Phase 1 Clinical Data of ORKA-001, a Novel Half-Life Extended IL-23p19 Monoclonal Antibody with Potential for Once-Yearly Dosing in Plaque Psoriasis

J Krueger[1], C Wynne[2], M Lebwohl[3], B Strober[4], JF Merola[5], JM Gelfand[6], JE Gudjonsson[7], B Blanchard[8], C Finch[8], E Levi[8], J Goncalves[8], A Blauvelt[9]

[1]The Rockefeller University, New York, NY, USA, [2]New Zealand Clinical Research, Christchurch, NZ, [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA, [4]Department of Dermatology, Yale University and Central Connecticut Dermatology, Cromwell, CT, USA
[5]Department of Dermatology and Department of Medicine, Division of Rheumatology, UT Southwestern Medical Center, Dallas, TX, USA, [6]University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, USA, [7]University of Michigan, Ann Arbor, MI, USA
[8]Oruka Therapeutics, Menlo Park, CA, USA, [9]Blauvelt Consulting, Annapolis, MD, USA

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
- The fragment crystallizable (Fc) has been engineered to ablate effector function (L237A/L238A) and to extend half-life (M255Y/S257T/T259E [YTE])[1]
- ORKA-001's extended half-life and optimized properties have the potential to enable extend dosing intervals (e.g., once yearly), enhanced efficacy, and more durable responses (including the potential for off-treatment remission) in plaque PsO
- A Phase 1 first-in-human trial evaluated the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of ORKA-001 in healthy participants (NCT06698939)

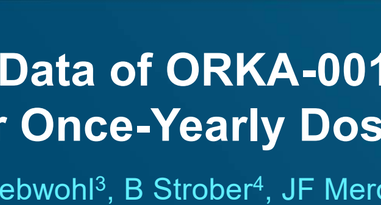
Reference: 1. Dall'Acqua 2006

Disclosures:

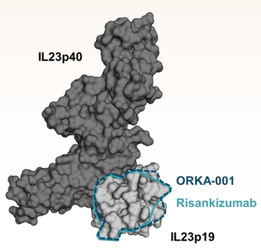
- Christopher Finch, Eugenia Levi and Joana Goncalves are employees of Oruka Therapeutics
- Christoper Finch, Eugenia Levi, Joana Goncalves and Andrew Blauvelt are stockholders of Oruka Therapeutics

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

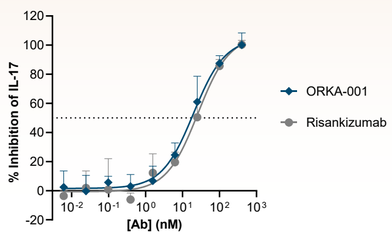
- ORKA-001 and risankizumab demonstrate comparable high affinity for IL-23p19 (K_D <5 pM)
- Cryo-EM structural analysis demonstrates ORKA-001 has a nearly identical epitope as risankizumab
- ORKA-001 shows similar potency to risankizumab



ORKA-001 and risankizumab epitopes



Inhibition of IL-17 release in human PBMCs



ORKA-001 Phase 1 Trial Design

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 to date

300 mg SC	~7 months
600 mg SC	~6 months
1200 mg SC	~5 months

Abbreviations: SC, subcutaneous

Table 1: Baseline characteristics were typical of healthy volunteers

ORKA-001 and placebo	300 mg	600 mg	1200 mg	All cohorts
N	8	8	8	24
Age, years Mean (SD)	48.3 (10.8)	47.8 (11.7)	46.6 (12.7)	47.5 (11.3)
Sex % Female	50%	13%	75%	46%
Race % White	88%	88%	63%	79%
Weight, kg Mean (SD)	78.1 (10.6)	79.6 (11.6)	69.6 (15.4)	75.7 (12.9)
BMI, kg/m² Mean (SD)	26.6 (4.0)	25.3 (2.2)	25.3 (2.9)	25.7 (3.0)

