ORKA-001, a Novel Extended Half-life Monoclonal Antibody Targeting IL-23 with the Potential to Improve upon Currently Available Therapies for Psoriasis

Byron Kwan[1], Mohammad Murshid Alam[1], Jacob Milligan[1], Soraia Oliveira[1], Christopher Finch[2], Joana Goncalves[2], Laura Sandler[2], Jason Oh[1], Hussam Shaheen[1]

[1] Paragon Therapeutics, Waltham, MA, United States | [2] Oruka Therapeutics, Waltham, MA, United States

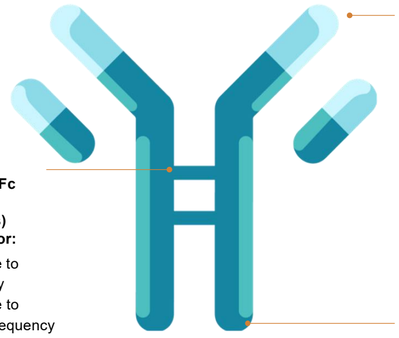
Introduction

- 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.
- The pipeline consists of molecules developed by Paragon Therapeutics, which employs a breadth of protein engineering technologies to discover and optimize biologics targeting established mechanisms.
- Interleukin 23 (IL-23) is a proinflammatory cytokine that helps to maintain and activate T helper 17 (Th17) cells, the primary pathogenic cells in psoriasis1. Antagonism of the p19 subunit of IL-23 (IL-23p19) has proven to have robust efficacy and a favorable safety profile in the treatment of psoriasis[2].
- ORKA-001 is a novel, highly specific, humanized IgG1 monoclonal antibody that potently inhibits IL-23p19.
- ORKA-001 is designed to have higher and longer antibody exposure due to half-life extension through YTE substitution, a validated Fc modification method (Figure 2).
- Since both affinity and antibody exposure of IL-23p19 inhibitors have been shown to have a positive correlation with efficacy in psoriasis[3,4], ORKA-001 has the potential to deliver an enhanced clinical profile compared to current treatments for psoriasis.

Disclosures

- Byron Kwan, Mohammad Murshid Alam, Jacob Milligan, Soraia Oliveira, Jason Oh, and Hussam Shaheen are employees and stockholders of Paragon Therapeutics.
- Christopher Finch, Joana Goncalves, and Laura Sandler are employees and stockholders of Oruka Therapeutics.

Figure 1: ORKA-001: A novel highly specific extended half-life monoclonal antibody targeting IL-23p19



Binds specifically to IL-23p19

- Validated mechanism of action
- Similar epitope to risankizumab
- Similar potency to risankizumab

Half-life extension through validated Fc modification (YTE substitutions) creates potential for:

- Higher exposure to increase efficacy
- Longer exposure to reduce dosing frequency

Effector-null human IgG1 Fc

Figure 2: 'YTE' substitution increases the pH-dependent affinity of the Fc region for FcRn, extending antibody half-life

- M252Y/S254T/T256E ("YTE") amino acid substitutions to the Fc region of antibodies increases the pH-dependent binding affinity to FcRn
- YTE substitution results in increased antibody recycling, causing less lysosomal degradation and thus a prolonged half-life of the antibody

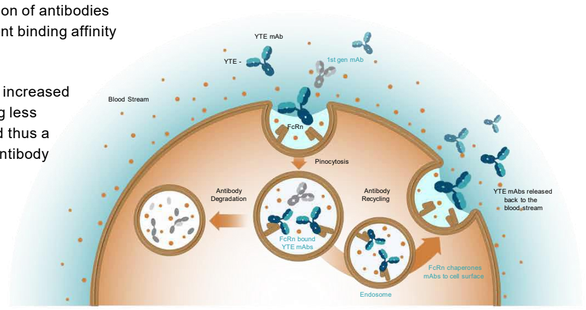


Figure adapted from Apogee Therapeutics

Methods

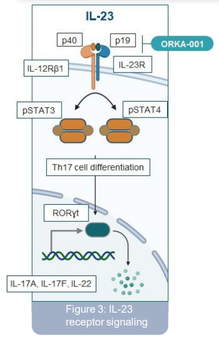


Figure 3: IL-23 receptor signaling

- ORKA-001 was evaluated in multiple in vitro and ex vivo assays in comparison to two benchmark antibodies that target IL-23p19: risankizumab (RIS) and guselkumab (GUS).
- Binding affinity to IL-23 was determined by surface plasmon resonance (SPR).
- Antagonism of human IL-23 signaling was evaluated via assays measuring STAT3 activity in cell lines (Figure 3).
- Inhibition of IL-23-induced IL-17 A secretion was assessed using in vitro cellular assays in human peripheral blood mononuclear cells (PBMC) and mouse splenocytes.
- Half-life extension was measured via pharmacokinetic (PK) analysis in cynomolgus monkeys dosed with a single bolus of ORKA-001.

