ORUKA THERAPEUTICS

Corporate Overview

NASDAQ: ORKA

September 2024

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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, half-life extended monoclonal antibodies** targeting mechanisms with **proven efficacy and safety**

PROGRAM	DISCOVERY	IND-ENABLING	CLINICAL	POTENTIAL INDICATIONS
ORKA-001	IL-23p19		**FIH 1Q25** **HV PK 2H25**	Psoriasis
ORKA-002	IL-17A/F		**FIH 3Q25**	Psoriasis, psoriatic arthritis, others
ORKA-003	Undisclosed			

Rights to development candidates acquired from Paragon Therapeutics, the source of the technology behind Apogee and Spyre

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Notes: Oruka has an option to acquire exclusive worldwide rights from Paragon Therapeutics, Inc., for all programs, with IL-23 rights for all therapeutic indications outside of IBD. Abbreviations: FIH, first-in-human dosing; HV, healthy volunteer; PK, pharmacokinetics

Psoriasis is the ideal indication space for our strategy

Large, well-validated market with proven ability for differentiated new entrants to gain share

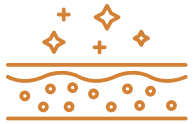
Best targets established with IL-23p19 and IL-17A/F – unlikely that new mechanisms can improve on the standard of care

Physicians want new and better biologics – the field has focused on orals, but they have consistently fallen short of biologic efficacy

Extensive clinical precedent exists from prior programs to inform development of an optimal biologic