RESULTS

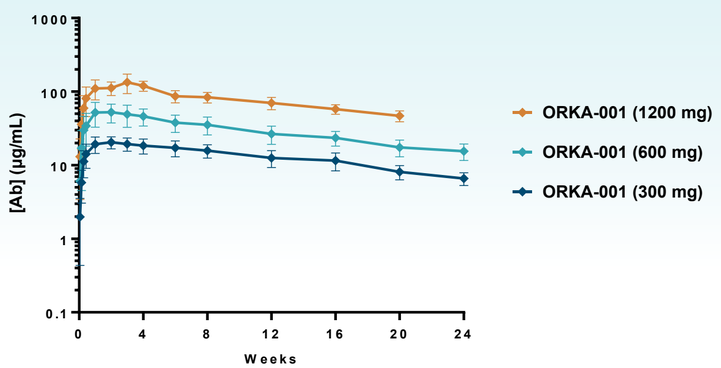
Table 2: ORKA-001 safety profile was consistent with the IL-23p19 class

ORKA-001 and placebo	300 mg	600 mg	1200 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%

AEs occurring in >2 subjects were headache, upper respiratory tract infection, and transient erythema at the injection site

Note: Data cut as of August 6, 2025

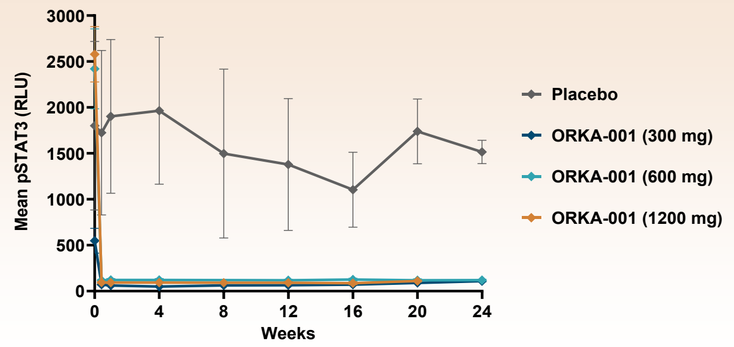
Figure 2: ORKA-001 demonstrates a half-life of ~100 days in humans



- Individual PK profiles show no indication of anti-drug antibodies

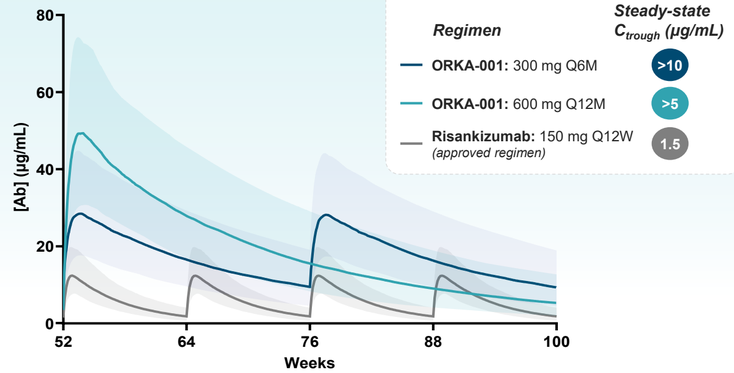
Note: Mean ± SD (N=6 per group). Data cut as of August 6, 2025.

Figure 3: ORKA-001 potently inhibited IL-23-mediated STAT3 signaling



Note: Mean ± SD (N=6 per group). Data cut as of August 6, 2025. ORKA-001 (600 mg) data slightly offset for visualization

Figure 4: ORKA-001's 100-day half-life could potentially enable 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.)

Conclusions

- PK and PD results in this Phase 1 study of ORKA-001 **support the potential for once-yearly dosing** while maintaining trough antibody concentrations above approved IL-23 targeting antibodies like risankizumab
- These Phase 1 data also support the ability to achieve sustained antibody exposures with ORKA-001 that could enable **higher rates of skin clearance** than the current standard of care and **extended off-treatment remission** in some patients
- ORKA-001 was well-tolerated across all dose levels, with a **favorable safety profile consistent with the IL-23p19 inhibitor class**
- These attributes are being further explored in an **ongoing Phase 2a study, EVERLAST-A,** which is evaluating efficacy and safety of ORKA-001 in adults with moderate-to-severe psoriasis

For further information please contact MedAffairs@orukatx.com

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