Created from: Moschen, et al. Nat Rev Gastroenterol Hepatol. (2019); Verstockt, et al. Nat Rev Gastroenterol Hepatol. (2023)

RESULTS

Figure 4: ORKA-001 binds IL-23p19 at a similar epitope as risankizumab with similar affinity

- ORKA-001 and RIS demonstrate comparable high affinity for IL-23p19 (KD <5 pM)
- Cryo-EM structural analysis demonstrates ORKA-001 has a nearly identical epitope as RIS (Figure 4)

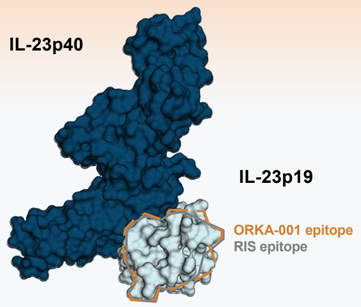
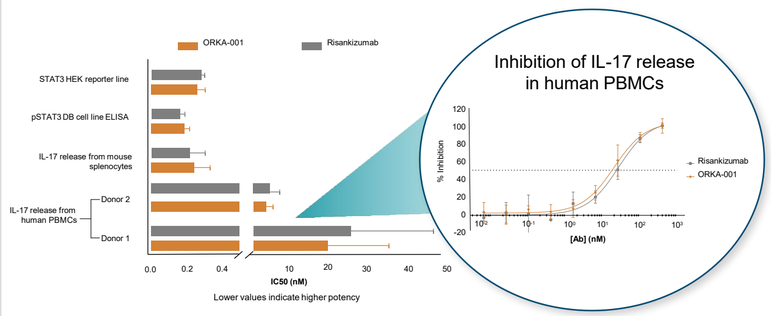


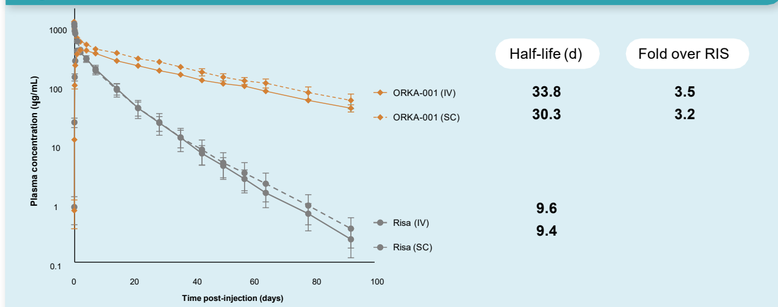
Figure 5: ORKA-001 shows equal or better potency to RIS across a variety of in vitro assays

- ORKA-001 potently inhibited STAT3 activity in cell lines and IL-17A secretion in IL-23-stimulated human PBMC and mouse splenocytes (Figure 5).
- ORKA-001 functional potencies for IL-23 antagonism were comparable to or better than those of RIS (Figure 5) and GUS (not shown).



Notes: IL-17A release assay from mouse splenocytes was conducted relative to risankizumab YTE

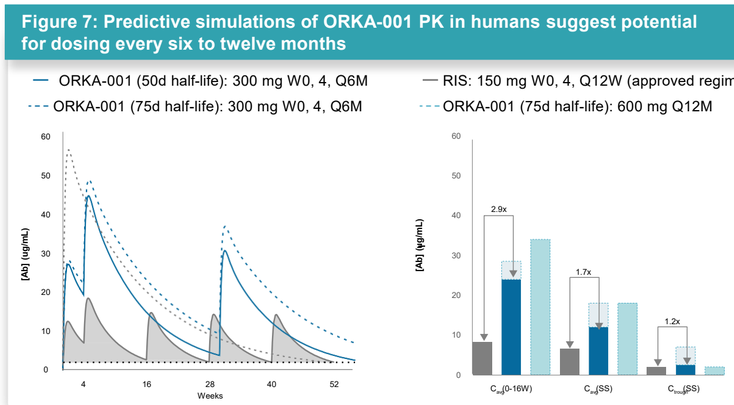
Figure 6: ORKA-001 demonstrates an extended half-life in non-human primates (NHP)



	Half-life (d)	Fold over RIS
ORKA-001 (IV)	33.8	3.5
ORKA-001 (SC)	30.3	3.2
Risa (IV)	9.6	
Risa (SC)	9.4	

The half-life of ORKA-001 was significantly extended in cynomolgus monkeys compared to RIS (Figure 6). Obvious timepoints affected by anti-drug antibodies due to cross-species reactivity were excluded from analysis in accordance with standard practice (N=1 in ORKA-001 SC group).

