ORUKA THERAPEUTICS

Corporate Overview

NASDAQ: ORKA

November 2025

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Fully funded through a potential psoriasis breakthrough

Potential to change the treatment paradigm in psoriasis, a $30B+ indication space

- **ORKA-001 (IL-23p19):** ~100d half-life and high AUC increases likelihood of achieving upside scenario, which ongoing EVERLAST-A Phase 2a will test (data in 2H 2026)
  - Once yearly dosing
  - Higher rates of disease clearance (PASI 100)
  - Off-treatment remissions in some patients
- **ORKA-002 (IL-17A/F):** HV PK data ~YE 2025 and Phase 2 initiation in 1H 2026
- **ORKA-021 (ORKA-002 → ORKA-001):** straightforward path to potential H2H win vs. Skyrizi and Bimzelx

Continued external tailwinds

- **Better biologics overdeliver in PsO**
  - UCB's Bimzelx launch exceeding expectations **– ~$2B annualized 2025 sales, with $5B+ peak sales consensus**
  - Skyrizi continues to exceed forecasts **– >$11B expected 2025 sales in psoriatic disease and growing**
- **Orals do not reach biologic efficacy –** e.g., icotrokinra (JNJ-2113)

Fully-funded >1 year beyond multiple Phase 2 catalysts

- Additional **$180M financing in September 2025 extends runway over one year past three key Phase 2 readouts:** ORKA-001 Phase 2a and 2b (EVERLAST-A and -B), and ORKA-002 Phase 2
- **67.1M total shares** of common stock and common stock equivalents

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On a mission to enable freedom from chronic skin disease

Our goal

Help patients with chronic skin conditions experience the **greatest possible freedom from disease**

Highest possible rates of disease clearance

+

Fewest number of doses

Our approach

Advance potentially **best-in-class antibodies** targeting mechanisms with **proven efficacy and safety**

PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	INDICATIONS
ORKA-001	IL-23p19		**Interim data 2H26**	PsO
ORKA-002	IL-17A/F	**HV PK ~YE25**	**Initiation 1H26**	PsO, PsA, HS, others
ORKA-021	Sequential combination regimen of ORKA-002 and -001			
ORKA-003	Undisclosed			

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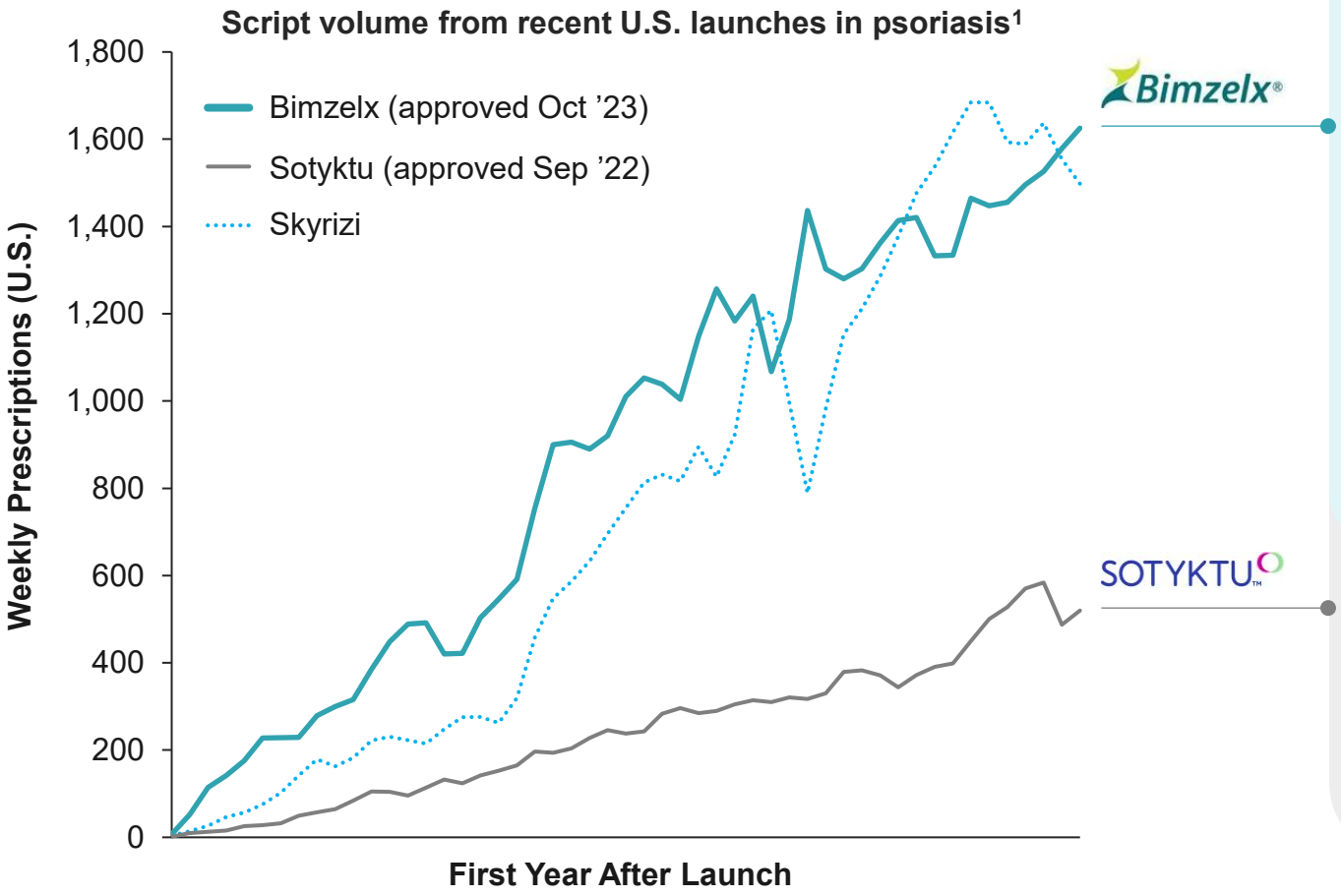
Notes: Oruka has exclusive worldwide rights to ORKA-001 (for all fields outside of IBD) and ORKA-002 (for all fields) from Paragon Therapeutics, Inc.
Abbreviations: FIH, first-in-human dosing; HV, healthy volunteer; HS, hidradenitis suppurativa; PK, pharmacokinetics; PsA, psoriatic arthritis; PsO, psoriasis

Bimzelx launch shows that better biologics will win in psoriasis

Bimzelx versus Sotyktu performance validates our thesis



- **UCB's Bimzelx launch has exceeded expectations, driven by strong demand –** ~$2B annualized 2025 sales, with $5B+ peak sales consensus
- **Market underestimated the opportunity –** UCB market cap ~$15B pre-launch vs. ~$50B two years later (>$30B market cap created on Bimzelx alone)
- **Strong launch driven by PsO in U.S. –** proof point that smaller, non-incumbent company can effectively commercialize in PsO

- **Sotyktu underperformed due to lack of demand –** sub-optimal efficacy with JAK-like safety overhang
- **Market access dynamics not meaningfully different from Bimzelx –** not a major driver

Notes & Sources: (1) Jefferies (based on IQVIA data), shown as 2-week moving average

The psoriasis market will continue to reward biologic innovation

Massive market size

$30B+

Growing moderate-to-severe psoriasis market, with further potential in mild-to-moderate disease

Continued pharma investment

Takeda — nimbus THERAPEUTICS

Lilly — DICE Therapeutics

J&J — Protagonist Therapeutics

Pharma has bet big on orals, sacrificing efficacy for perceived convenience

Better biologics continue to win

$5B+ Bimzelx® (bimekizumab-bkzx)

peak sales forecast

Bimzelx launch shows non-incumbents can achieve access if they have a drug physicians want

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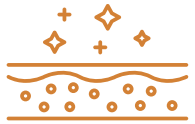
ORKA-001 & -002 complement each other to address all PsO/PsA

ORKA-001

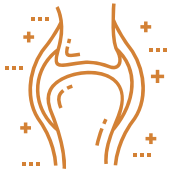
For patients with purely skin disease



Majority of dermatologists prefer an anti-IL-23p19

ORKA-002

For patients with joint involvement, including PsA, or recalcitrant skin disease



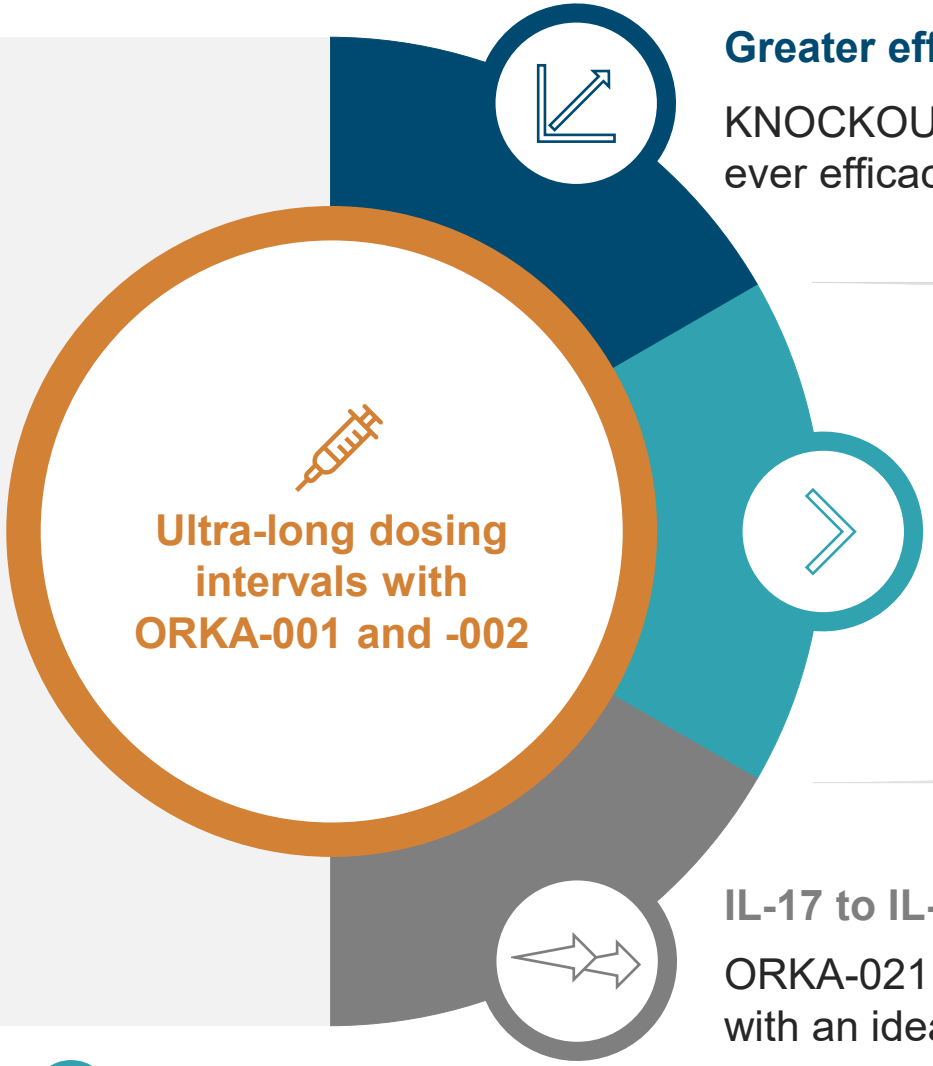
Anti-IL-17 preferred, and **IL-17A/F emerging as the best approach**

ORKA-021

Sequential **combination of -002 and -001 –** rapid response with ideal maintenance profile

Creates **another way to "win"** in defining the best possible regimen in PsO and PsA

1-2 doses per year is enough to win, but we are aiming far higher



Greater efficacy

KNOCKOUT demonstrates potential for highest ever efficacy from higher IL-23 antibody exposure