ORKA-001 and ORKA-002 complement each other

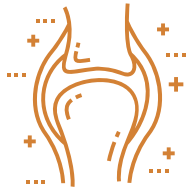
ORKA-001



For patients with purely skin disease

Majority of dermatologists prefer an anti-IL-23p19

ORKA-002

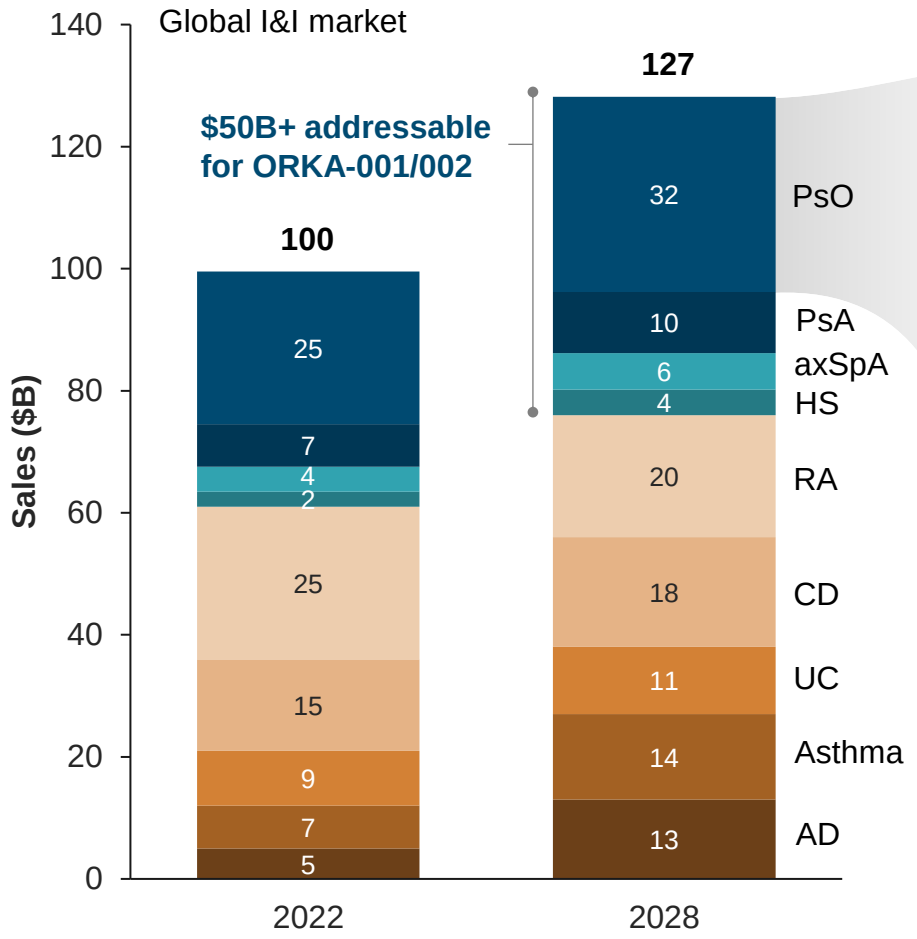


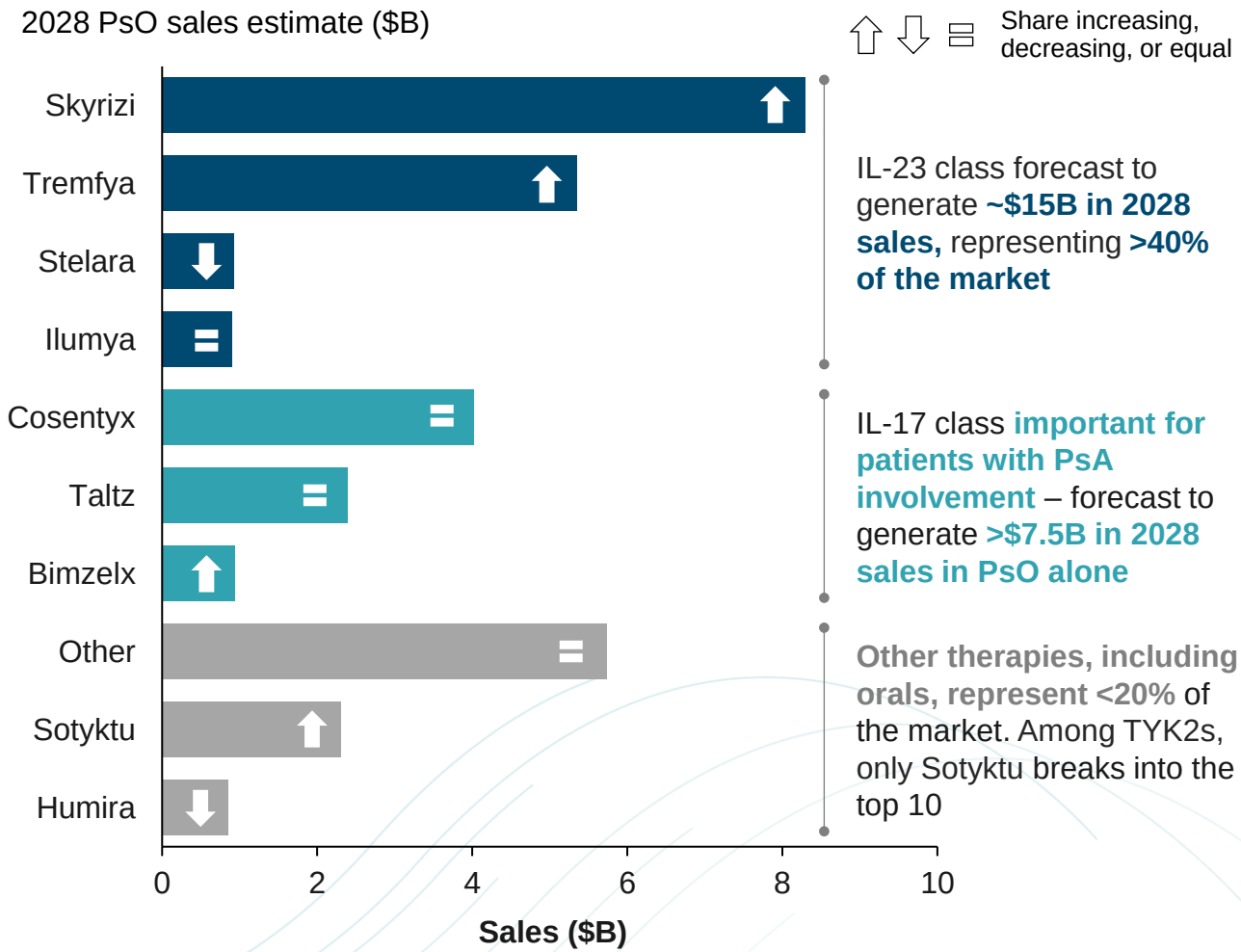
For patients with joint involvement, including PsA, or recalcitrant skin disease