Figure 7: Predictive simulations of ORKA-001 PK in humans suggest potential for dosing every six to twelve months



- Predictive simulations of ORKA-001 PK in humans suggest that a half-life of ~50 days would enable subcutaneous maintenance dosing every 6 months while a half-life of ~75 days would enable subcutaneous maintenance dosing every 12 months while maintaining trough antibody concentrations equal to or above risankizumab (Figure 7).
- YTE-modified antibodies on average have a human half-life that equals approximately 2-4x the NHP half-life. The half-life for ORKA-001 observed in NHPs (Figure 6) therefore supports the potential to achieve at least Q6M and even Q12M dosing.
- All half-life and dosing scenarios result in higher average exposures for ORKA-001 compared to risankizumab, which has the potential to lead to higher efficacy based on published results with risankizumab[3,5]

Conclusions

- ORKA-001 exhibits high affinity and selectivity for IL-23p19 in vitro and potent inhibition of downstream cellular signaling.
- ORKA-001 demonstrated half-life of over 30 days in non-human primates, which exceeds that of risankizumab by over 3-fold
- ORKA-001 has the potential to match or exceed RIS and GUS on potency while requiring only twice or once per year dosing
- These data provide preclinical evidence of ORKA-001's clinical potential to meaningfully improve upon currently available therapies for psoriasis

Reference: 1. Harrington et al. 2005, Nat Immunol; 2. Ruggiero et al. 2023, Immunol Res, 3: Blauvelt et al. Presented at AAD 2024, San Diego, CA, 4. Daniele et al. 2024 JID Innov; 5. Khatri et al. 2019 J Clin Pharmacol

For further information please contact MedAffairs@orukatx.com

ORUKA THERAPEUTICS

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

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[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)

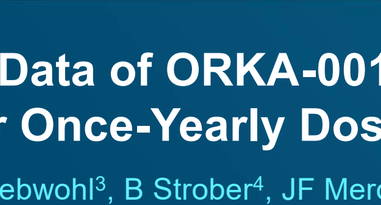
Reference: 1. Dall'Acqua 2006

Disclosures:

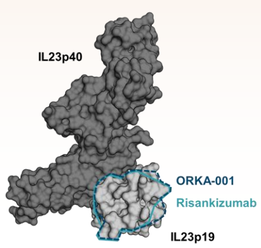
- Christopher Finch, Eugenia Levi and Joana Goncalves are employees of Oruka Therapeutics
- Christoper Finch, Eugenia Levi, Joana Goncalves and Andrew Blauvelt are stockholders of Oruka Therapeutics

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

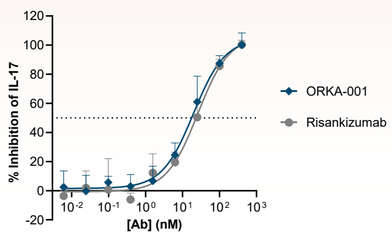
- ORKA-001 and risankizumab demonstrate comparable high affinity for IL-23p19 (K_D <5 pM)
- Cryo-EM structural analysis demonstrates ORKA-001 has a nearly identical epitope as risankizumab
- ORKA-001 shows similar potency to risankizumab



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

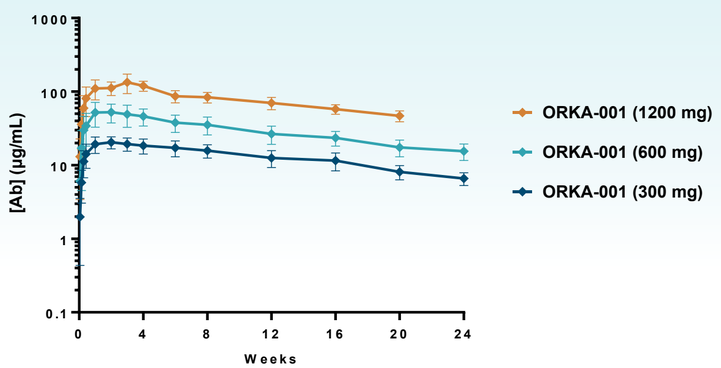
Table 2: ORKA-001 safety profile was consistent with the IL-23p19 class

