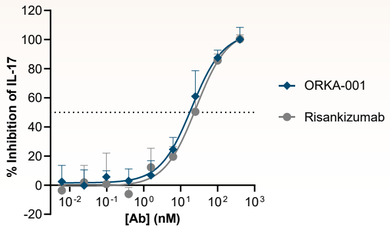
- ORKA-001 and risankizumab demonstrate comparable high affinity for IL-23p19 ($K_D$ <5 pM)
- Cryo-EM structural analysis demonstrates ORKA-001 has a nearly identical epitope as risankizumab
- ORKA-001 shows similar potency to risankizumab



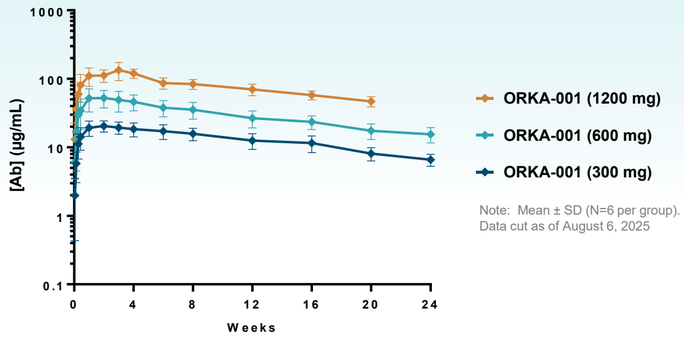

### ORKA-001 and risankizumab epitopes




### Inhibition of IL-17 release in human PBMCs




## Figure 2: ORKA-001 demonstrated a half-life of ~100 days in humans

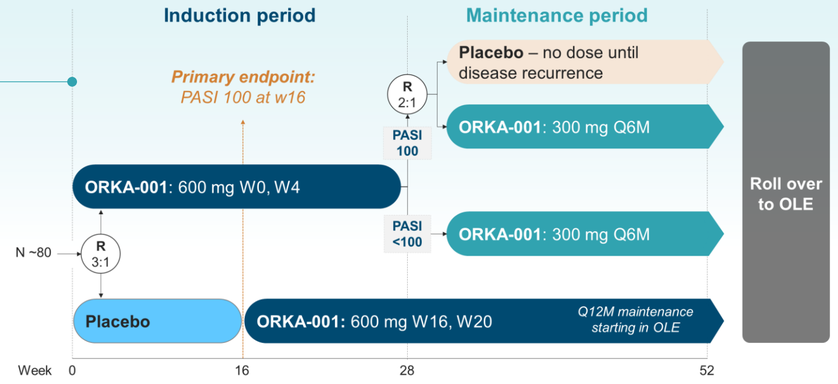



Note: Mean ± SD (N=6 per group).
Data cut as of August 6, 2025

## Figure 3: EVERLAST-A study design (NCT07090330)

The EVERLAST-A Phase 2a study evaluating the efficacy and safety of ORKA-001 in patients with moderate-to-severe psoriasis has an innovative design, including:

- Primary endpoint of PASI 100 at Week 16
- "No-dose" arm that will test the potential for annual dosing, higher rates of complete skin clearance and off-treatment remissions



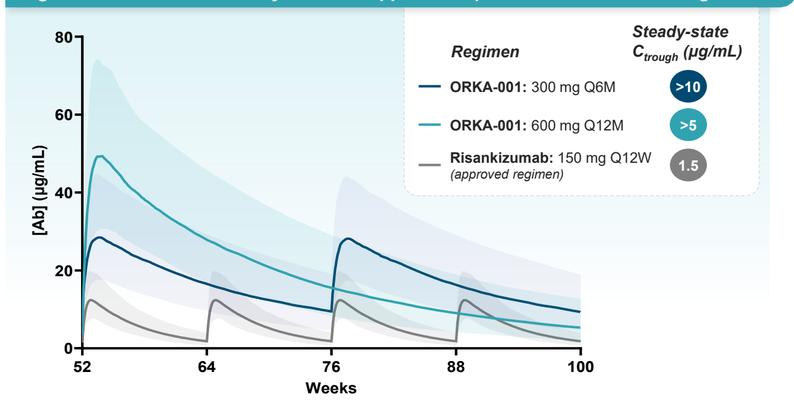

**Key Inclusion Criteria:**

- Adults
- Plaque psoriasis for >6 months
- Moderate-to-severe psoriasis: BSA ≥10%, PASI ≥12, and IGA score of ≥3