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

Our programs target a $50B+ total market opportunity

ORKA-001/002 target the dominant mechanisms in the largest I&I market





Notes: Asthma sales represent biologic treatments only
Sources: EvaluatePharma; GlobalData; Barclays; TD Cowen; Oruka analysis

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

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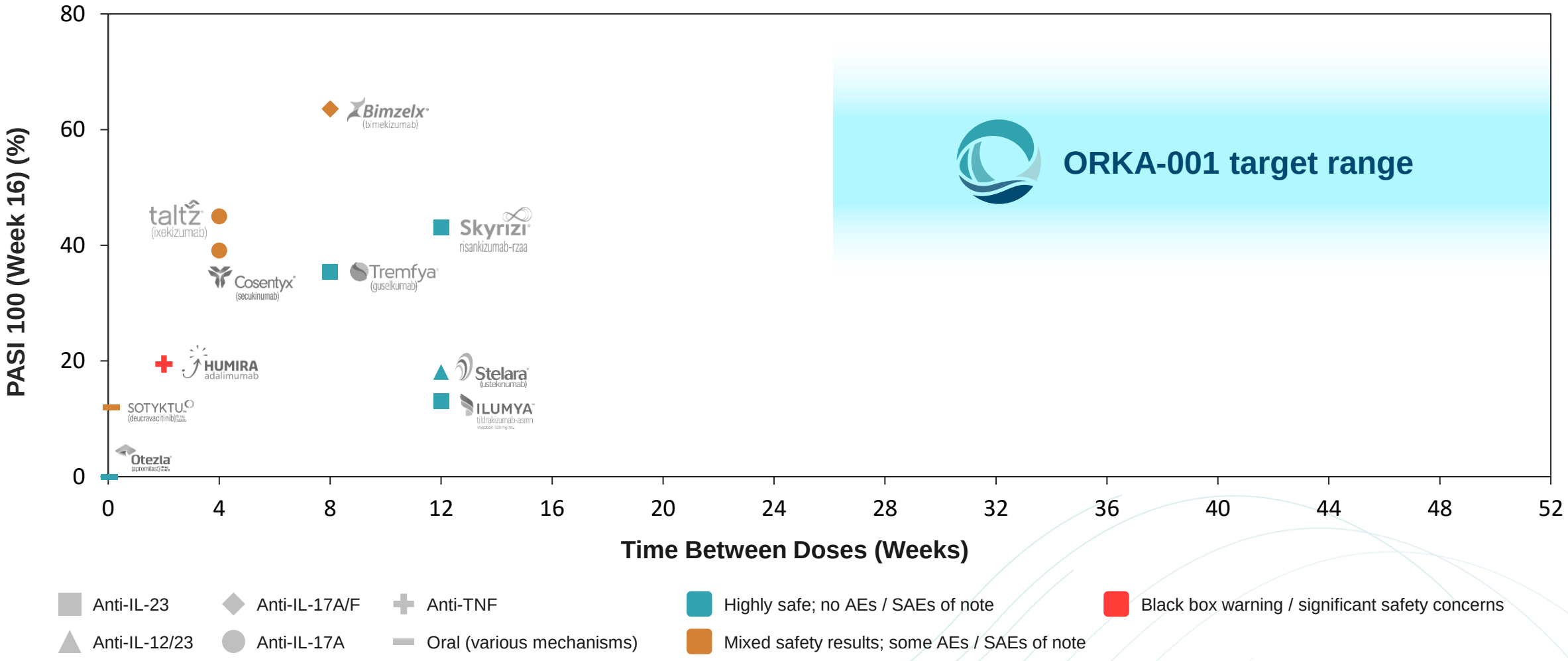
Biologics have raised the bar on standard of care in PsO, but there is ample room for improvement