Off-treatment remission

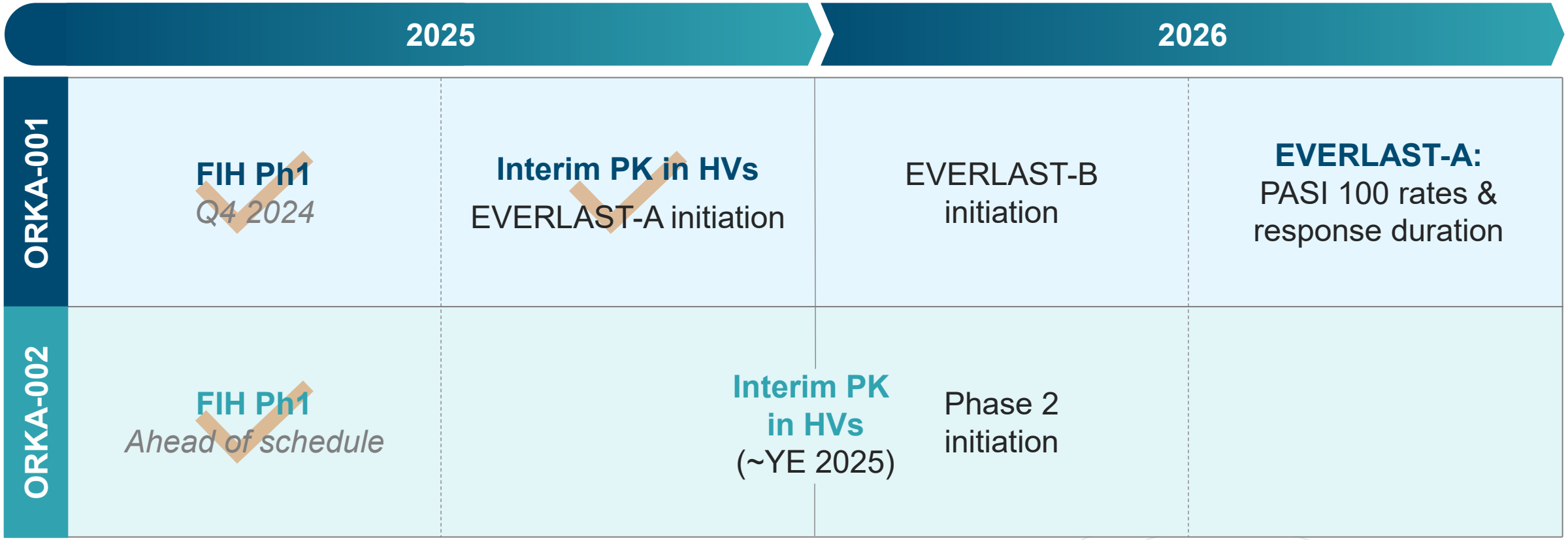
High anti-IL-23 exposures could lead to immune reset and long-lasting disease clearance in some patients

IL-17 to IL-23 combination

ORKA-021 could deliver rapid and deep responses with an ideal maintenance profile

Maximizes odds of having a strong value proposition to achieve preferred access and price for innovation

Advancing co-leads rapidly towards multiple clinical data catalysts



Strong cash position provides runway >1 year beyond three major readouts:
EVERLAST-A Ph2a in 2H 2026, EVERLAST-B Ph2b in 2027, and ORKA-002 Ph2 in 2027

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ORKA-001: potentially best-in-class anti-IL-23p19

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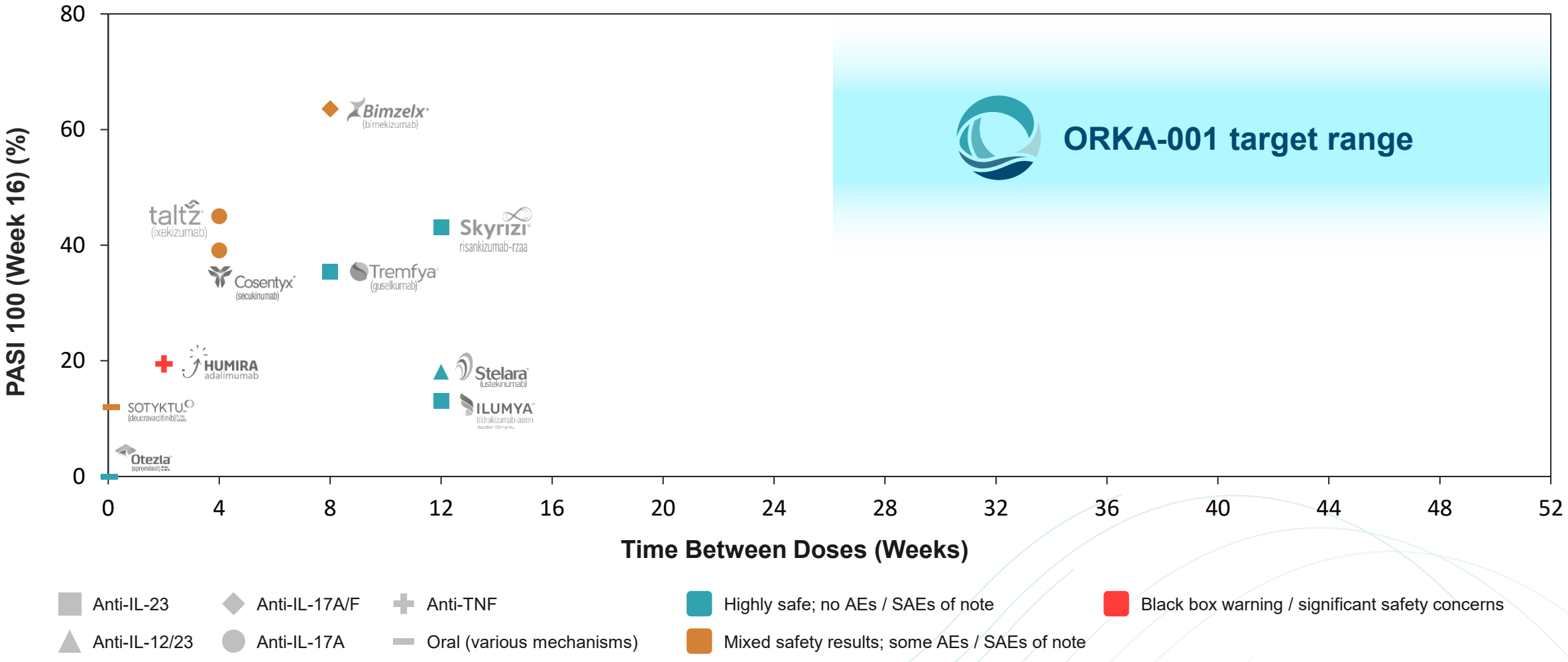
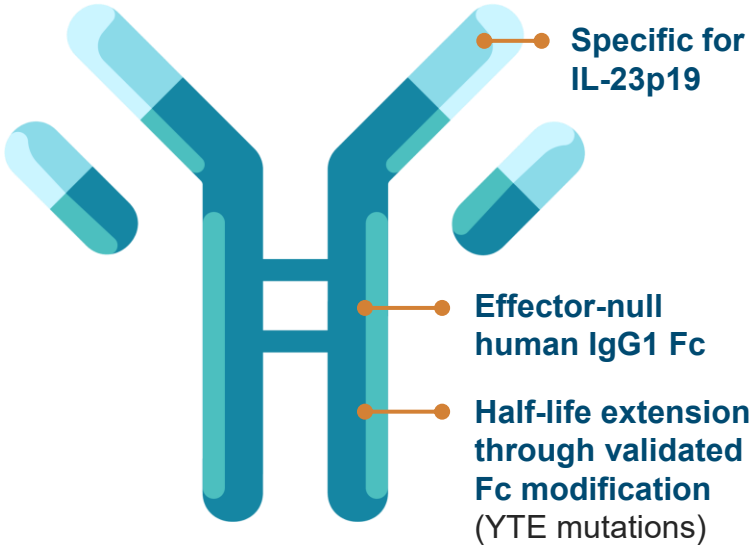
Biologics have raised the bar on standard of care in PsO, but there is ample room for improvement



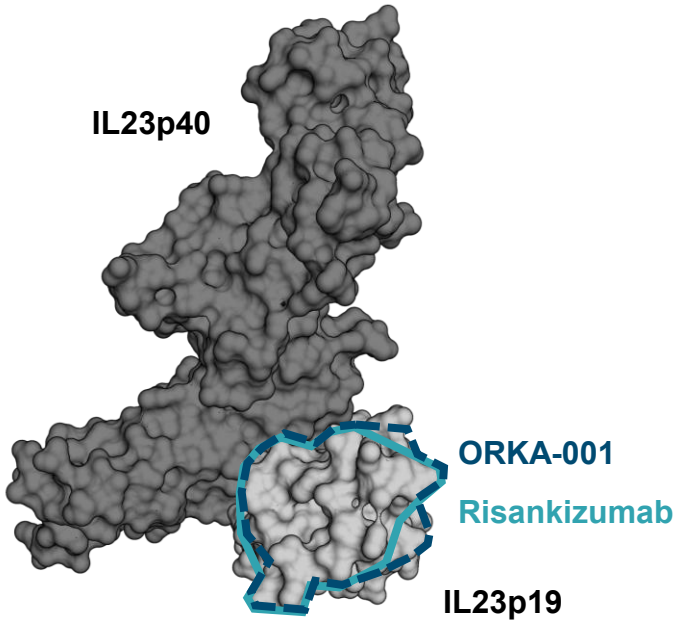
Notes & Sources: FDA Approval Labels and publications of Phase 3 trials supporting approval; W16 PASI 100 not reported for Ilumya (W12 data shown), Otezla (W16 data shown from comparator arm in Sotyktu label), or Stelara (W16 data shown from comparator arm in Skyrizi UltIMMa-1/2 trials)

ORKA-001 targets validated biology with significantly extended PK

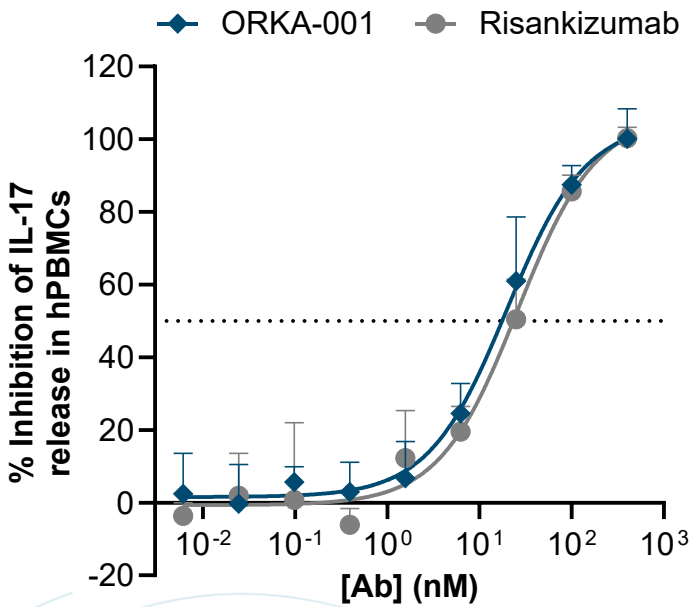
ORKA-001 could be the last word in IL-23p19 inhibitors



Binds a nearly identical epitope to risankizumab



Comparable potency to risankizumab in a variety of assays



ORKA-001 is designed to match the validated biology of Skyrizi (risankizumab), but with a dramatically extended half-life

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ORKA-001 Phase 1 results set the stage for a step-change in PsO

Phase 1 results

- Half-life of ~100 days
- C_{max} and AUC that enable "KNOCKOUT" exposures
- PD biomarkers linking antibody PK to target engagement
- Safety and tolerability consistent with the IL-23 class