**Secondary Endpoints:**

- IGA 0, PASI 90, and IGA 0/1 at Week 16
- PASI 100 and IGA 0 at Week 52
- PASI 90 and IGA 0/1 at Week 52
- Safety assessments
- PK parameters

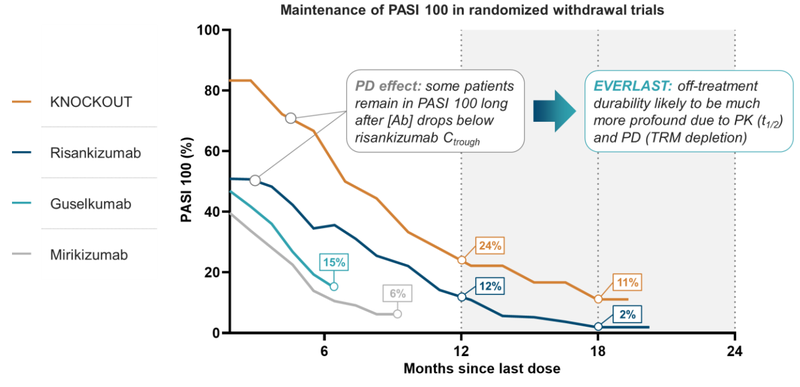
## Figure 4: ORKA-001's 100-day half-life supports the potential for annual dosing




Risankizumab $C_{max}$ in IBD (median 350 µg/mL) supports safety of high anti-IL-23 exposures

Note: modeling based on internal data and published population PK model for risankizumab; error bars reflect 5th and 95th percentiles; risankizumab exposures in ulcerative colitis from 2024 Thrake (Clin Pharmacol Ther.)

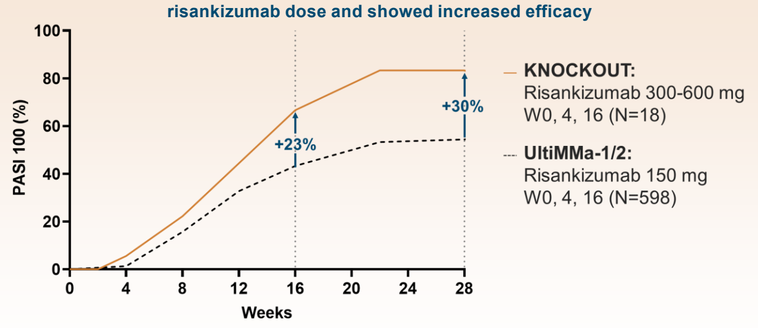
## Figure 5: Greater IL-23 inhibition may enable off-treatment remission by depleting TRMs




Reference: Blauvelt et al., G2C (2024); Blauvelt et al., JAMA Dermatol (2020); Reich et al., JAAD (2017); Blauvelt et al., Br J Dermatol (2022); FDA Labels

## Figure 6: Higher exposures with ORKA-001 may lead to higher efficacy

**The KNOCKOUT study tested 2-4x the approved risankizumab dose and showed increased efficacy**




ORKA-001 exposures in EVERLAST-A are expected to match or exceed exposures in KNOCKOUT, testing whether higher exposures can lead to greater efficacy

Reference: Cross-trial comparison of pooled data from KNOCKOUT and UltIMMa-1/2 from Blauvelt et al., G2C (2024) and Gordon et al., Lancet (2018), respectively

## Conclusions

- **ORKA-001** is a novel IL-23p19 inhibitor with an extended half-life and has demonstrated PK and PD results that support the potential for:
  - **Once-yearly dosing** while maintaining trough antibody concentrations above approved IL-23 targeting antibodies like risankizumab
  - Sustained antibody exposures that may allow ORKA-001 to achieve **higher rates of skin clearance** than the current standard of care and **extended off-treatment remission** in some patients
- **EVERLAST-A is an ongoing Phase 2a study** evaluating ORKA-001 in patients with moderate-to-severe psoriasis. The study aims to determine whether ORKA-001 can lead to once or twice a year dosing intervals, higher rates of complete skin clearance, and extended off-treatment disease remission in some patients, while maintaining a favorable safety profile consistent with the IL-23i class

*For further information please contact MedAffairs@orukatx.com*

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