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)

Base case is best-in-class, upside could be paradigm changing

	Base case scenario	Upside scenario
Dosing interval	**Once per six months**	**Once per year** and/or **patient-specific**
Efficacy	**Comparable PASI 100 to Skyrizi**	**Better PASI 100 than Skyrizi**
	Best-in-class profile	*Paradigm-changing*

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

Binds similar epitope to Skyrizi (risankizumab) with similar potency

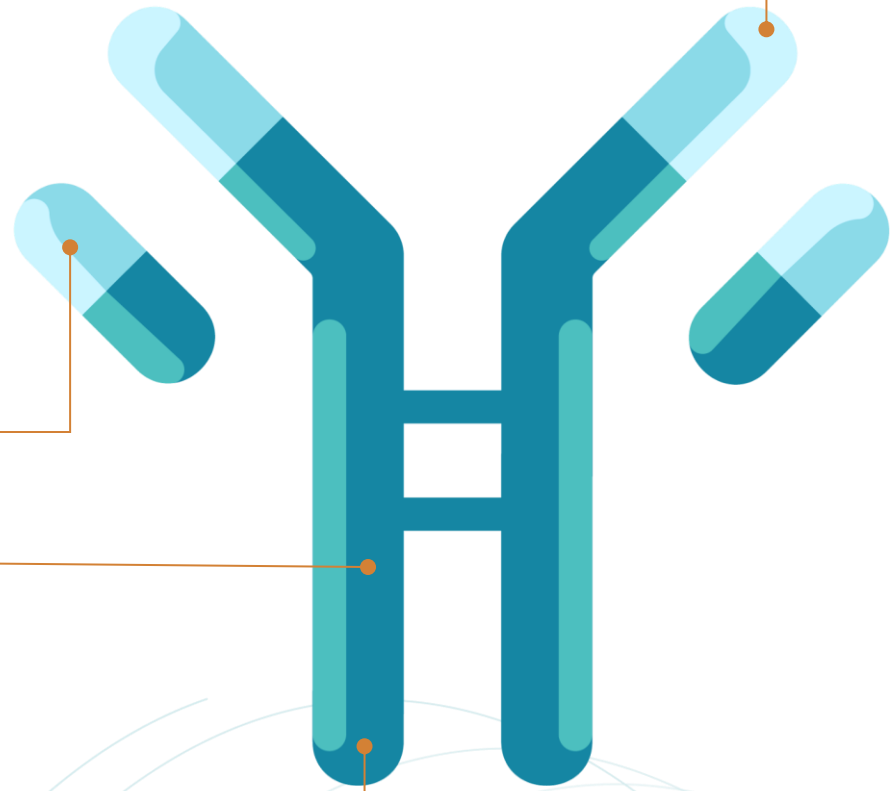
- Validated mechanism of action
- **Specific for IL-23p19** (not IL-12/23 p40)
- **K_D < 5 pM**
- Predicted **equivalent safety**
- Predicted to **meet or beat efficacy**

Novel IP for composition of matter into 2040s

Half-life extension through validated Fc modification (YTE mutations)