Three major "ways to win"

Annual dosing	**Once per year dosing,** with a Q6M option if needed for hard-to-treat patients
Best-in-class efficacy	**"KNOCKOUT"** antibody exposures could lead to **highest anti-IL-23 efficacy**
Off-treatment remission	**Multi-year off-treatment remissions** for some patients – **a first in PsO** and a potential paradigm change

Ongoing EVERLAST-A Phase 2a trial in PsO will validate this potential – efficacy data expected in 2H 2026

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ORKA-001 Phase 1 trial design

Phase 1 trial to evaluate the safety, tolerability, and PK of ORKA-001 in healthy participants (NCT06698939)

Design

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

Population

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

Endpoints

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

Dose levels and length of follow-up to date

Notes: Data cut as of August 6, 2025
Abbreviations: SC, subcutaneous

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

ORKA-001 and placebo	300 mg	600 mg	1200 mg	All
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 headache, upper respiratory tract infection, and transient erythema at the injection site

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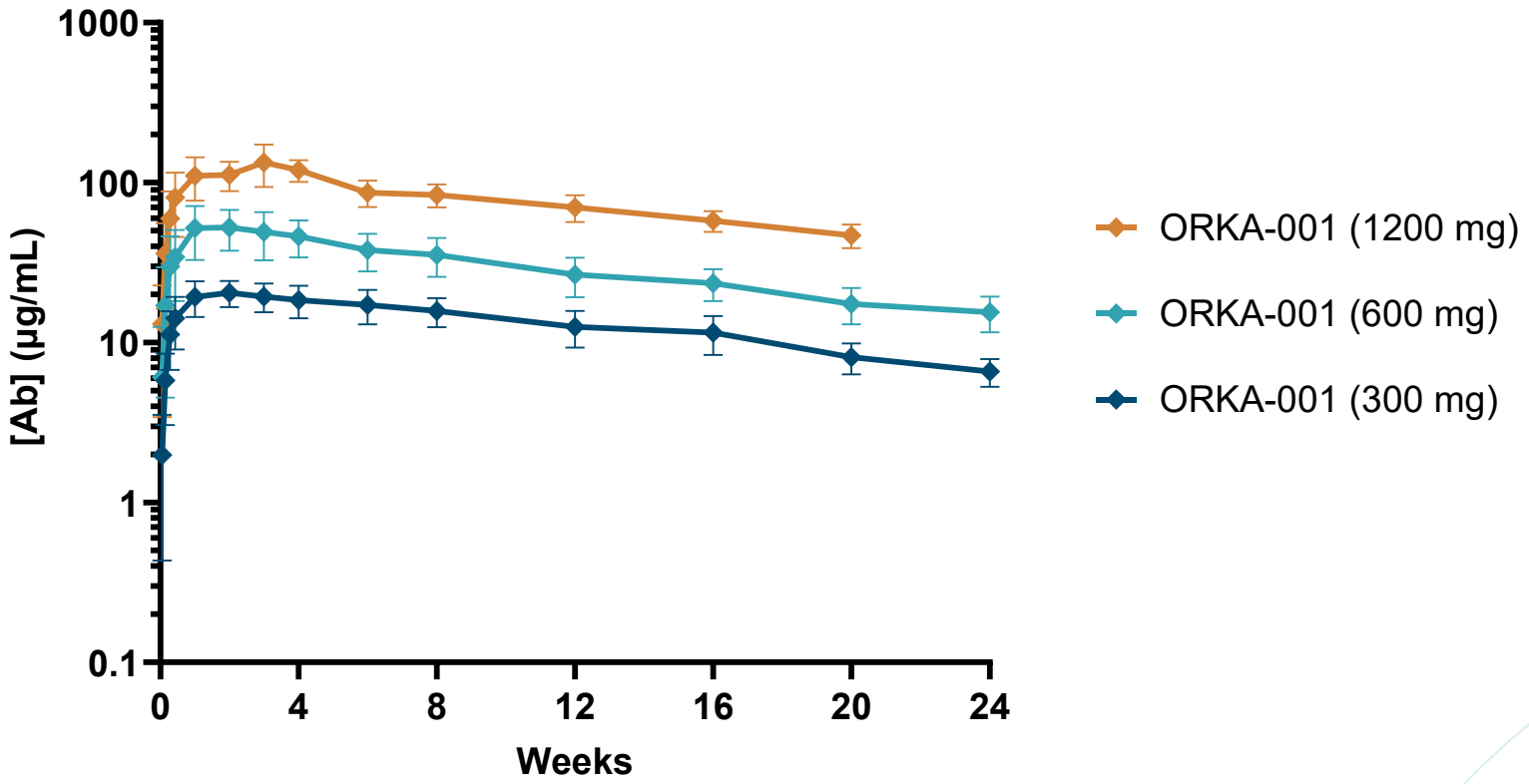
Notes: Data cut as of August 6, 2025

Approximately 100-day half-life and high AUC derisks upside case

Pharmacokinetic profile of a single subcutaneous dose of ORKA-001

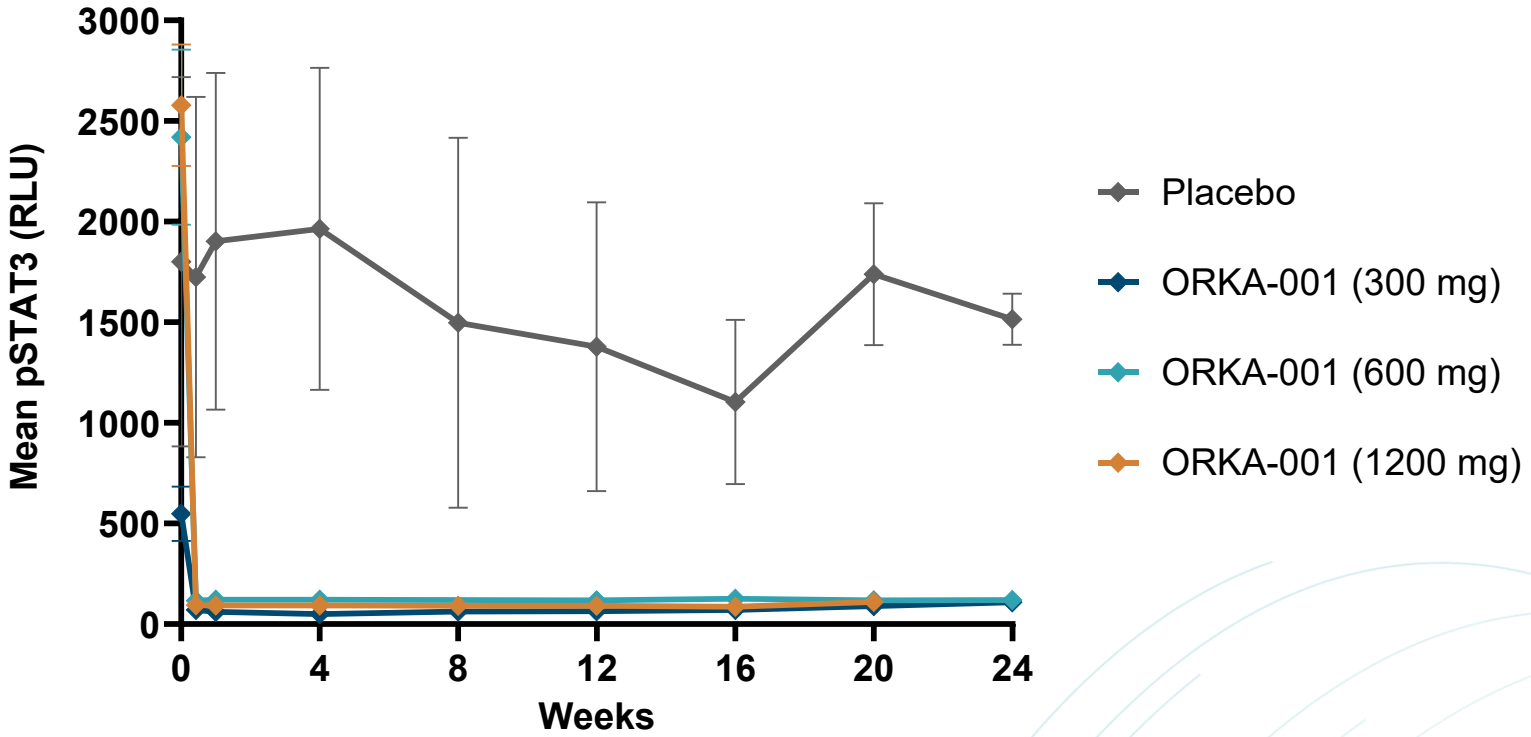


- **~100-day half-life** in humans, >3x longer than risankizumab
- C_{max} exceeds risankizumab's at an equivalent dose[1], suggesting ORKA-001 has **high bioavailability**
- High AUC confirms ability to achieve **exposures matching or exceeding KNOCKOUT**
- Individual PK profiles **show no indication of ADAs**

Notes & Sources: Mean ± SD (N=6 per group). Data cut as of August 6, 2025. (1) Single 300 mg subcutaneous dose of risankizumab in n=6 white healthy volunteers reported in Skyrizi BLA Multi-disciplinary Review and 2019 Khatri (J Clin Pharmacol)

ORKA-001 demonstrated deep and sustained inhibition of STAT3 signaling, a downstream marker of IL-23 activity, through 24 weeks

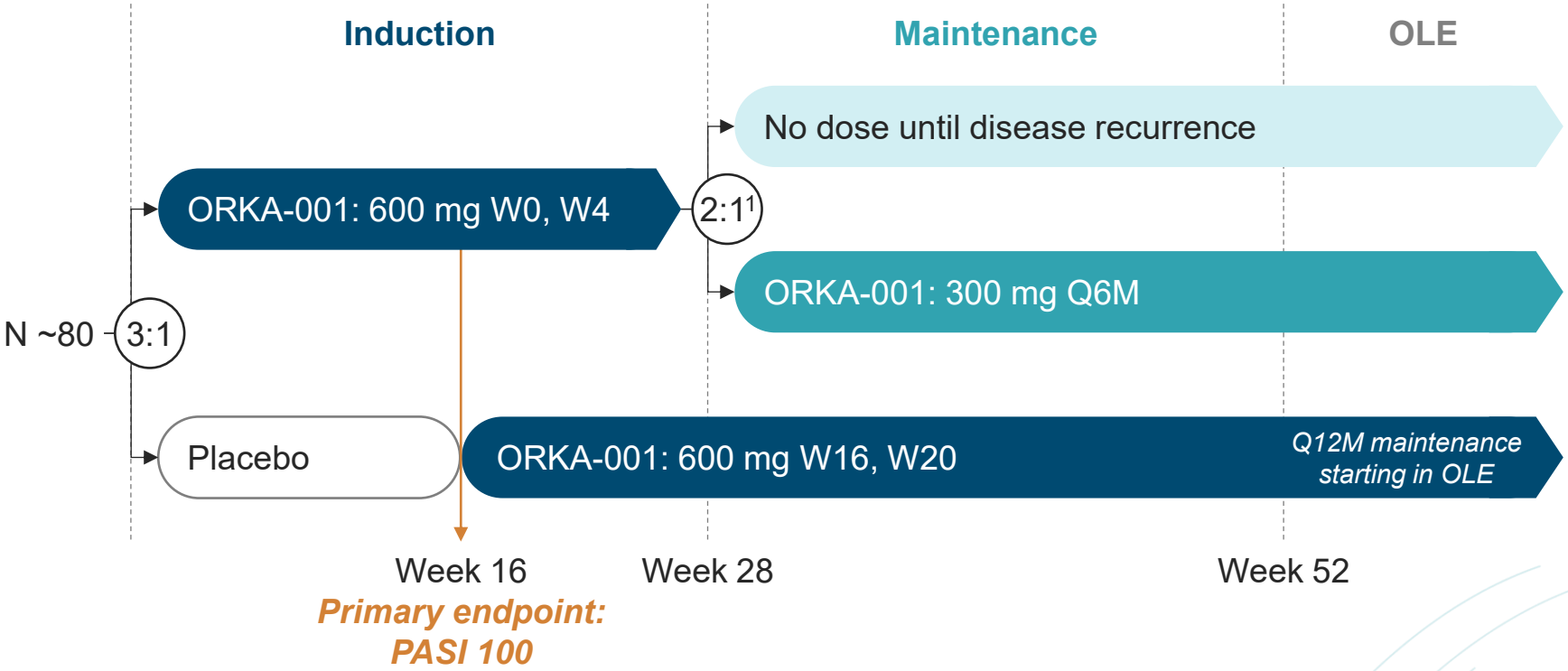
ORKA-001 from serum inhibits STAT3 phosphorylation following *ex vivo* IL-23 stimulation



