Phase 1 Clinical Trial of ORKA-002, a Novel Half-Life Extended IL-17A/F Monoclonal Antibody with Potential for Twice Yearly Dosing in Psoriasis and Psoriatic Arthritis

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INTRODUCTION

- Oruka Therapeutics is advancing a portfolio of potentially best-in-class antibodies that target the core mechanisms underlying psoriasis (PsO), psoriatic arthritis (PsA), and other dermatologic and inflammatory diseases such as hidradenitis suppurativa (HS)
- ORKA-002 is a novel, highly specific, humanized IgG1 monoclonal antibody that selectively binds to both IL-17A and IL-17F to prevent homodimer and heterodimer signaling
- The fragment crystallizable (Fc) region of ORKA-002 has been engineered to extend half-life (M260Y/S262T/T264E [YTE])[1]
- A Phase 1 first-in-human trial is evaluating the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of ORKA-002 in healthy participants (NCT06944379)

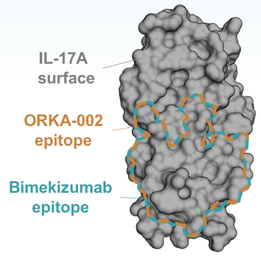
Disclosures:

- Becky Blanchard, Shauna Jardon and Joana Goncalves are employees of Oruka Therapeutics
- Becky Blanchard, Shauna Jardon, Joana Goncalves and Andrew Blauvelt hold equity interests in Oruka Therapeutics

Fig 1: ORKA-002 is a novel IL-17A/F inhibitor with binding similar to bimekizumab

- ORKA-002 and bimekizumab have comparable affinity for IL-17A and IL-17F
- ORKA-002 binds a similar epitope as bimekizumab for both IL-17A and IL-17F
- ORKA-002 shows similar potency to bimekizumab across multiple *in vitro* assays
- Dual inhibition of IL-17A/F has demonstrated improved efficacy compared with IL-17A inhibition alone[2,3]

Binding epitopes on IL-17A



ORKA-002 also binds a similar epitope for IL-17F

ORKA-002–mediated NF-κB inhibition

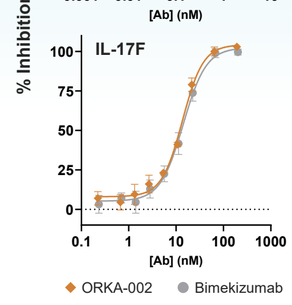


Fig 2: ORKA-002 Phase 1 trial design (NCT06944379)

Design
- Double-blind and placebo-controlled
- Single ascending dose

Population
- Healthy adult volunteers
- N=8 per dose cohort (6:2 active:placebo)

Endpoints
- Primary: Safety and tolerability
- Secondary: Pharmacokinetics
- Exploratory: Pharmacodynamic markers

Dose levels and length of follow-up as of the January 6, 2026 data cut

160 mg SC	~6 months
320 mg SC	~5 months
640 mg SC	~4 months

Baseline characteristics were typical of healthy adult volunteers

Abbreviations: SC, subcutaneous

References: 1. Dall'Acqua 2006 (J Biol Chem); 2. Reich 2021 (NEJM); 3. Kokolakis 2023 (BJD)

RESULTS

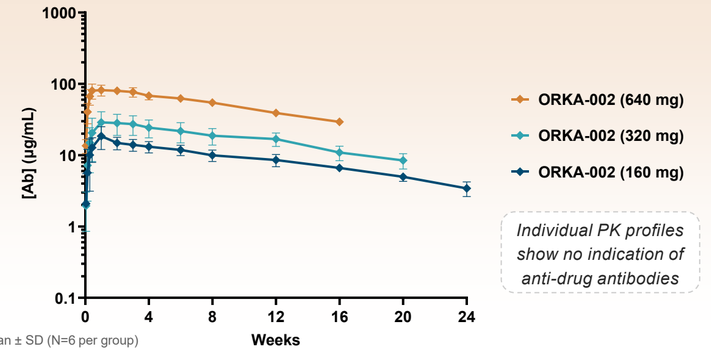
Table 1: ORKA-002 blinded safety profile was consistent with the anti-IL-17 class

ORKA-002 and placebo (blinded)	160 mg	320 mg	640 mg	All cohorts
N	8	8	8	24
≥1 TEAE	8 (100%)	8 (100%)	7 (87.5%)	23 (95.8%)
≥1 SAE	0%	0%	0%	0%
≥1 severe TEAE	0%	0%	0%	0%
Discontinued due to TEAE	0%	0%	0%	0%

Only AEs occurring in >2 subjects were contusion[1], headache, skin abrasion[1], and upper respiratory tract infection

(1) contusions and skin abrasions were not at the injection site and were not considered related to the Investigational Medicinal Product by the Investigator. Abbreviations: TEAE, Treatment- Emergent Adverse Event; SAE, Serious Adverse Event