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

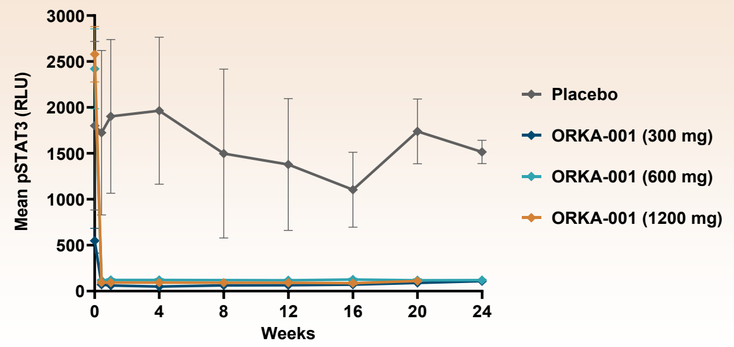
Figure 2: ORKA-001 demonstrates a half-life of ~100 days in humans



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

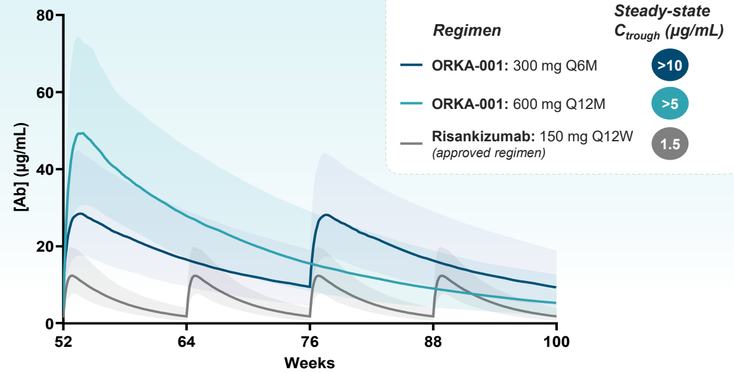
Note: Mean ± SD (N=6 per group). Data cut as of August 6, 2025.

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

ORUKA THERAPEUTICS

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

Andrew Blauvelt[1], Bruce Strober[2], Joseph Merola[3], James Krueger[4], Joel Gelfand[5], Johann E. Gudjonsson[6], Eugenia Levi[7], Joana Goncalves[7], Mark Lebwohl[8]

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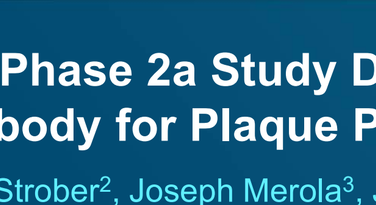
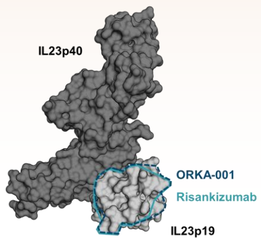


ORKA-001 and risankizumab epitopes



Inhibition of IL-17 release in human PBMCs

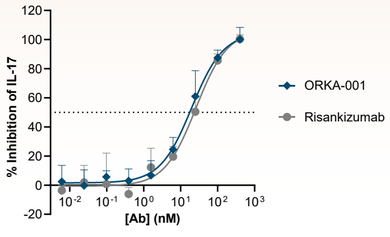
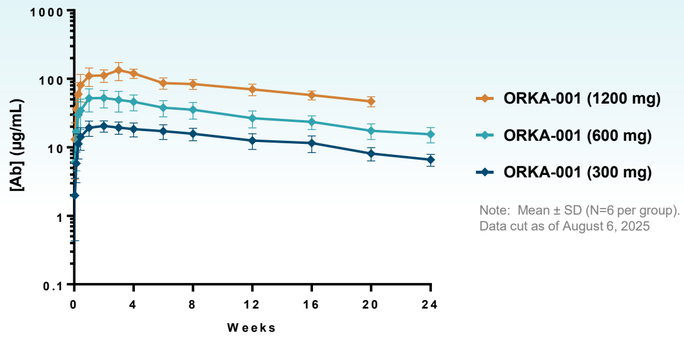