Notes: Mean ± SD (N=6 per group). 24 weeks is the longest follow-up available as of the data cut on August 6, 2025.
ORKA-001 (600 mg) data slightly offset for visualization

EVERLAST-A Phase 2a – a potential game changer in PsO

EVERLAST-A Phase 2a proof-of-concept trial in moderate-to-severe psoriasis (NCT07090330)



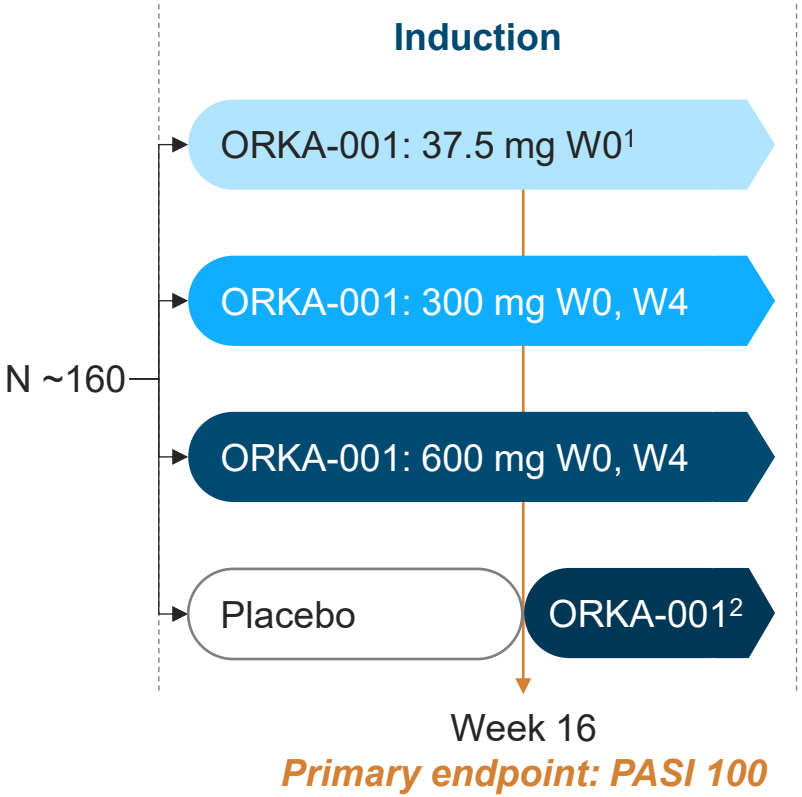
Initial data in 2H 2026 has potential to deliver on all "upside" scenarios:

- **Definitive test of higher efficacy at higher exposures:** PASI 100 at W16, W28, and beyond
- **Evidence for annual dosing and off-treatment remissions** from durability in "no dose" cohort

Notes: (1) Patients in PASI <100 at Week 28 do not undergo randomization and instead receive ORKA-001 300 mg Q6M
Abbreviations: OLE, open-label extension

EVERLAST-B Phase 2b expected to begin in 1H 2026

EVERLAST-B Phase 2b dose-ranging trial in moderate-to-severe psoriasis



Maintenance period will evaluate no dose, Q6M, and Q12M regimens

EVERLAST-B dosing projected to begin in 1H 2026, before the end of EVERLAST-A

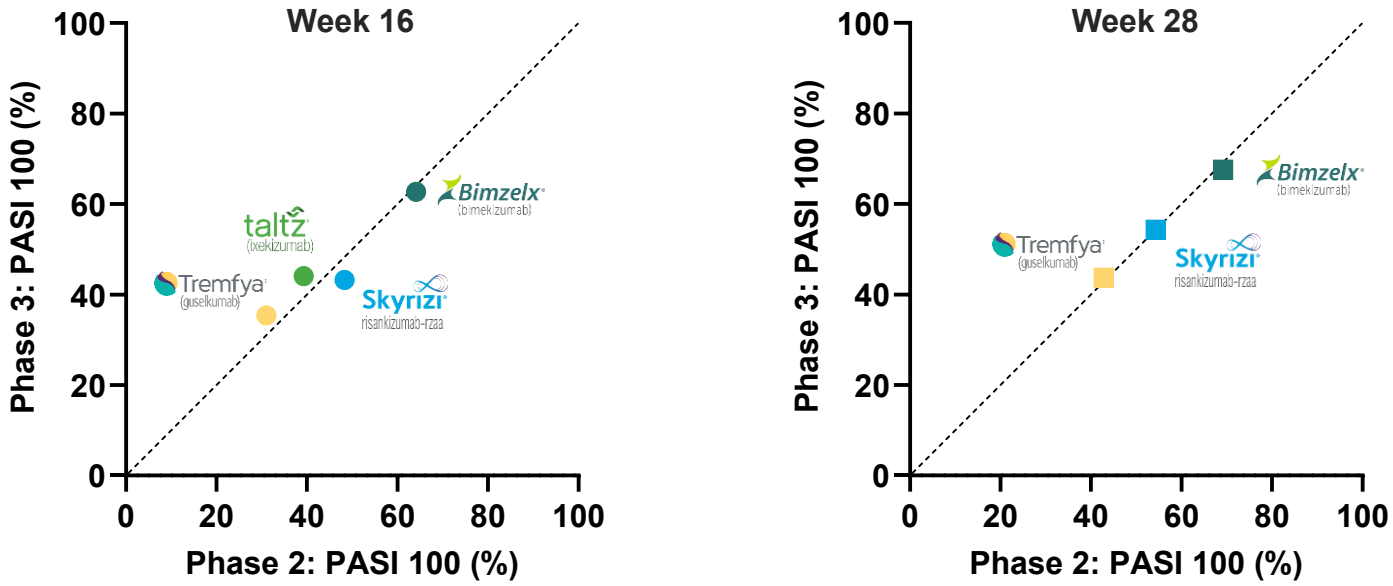
- **Expediting start** by adding additional sites (North America and Europe) and then rolling over EVERLAST-A sites onto EVERLAST-B enrollment
- **Maximizes speed to BLA**

Notes: (1) Expected to be sub-optimal and included for dose-ranging purposes; (2) Placebo patients receive ORKA-001 starting at Week 16

Phase 2 psoriasis data is robust and predictive of Phase 3

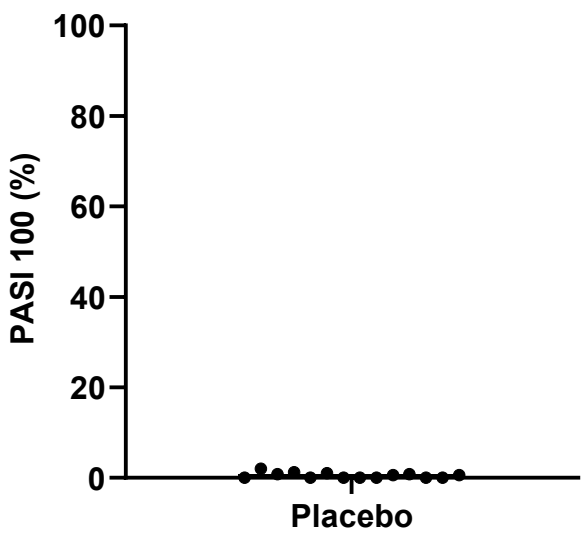
Consistent Phase 2 to 3 translation

Phase 2 PASI 100 rates strongly correlate with Phase 3 at both Week 16 and 28



Low placebo rates

<1% PASI 100 placebo rate



Facilitates rapid FIH to BLA/NDA timeline (e.g., 6 years for Skyrizi and 6.1 years for Sotyktu)

Notes & Sources: (left) Shown for closest dose from Phase 2 to Phase 3; Phase 2: weighted average of highest doses for Skyrizi and Tremfya used to approximate Phase 3 dose, Bimzelx data estimated from BE ABLE 1 and 2, Taltz Phase 2 only ran to W20; Phase 3: weighted average of pivotal trials for Skyrizi (N=2), Bimzelx (N=3 W16, N=2 W28), Tremfya (N=2), Taltz (N=3). (right) Placebo data at primary endpoint (W12 or W16) from N=14 Phase 3 trials of IL-23 and IL-17 mAbs

EVERLAST-A provides multiple “ways to win” in 2H 2026

Provide definitive test of higher efficacy at higher exposures

PASI 100 data at Week 16, Week 28, and beyond

Establish evidence for annual dosing and lock in Q6M

Open-ended cohort will validate annual dosing; Q6M dosing arm to show response maintenance

Show compelling signs of off-treatment remissions[1]

Kaplan-Meier curve of PASI 100 durability after induction, with some patients out to ~1 year

Durability data will mature in open label portion creating opportunities for future data releases