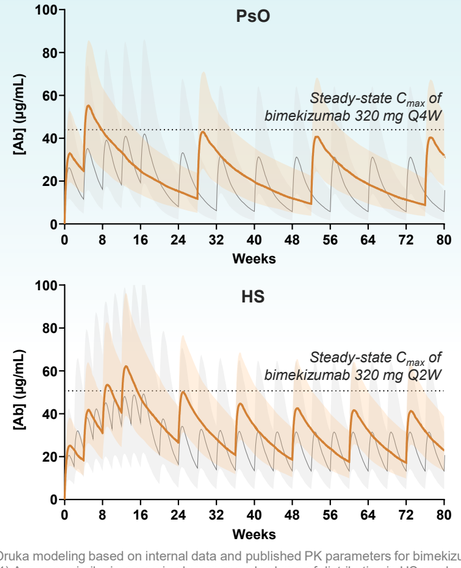
Fig 3: ORKA-002 demonstrated a half-life of 75-80 days in humans



Individual PK profiles show no indication of anti-drug antibodies

Mean ± SD (N=6 per group)

Fig 4: ORKA-002 PK supports potential for Q6M dosing in PsO/PsA & Q3M dosing in HS

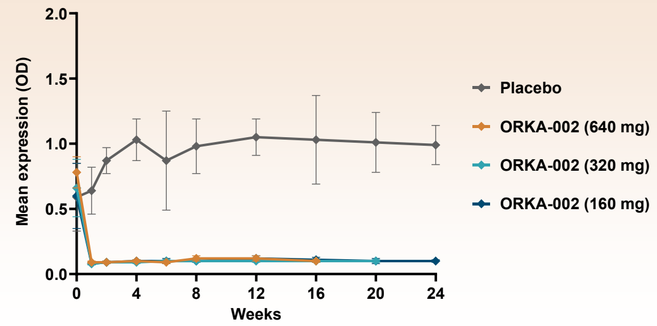


- **ORKA-002:** 320 mg W0, 4 then Q6M
- **Bimekizumab:** 320 mg Q4W from W0-16, then Q8W

- **ORKA-002[1]:** 320 mg W0, 4, 8, 12 then Q3M
- **Bimekizumab:** 320 mg Q2W from W0-16, then Q4W

Oruka modeling based on internal data and published PK parameters for bimekizumab; error bars reflect 5th and 95th percentiles; (1) Assumes similar increase in clearance and volume of distribution in HS as observed with bimekizumab

Fig 5: ORKA-002 durably inhibits IL-17 signaling in an *ex vivo* IL-17 stimulation assay

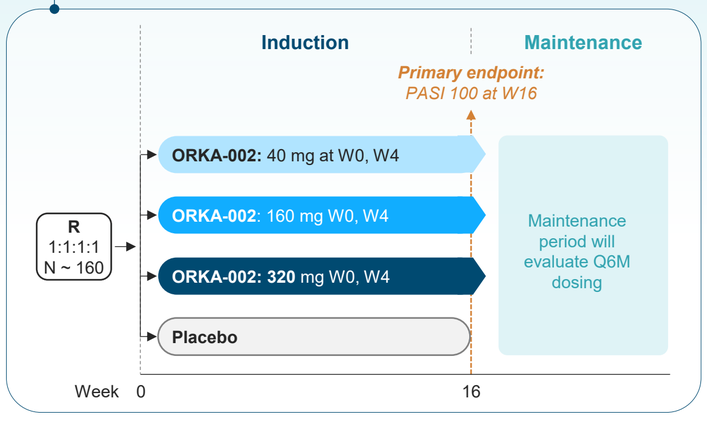


Mean ± SD (N=6 per group). 24 weeks is the longest follow-up available as of the data cut on January 6, 2026

Fig 6: ORKA-002 will be evaluated in the Phase 2 ORCA-SURGE trial in PsO

ORCA SURGE

ORCA-SURGE is a Phase 2 dose-ranging trial evaluating the efficacy and safety of ORKA-002 in adults with moderate-to-severe psoriasis.



Conclusions

- PK and PD results from this Phase 1 trial of ORKA-002, including a **half-life of 75-80 days, support the potential for twice-yearly dosing in psoriatic disease and quarterly dosing in HS** while maintaining trough antibody concentrations above bimekizumab
- ORKA-002 was well-tolerated across all dose levels, with a **safety profile consistent with the IL-17 inhibitor class**
- **ORCA-SURGE is a Phase 2 dose-ranging trial** evaluating the efficacy and safety of ORKA-002 in moderate-to-severe PsO **starting in the first half of 2026**
- In addition, a Phase 2 trial evaluating ORKA-002 in **HS is expected to start in the second half of 2026**

For further information please contact MedAffairs@orukatx.com

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