Figure 2: ORKA-001 demonstrated a half-life of ~100 days in humans

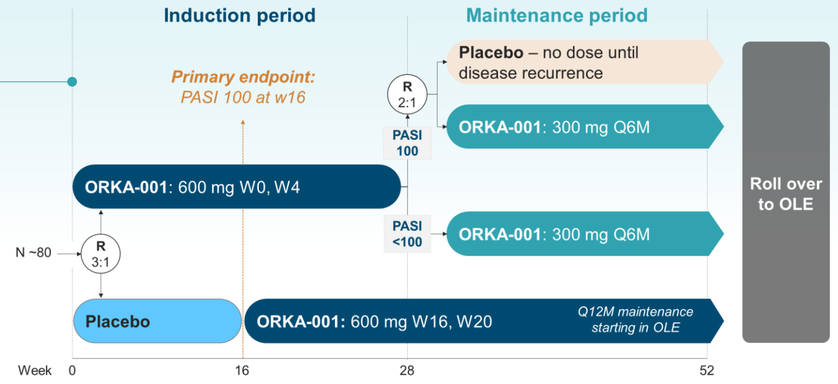


Note: Mean ± SD (N=6 per group).
Data cut as of August 6, 2025

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



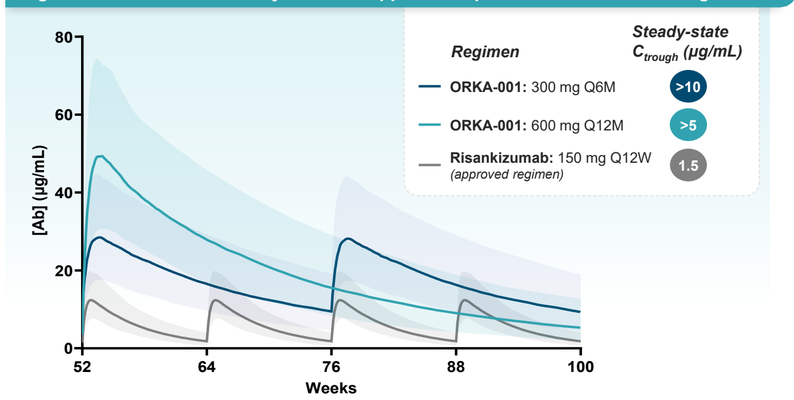
Key Inclusion Criteria:

- 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



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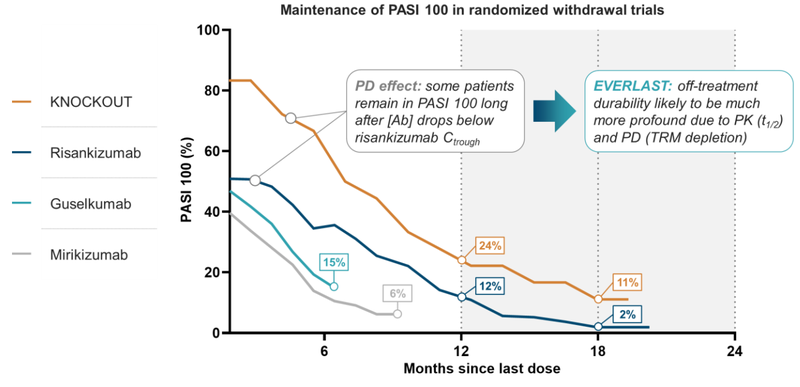
Note: modeling based on internal data and published population PK model for risankizumab; error bars reflect 5th and 95th percentiles; risankizumab exposures in ulcerative colitis from 2024 Thrake (Clin Pharmacol Ther.)

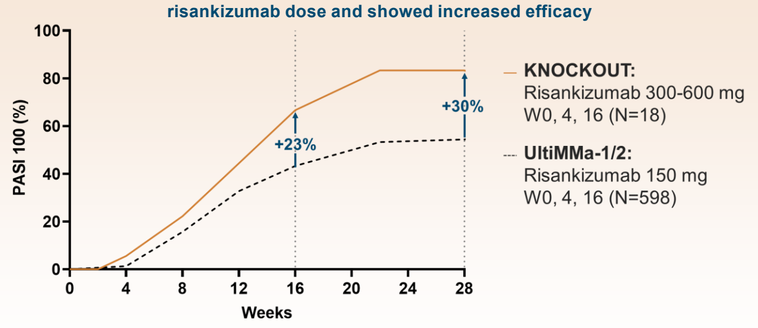
Figure 5: Greater IL-23 inhibition may enable off-treatment remission by depleting TRMs



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

ORUKA THERAPEUTICS

Characterization of ORKA-002, a Novel Extended Half-life Monoclonal Antibody Targeting IL-17A/F for the Treatment of Psoriasis and Other Indications

B Kwan[1], JF Merola[2], A Blauvelt[3], D Rios[1], J Ministro[1], J Milligan[1], G Fayad[1], C Finch[4], E Levi[4], J Senn[4], J Oh[1], H Shaheen[1]

[1] Paragon Therapeutics, Waltham, MA, [2]Departments of Dermatology and Medicine, Division of Rheumatology, UT Southwestern Medical Center, Dallas, TX, USA; Blauvelt Consulting, LLC, Annapolis, MD, USA; [4]Oruka Therapeutics, Waltham, MA, USA