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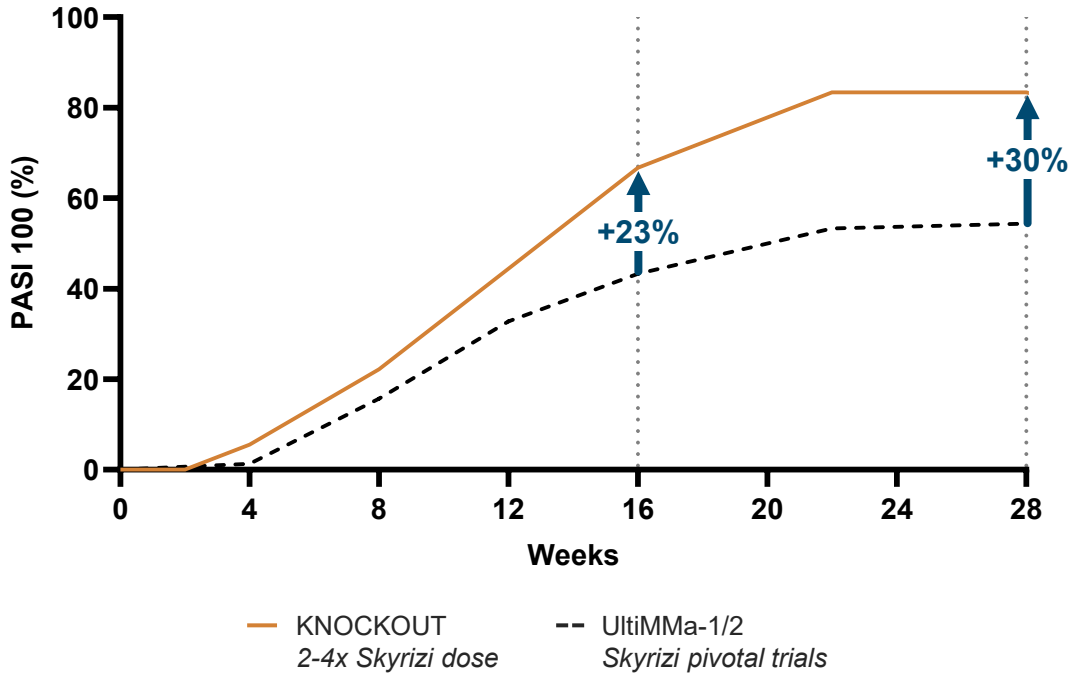
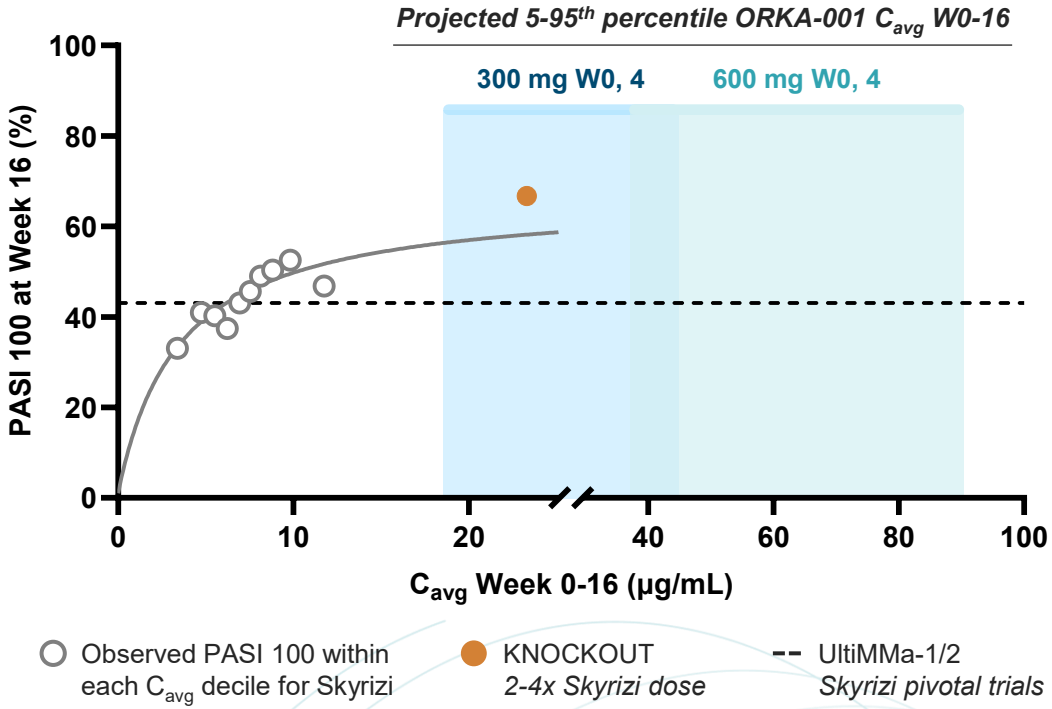
Notes & Sources: (1) Defined in the literature as clear skin for a period of 1 year or more after the completion of the last dose of a prescription therapy for psoriasis (2020 Armstrong in BJD)

ORKA-001 PK profile could enable higher efficacy in PsO

KNOCKOUT study testing 2-4x the approved Skyrizi dose showed the highest anti-IL-23 efficacy to date



Skyrizi exposure-response model indicates potential to increase efficacy with higher exposure

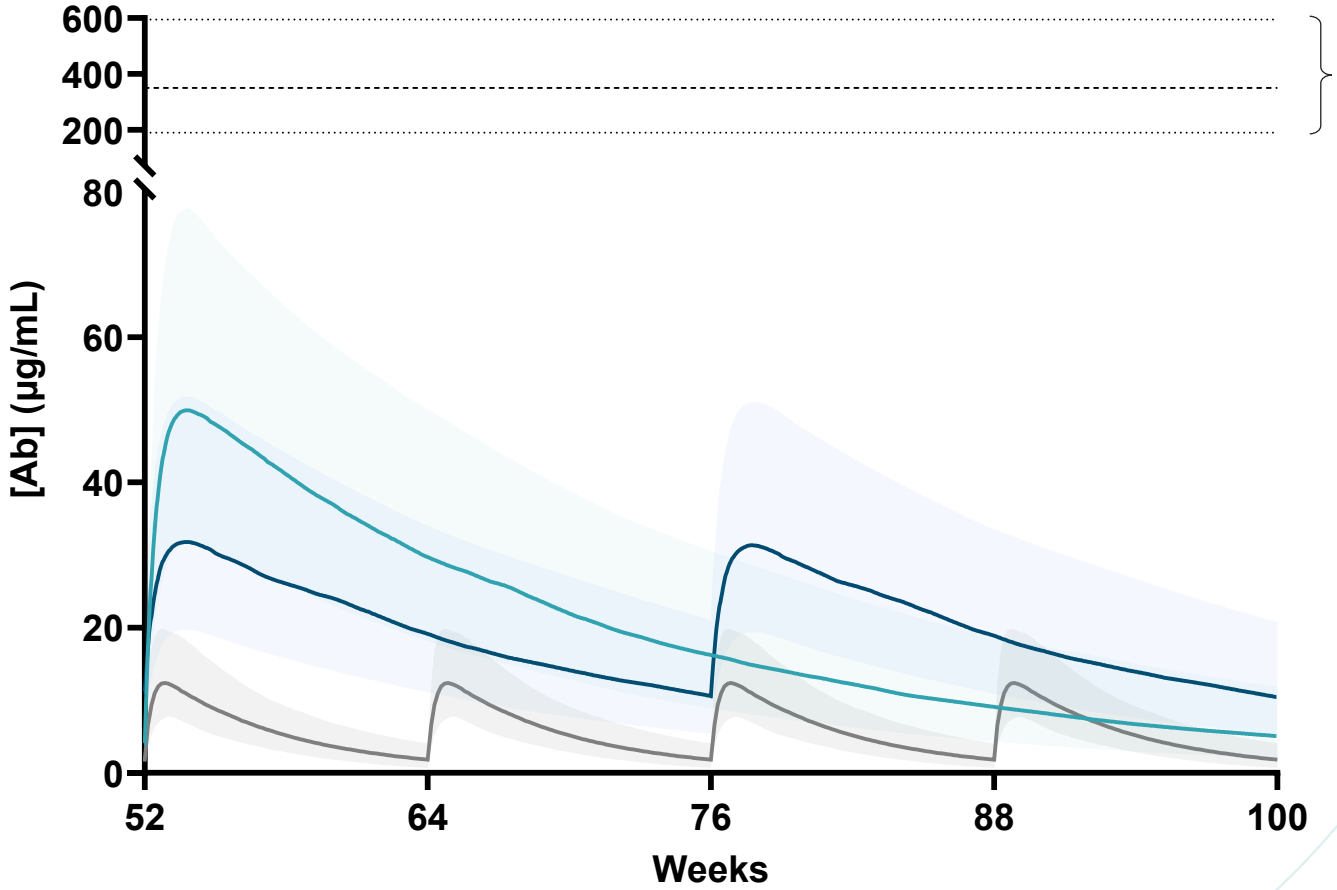


Higher efficacy observed with higher anti-IL-23 exposure, with separation increasing from W16 to W28 as efficacy reaches peak

Notes & Sources: (left) Cross-trial comparison of pooled data from KNOCKOUT (N=18) and UltIMMa-1/2 (N=598) from 2024 Blauvelt (AAD presentation) and 2018 Gordon (Lancet). (right) Adapted from 2019 Khatri (Clin Pharmacol Ther) and Skyrizi BLA MDR (Fig. 20); gray line shows model-estimated probabilities for PASI 100 for all patients, including Asian ethnicity; KNOCKOUT exposures estimated from population pharmacokinetic model for Skyrizi

100-day half-life brings once annual dosing within reach

ORKA-001 projected steady-state exposures significantly exceed Skyrizi and make annual dosing likely



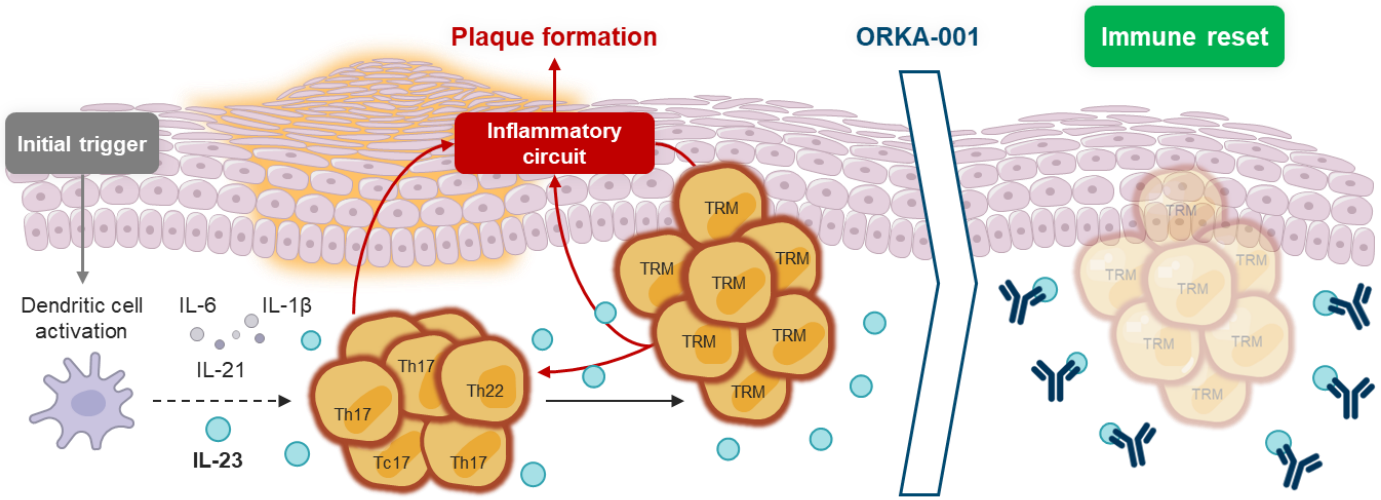
Skyrizi C_{max} in UC (median ± 5th and 95th percentiles) supports safety of high anti-IL-23 exposures

Maintenance dosing	Steady-state C_{trough} (µg/mL)
ORKA-001: 300 mg Q6M	>10
ORKA-001: 600 mg Q12M	>5
Skyrizi: 150 mg Q12W (approved PsO regimen)	1.5

Notes & Sources: Oruka modeling based on internal data and published population pharmacokinetic model for Skyrizi; error bars reflect 5th and 95th percentiles. Skyrizi exposures in ulcerative colitis from 2024 Thrake (Clin Pharmacol Ther). Steady-state C_{trough} reflects projected values from PK model for ORKA-001 and observed value from Phase 3 trials for Skyrizi in BLA MDR

“KNOCKOUT” IL-23 inhibition could generate off-treatment remissions by depleting pathogenic TRMs

Robust inhibition of IL-23 could create an “immune reset” in PsO

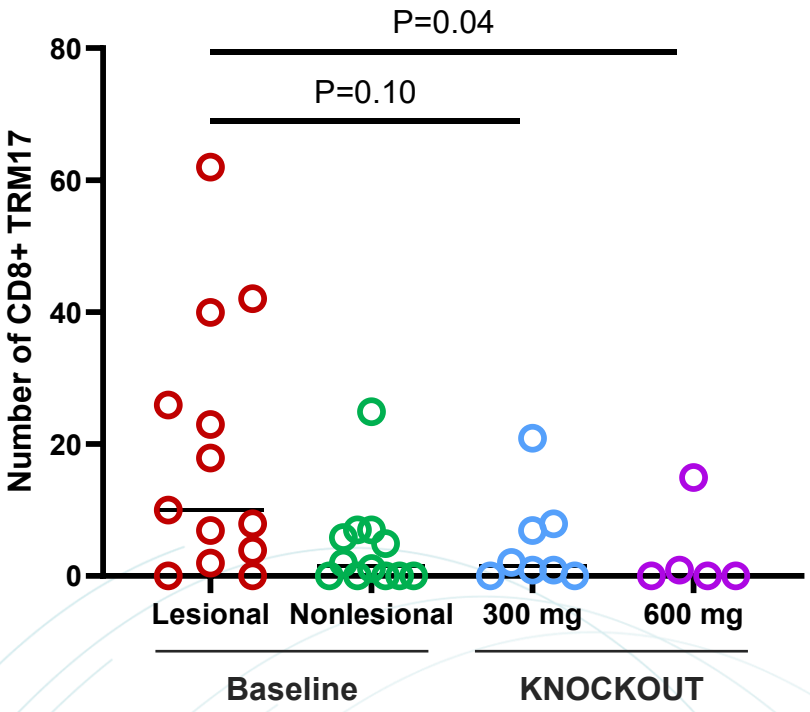


IL-23 drives differentiation of naive T cells into proinflammatory T cells and TRMs