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- The pipeline consists of molecules developed by Paragon Therapeutics, which employs a breadth of protein engineering technologies to discover and optimize biologics targeting established mechanisms.
- The IL-17 family of cytokines includes 6 members (IL-17A to IL-17F). Both IL-17A and IL-17F are key drivers in the pathogenesis of psoriatic disease, being highly overexpressed in psoriatic plaques and the inflamed synovium of patients with psoriatic arthritis.
- Recently, a biologic targeting both IL-17A and IL-17F, bimekizumab, has demonstrated high efficacy that exceeds therapies targeting IL-17A only.
- ORKA-002 is a novel, extended half-life, humanized monoclonal antibody that potently inhibits IL-17A and IL-17F.
- ORKA-002 has been engineered to have optimized properties with the aim of delivering an enhanced clinical profile compared to currently available treatments for psoriasis and other inflammatory diseases

Disclosures

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- Christopher Finch, Eugenia Levi, and Joseph Senn are employees and of Oruka Therapeutics.
- Christopher Finch, Eugenia Levi, Andrew Blauvelt and Joseph Senn are stockholder of Oruka Therapeutics.

Reference: 1. Prinz I, et. al. Interleukin-17 cytokines: Effectors and targets in psoriasis-A breakthrough in understanding and treatment. J Exp Med. 2020 Jan 6;217(1):e20191397.

Figure 1: ORKA-002: A novel highly specific extended half-life monoclonal antibody targeting IL-17A and IL-17F

- Binds specifically to IL-17A and IL-17F to prevent homodimer and heterodimer signaling, a validated mechanism of action
- Half-life extension through validated Fc modification (YTE substitutions) creates potential for reduced dosing frequency

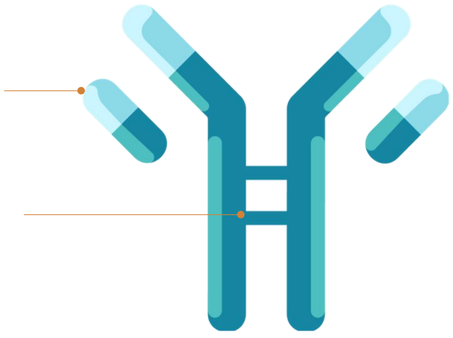


Figure 2: 'YTE' substitution increases the pH-dependent affinity of the Fc region for FcRn, extending antibody half-life

- M252Y/S254T/T256E ("YTE") amino acid substitutions to the Fc region of antibodies increases the pH-dependent binding affinity to FcRn
- YTE substitution results in increased antibody recycling, causing less lysosomal degradation and thus a prolonged half-life of the antibody

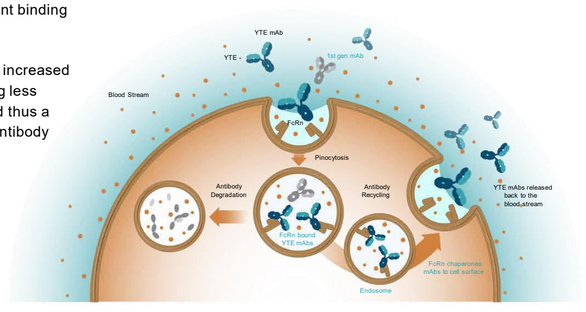


Figure adapted from Apogee Therapeutics

Methods

- ORKA-002 was evaluated in multiple in vitro and ex vivo assays in comparison to the benchmark antibody that targets IL-17A and IL17F: bimekizumab (BIME).
- Binding affinity to IL-17A and IL-17F was determined by surface plasmon resonance (SPR).
- Antagonism of Il-17A and IL-17F signaling was assessed NFκB activation assays in reporter cell lines.
- Inhibition of IL-17A-induced or IL-17F-induced IL-6 secretion was measured in vitro using normal human dermal fibroblasts.
- Half-life extension was evaluated via pharmacokinetic (PK) analysis in cynomolgus monkeys following a single bolus dose of ORKA-002.

RESULTS

Figure 3: ORKA-002 binds IL-17A and F at a similar epitope as bimekizumab with similar affinity

- Cryo-EM structural analysis demonstrates that ORKA-002 has a nearly identical epitope as bimekizumab for both IL-17A (above) and IL-17F (not shown)
- ORKA-002 and bimekizumab have comparable picomolar affinity for IL-17A and IL-17F by surface plasmon resonance (SPR)