IL-23 maintains TRMs, which react to external triggers to cause PsO recurrence

Inhibition of IL-23 can normalize TRMs in the skin, which could lead to long-term disease control

High anti-IL-23 exposures deplete pathogenic TRMs in the skin



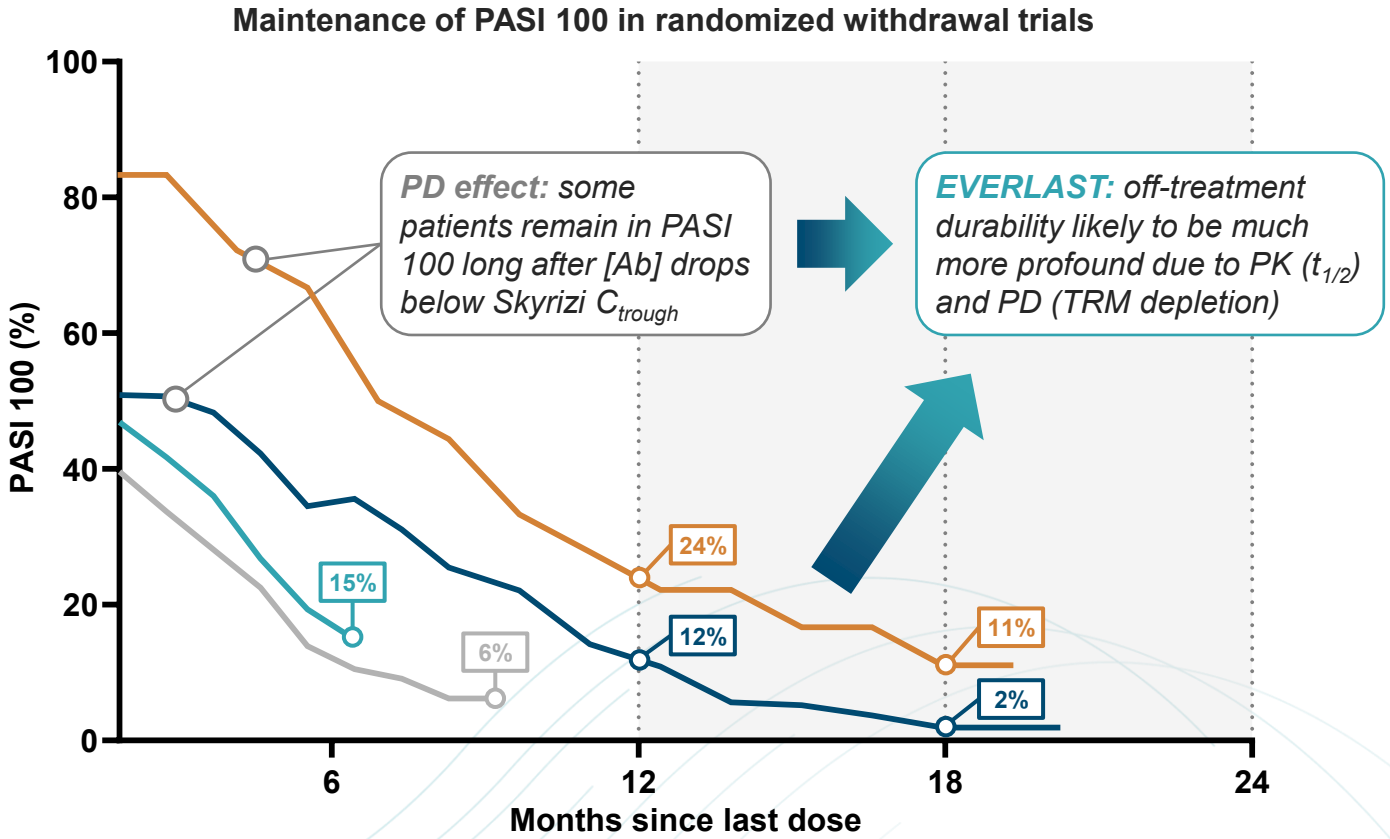
Sources: (left) Figure modified from 2024 Schakel (poster at EADV); (right) 2024 Blauvelt (presentation at G2C)
Abbreviations: TRM, tissue resident memory T cell

EVERLAST could enable compelling rates of “off-treatment remission” for the first time in psoriasis

ORKA-001 could affect the disease biology in a unique way due to optimized exposure and PK…

…potentially resulting in longer-term responses that exceed those seen with prior IL-23 inhibitors

	Dose	Half-life
EVERLAST-A	600 mg	~100d
KNOCKOUT	300-600 mg	28d
Risankizumab	150 mg	28d
Guselkumab	100 mg	17d
Mirikizumab	250 mg	9d



Sources: 2024 Blauvelt (presentation at G2C); 2020 Blauvelt (JAMA Dermatol); 2017 Reich (JAAD); 2022 Blauvelt (Br J Dermatol); FDA Labels

Looking forward to a potential label – illustrating the paradigm-changing potential of ORKA-001

Induction

Induction with ORKA-001 at a dose level selected based on EVERLAST studies

Maintenance

Evaluate at 6 and 12 months after induction dosing to inform whether to give ORKA-001 on one of the following regimens:

- Every 6 months
- Every 12 months
- **For patients in remission, i.e., clear skin beyond 12 months, initiate maintenance dosing only if disease recurs**

Treatment upon recurrence

Administer ORKA-001 as a subcutaneous injection on recurrence based on clinical evaluation using a dosing regimen of either every 6 or 12 months

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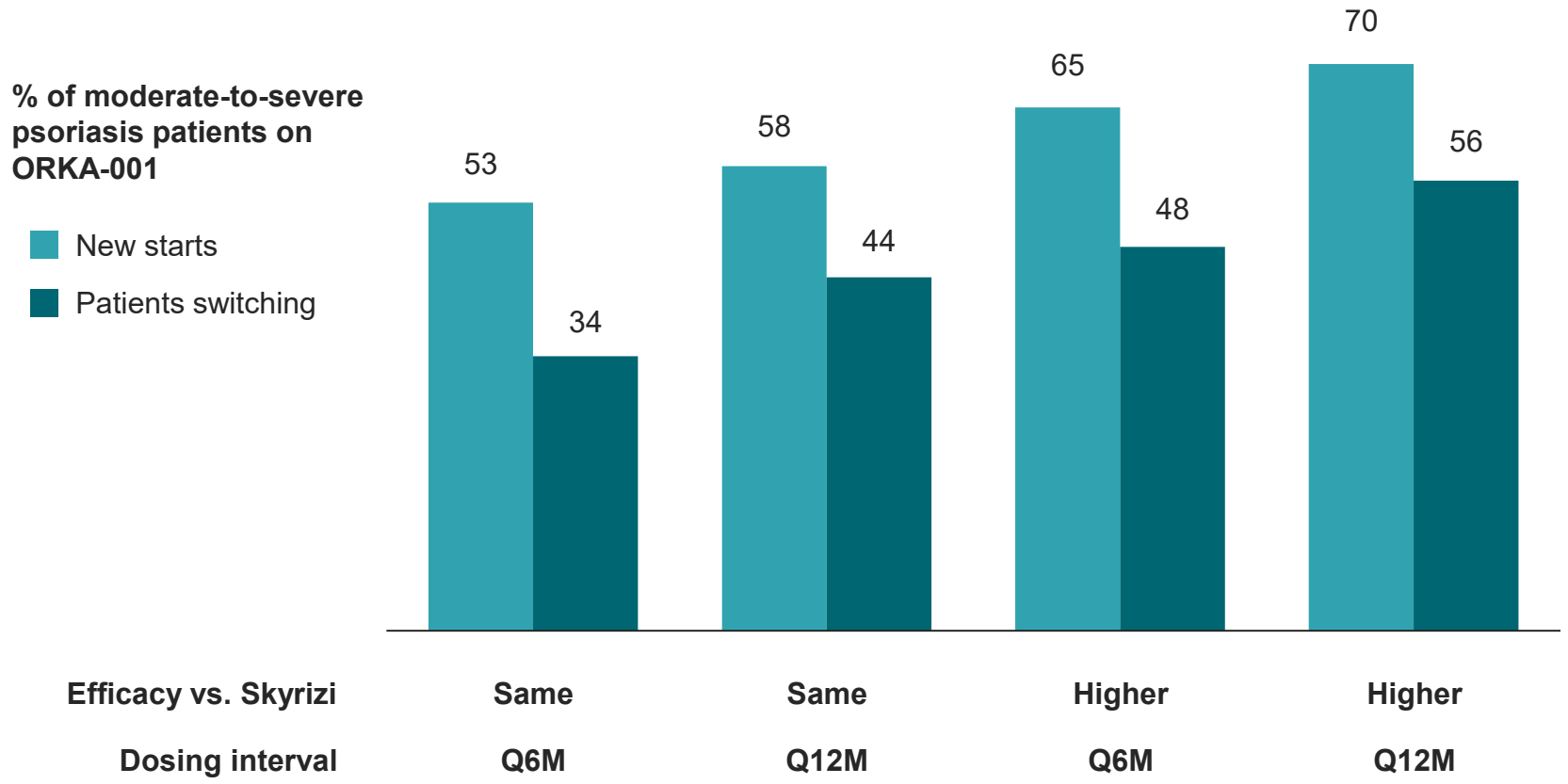
Dermatologists value both extended dosing and higher efficacy

Dermatologists say that annual dosing and higher efficacy would drive similar 50%+ share for ORKA-001, even when accounting for entry of icotrokinra



Sources: Survey of N=22 practicing dermatologists

ORKA-002:
potentially best-in-class anti-IL-17A/F

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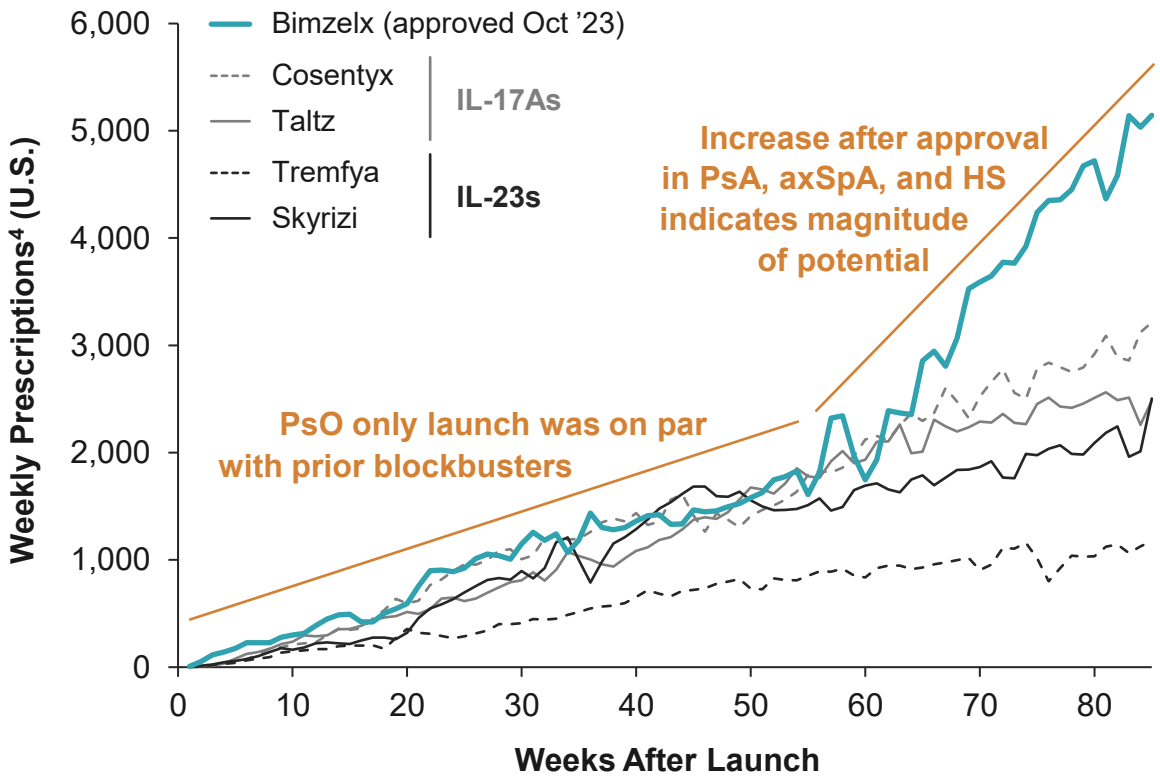
ORKA-002 targets IL-17A/F, a new mega-blockbuster class with an ideal setup for a longer-acting entrant

- **Brand new class –** superior efficacy vs. IL-17A[1] across multiple indications and high levels of skin clearance in IL-17A non-responders[2]
- **Long timeline to biosimilars –** Bimzelx recently approved, and only one other IL-17A/F antibody (sonelokimab) in clinical development
- **Very strong launch –** Bimzelx peak sales estimate now exceeds $5B[3]; strong formulary positioning achieved soon after approval
- **Pipeline-in-a-product expansion potential –** PsA, HS, axSpA, and others

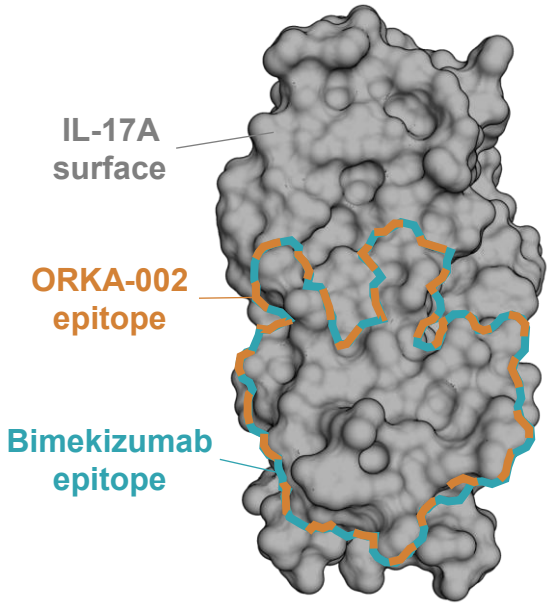
Bimzelx launch validates both the IL-17A/F class and ability to differentiate in PsO



Notes: (1) 2021 Reich (NEJM); (2) 2023 Kokolakis (BJD); (3) Visible Alpha; (4) Jefferies (based on IQVIA data), shown as 2-week moving average
Abbreviations: axSpA, axial spondyloarthritis; HS, hidradenitis suppurativa; PsA, psoriatic arthritis

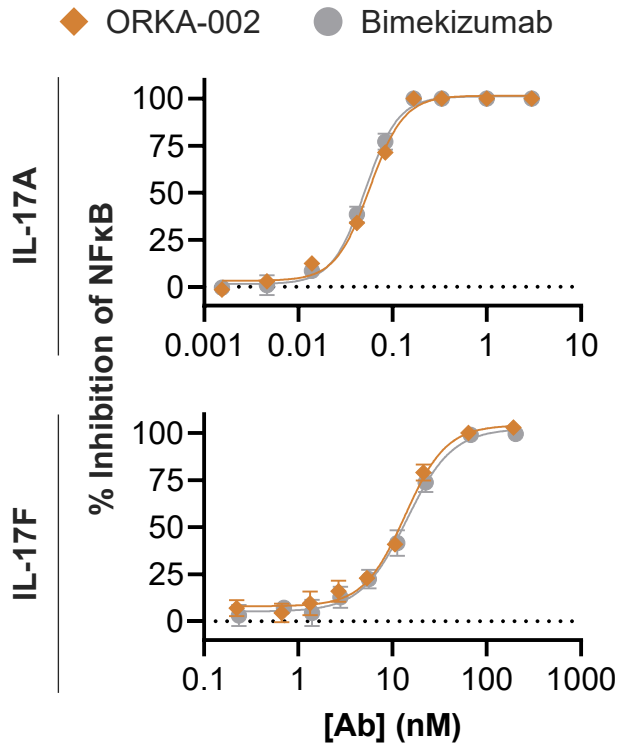
ORKA-002 has a dramatically extended half-life vs. bimekizumab

ORKA-002 binds a similar epitope to bimekizumab with similar potency



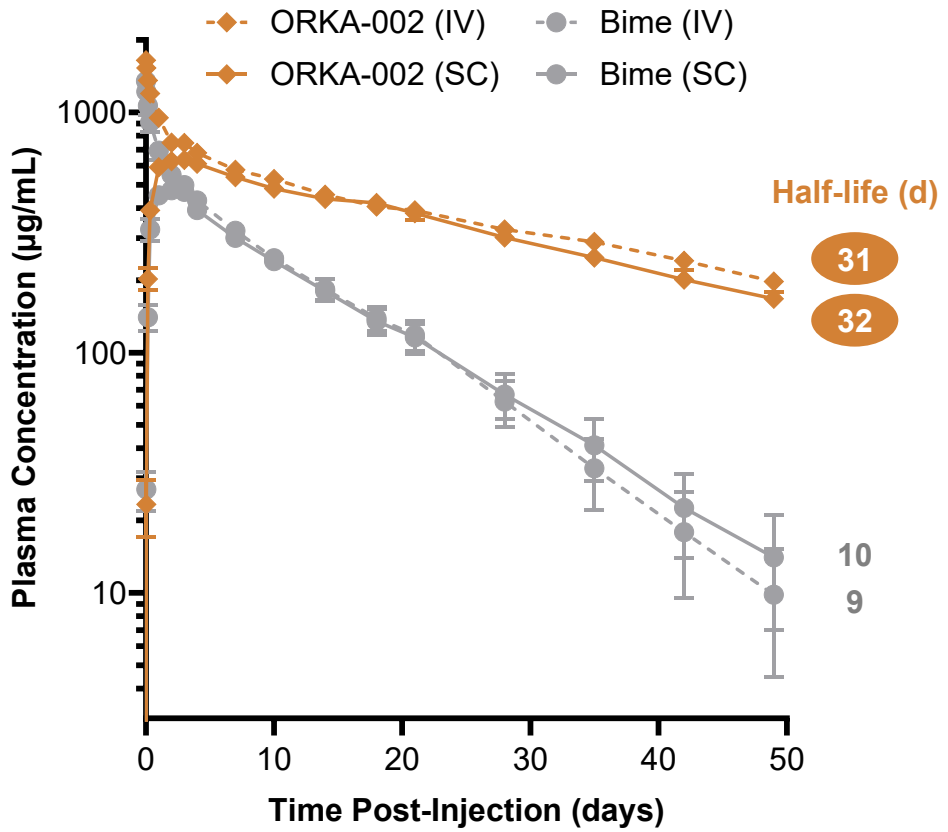
Similar epitope for IL-17F as well

Comparable picomolar affinity for IL-17A and IL-17F



Similar results observed across multiple in vitro *assays*

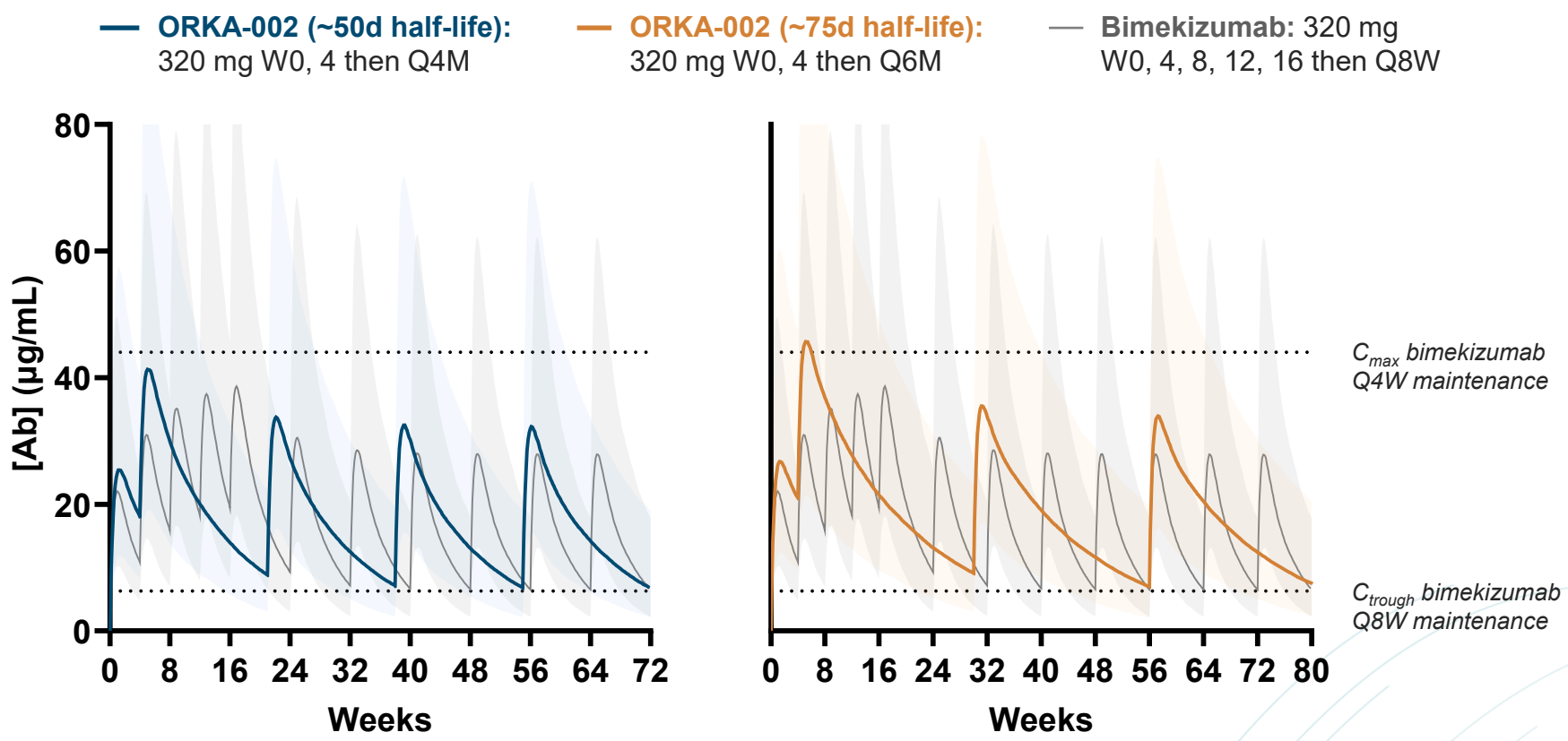
ORKA-002 has a >3x longer half-life than bimekizumab in NHPs