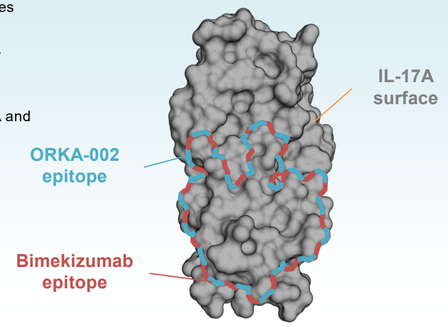
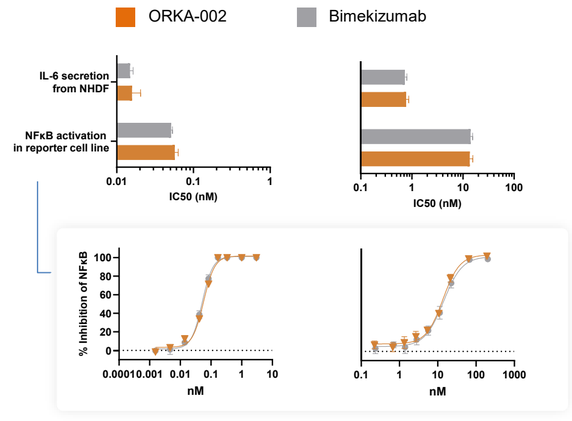


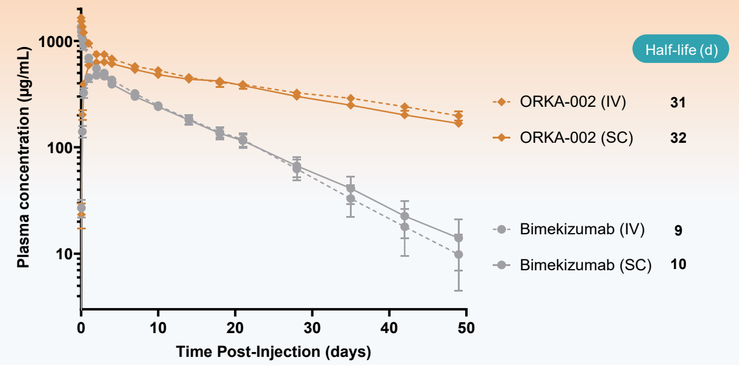
Figure 4: ORKA-002 shows similar potency to bimekizumab across multiple in vitro assays

- ORKA-002 bound specifically to human IL-17A and IL-17F with high affinity.
- IL-17A and IL-17F binding affinity and functional potencies for IL-17A and IL-17F antagonism were comparable to BIME (Figure 4).



Abbreviations: NHDF, normal human dermal fibroblasts

Figure 5: ORKA-002 demonstrates an extended half-life in non-human primates (NHP)



Notes: Study completed at Day 49

The half-life of ORKA-002 was significantly extended in cynomolgus monkeys compared to BIME (Figure 5). Obvious timepoints affected by anti-drug antibodies due to cross-species reactivity were excluded from analysis in accordance with standard practice (N=1 in ORKA-002 SC group).

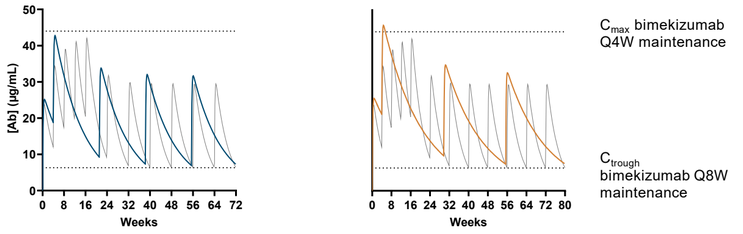
Figure 6: Predictive simulations of ORKA-002 PK in humans support dosing every four to six months

Projected exposure of illustrative ORKA-002 regimens vs. approved bimekizumab regimens

ORKA-002 (50d half-life): 320 mg W0, 4 then Q4M

ORKA-002 (75d half-life): 320 mg W0, 4 then Q6M

Bimekizumab: 320 mg W0, 4, 8, 12, 16 then Q8W



- Predictive simulations of ORKA-002 PK in humans suggest that a half-life of ~50 days would enable subcutaneous maintenance dosing every 4 months and a half-life of ~75 days would enable dosing every 6 months while maintaining trough antibody concentrations equal to or above bimekizumab (Figure 6).
- YTE-modified antibodies on average have a human half-life that equals approximately 2-4x the NHP half-life. The half-life for ORKA-002 observed in NHPs therefore supports the potential to achieve at least Q4M and even Q6M dosing.

Notes: Bimekizumab modeling, Cmax, and Ctrough are based on published PK parameters from FDA and EMA review documents

Conclusions

- ORKA-002 exhibits high affinity and selectivity for IL-17A and IL-17F and potent inhibition of downstream cellular signaling
- ORKA-002 demonstrated a half-life of ~25 days in cynomolgus monkeys, which exceeds that of bimekizumab by ~3-fold
- ORKA-002 has the potential to match bimekizumab on potency while requiring only two or three doses per year
- These data provide preclinical evidence of ORKA-002's clinical potential to meaningfully improve upon currently available therapies for psoriasis and psoriatic arthritis

For further information please contact MedAffairs@orukatx.com

ORUKA THERAPEUTICS

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

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

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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)

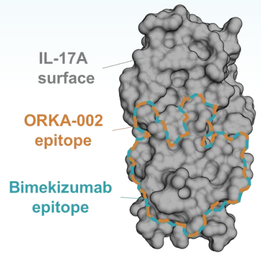
Disclosures:

- 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

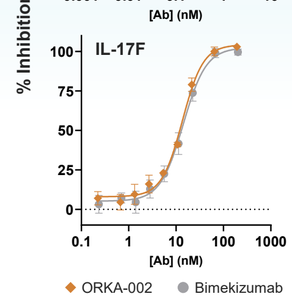


Fig 2: ORKA-002 Phase 1 trial design (NCT06944379)

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

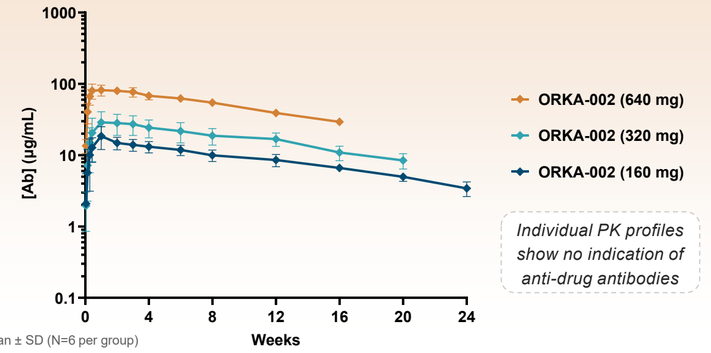
Table 1: ORKA-002 blinded safety profile was consistent with the anti-IL-17 class

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

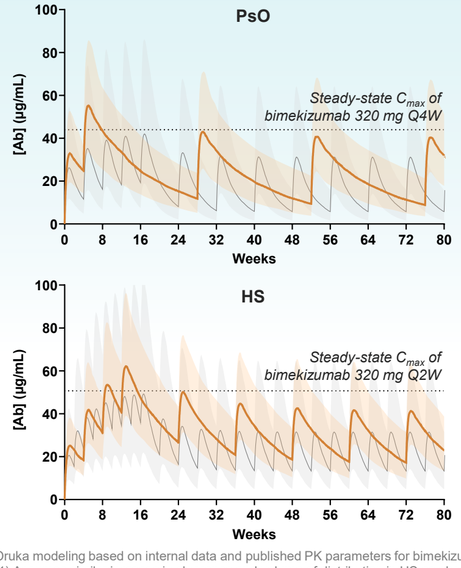
Fig 3: ORKA-002 demonstrated a half-life of 75-80 days in humans



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

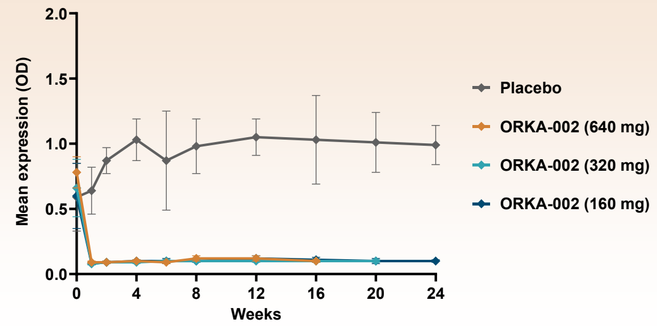


- **ORKA-002:** 320 mg W0, 4 then Q6M
- **Bimekizumab:** 320 mg Q4W from W0-16, then Q8W

- **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

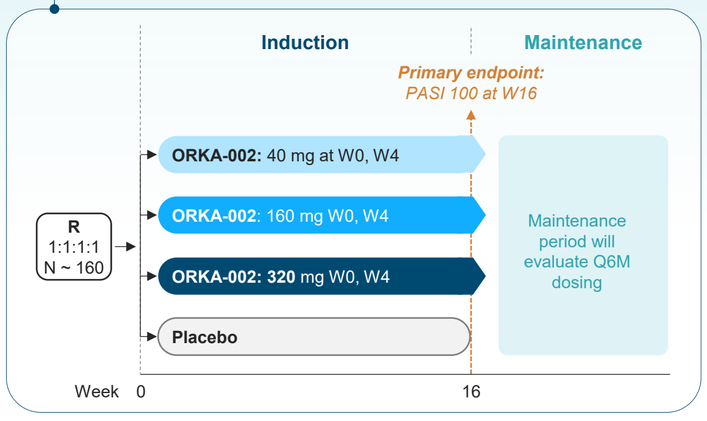


Mean ± SD (N=6 per group). 24 weeks is the longest follow-up available as of the data cut on January 6, 2026

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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