Notes: Presented at AAD 2025

Potential for 2-3 doses per year enabled by half-life extension

Projected C_{trough} of illustrative ORKA-002 regimens exceeds approved bimekizumab regimen in PsO



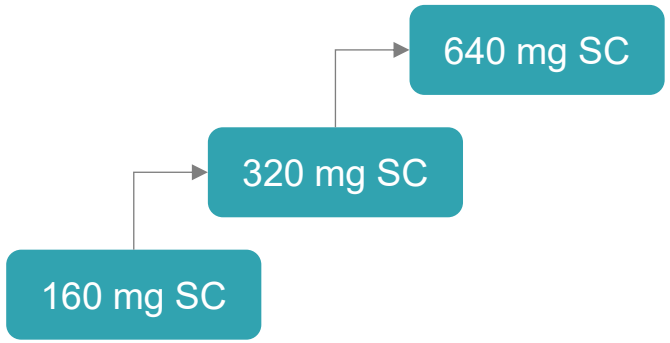
A ~50-day half-life could enable Q4M dosing and **~75-day half-life could enable Q6M dosing** while maintaining trough antibody levels above bimekizumab

Notes: Presented at AAD 2025; bimekizumab modeling, C_{max}, and C_{trough} based on published population PK parameters from FDA and EMA review documents; error bars represent 5th and 95th percentiles

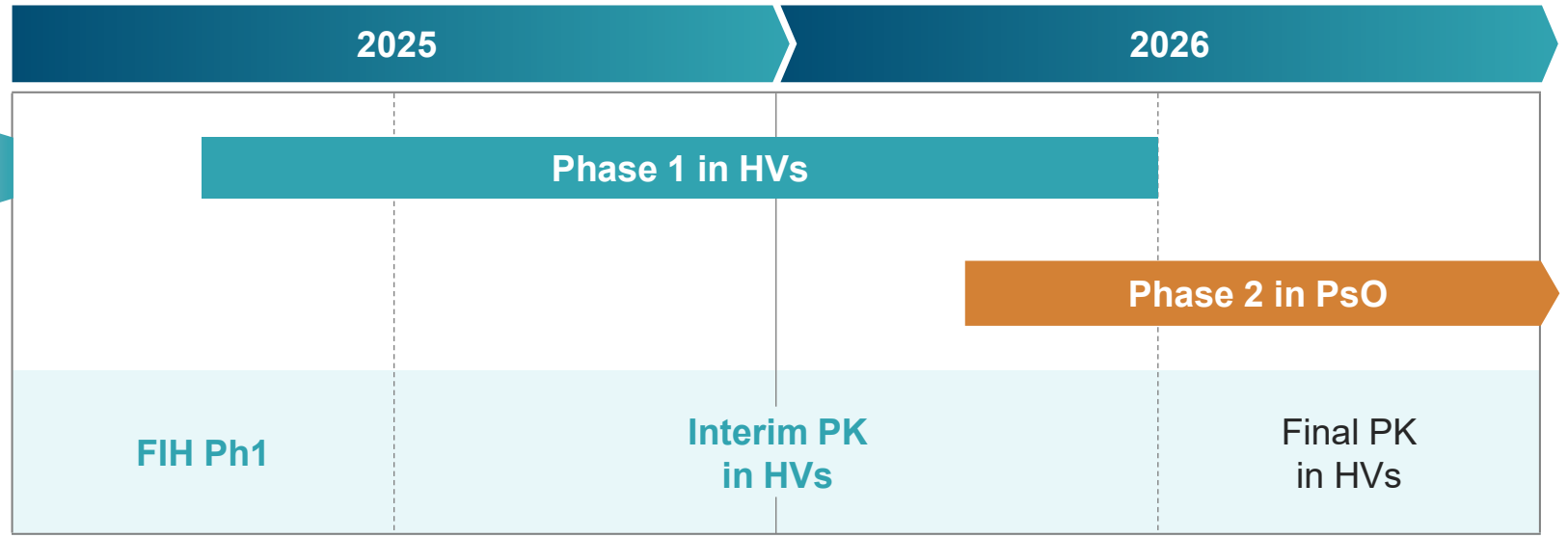
ORKA-002 is advancing just ~6 months behind ORKA-001

Phase 1 study to evaluate the safety, tolerability, and PK of ORKA-002 in healthy participants

- Placebo-controlled, single ascending dose study (NCT06944379)



- Conducted at a single center in New Zealand
- ~24 healthy volunteers



- **Ph1 interim PK is highly validating,** showing both basis for differentiation and early safety
- **Ph2 in PsO can provide robust efficacy data quickly,** supporting ORKA-002 as the best-in-class IL-17
- **Rapid expansion into additional large indications with validated IL-17A/F efficacy,** e.g., PsA, HS

Abbreviations: HS, hidradenitis suppurativa; PsA, psoriatic arthritis; SC, subcutaneous

ORKA-021

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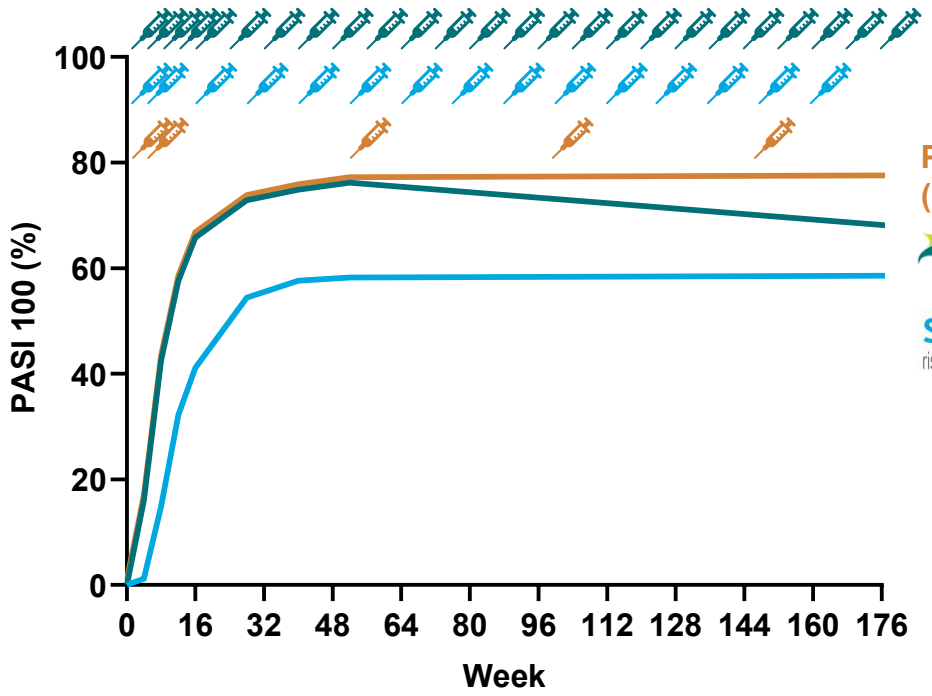
ORKA-021: Potential to combine the best of IL-17s and IL-23s

IL-17s: fastest onset and highest peak response + **IL-23s: less frequent dosing and best durability and safety**

Combining the two mechanisms sequentially could provide the "best of both worlds"



Possible with ORKA-021 (ORKA-002 → ORKA-001)

Bimzelx® (bimekizumab-bkzx)

Skyrizi® risankizumab-rzaa

Feedback from U.S. dermatologists:

*"It really sounds like a **great option**"*

*"**Conceptually beautiful**"*

*"The only reason this hasn't been done is that **no company has both**"*

Sources: Long-term efficacy from BE BRIGHT (Bimzelx) and LIMMitless (Skyrizi) open-label extension trials

Four ways to deliver a best-in-class regimen for psoriatic disease

- **Once yearly dosing** and **off-treatment remissions** go beyond convenience to **change the treatment paradigm**


ORKA-001

- Clinical precedent supports potential for **best efficacy** in the IL-23 class


ORKA-001

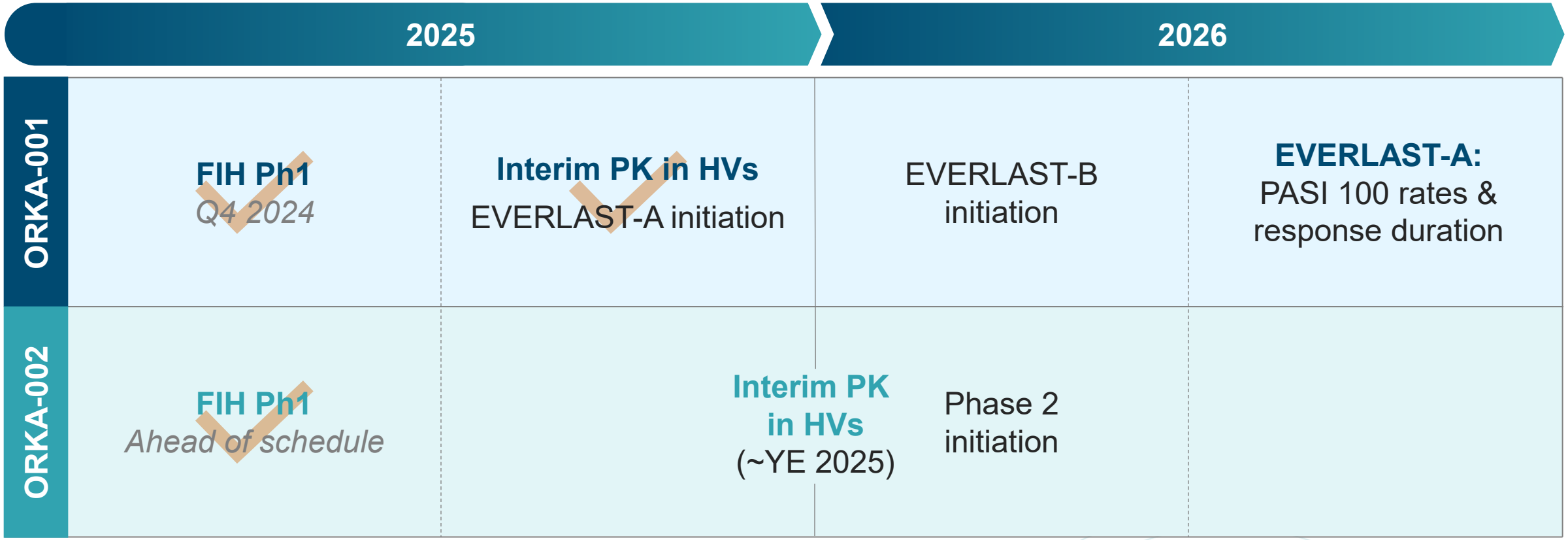
- Only long-acting IL-17A/F in a **brand-new, mega-blockbuster class** with **a long timeline to biosimilars** and **indication expansion potential**


ORKA-002

- Straightforward path to a potential H2H win – **faster and deeper responses** vs. Skyrizi and **superior maintenance profile** vs. Bimzelx


ORKA-021

Advancing co-leads rapidly towards multiple clinical data catalysts



Strong cash position provides runway >1 year beyond three major readouts:
EVERLAST-A Ph2a in 2H 2026, EVERLAST-B Ph2b in 2027, and ORKA-002 Ph2 in 2027

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Shares outstanding

As of September 30, 2025		Number of shares[1]
Common stock	• Shares outstanding	48.4M
Common stock equivalents	• Preferred stock (as-converted to common stock)	11.4M
	• Pre-funded warrants	7.3M
Common stock and common stock equivalents	• **Total outstanding[2]**	**67.1M**

Notes: Please refer to SEC filings for additional information. (1) Shown on an as-converted-to-common basis; (2) Excludes stock options and warrants held by employees, directors, and service providers