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

Effector-null human IgG1 Fc



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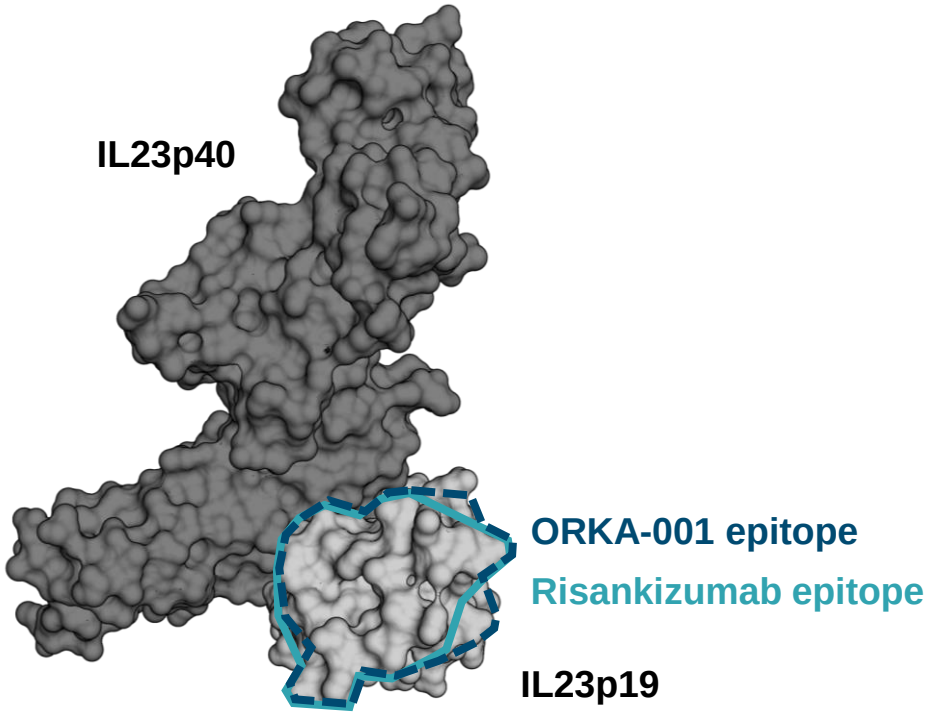
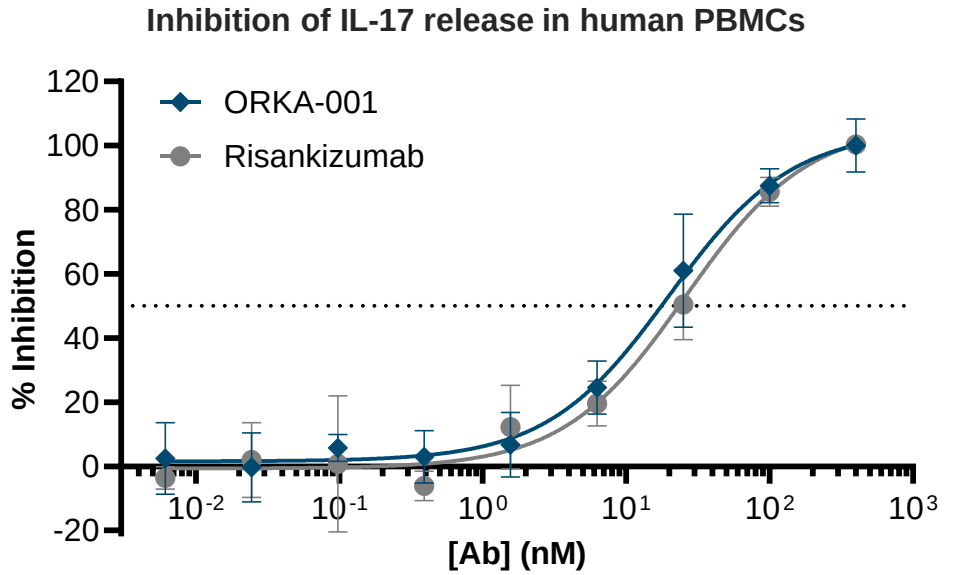
Notes: Oruka holds worldwide rights to all therapeutic indications outside of IBD

ORKA-001 binds a similar epitope as risa with similar potency

ORKA-001 binds a nearly identical epitope to risankizumab



ORKA-001 shows comparable potency to risankizumab



	ORKA-001	Risankizumab	Guselkumab
Relative IC50	0.76	1.0	4.83

Comparable affinity (<5 pM) as well

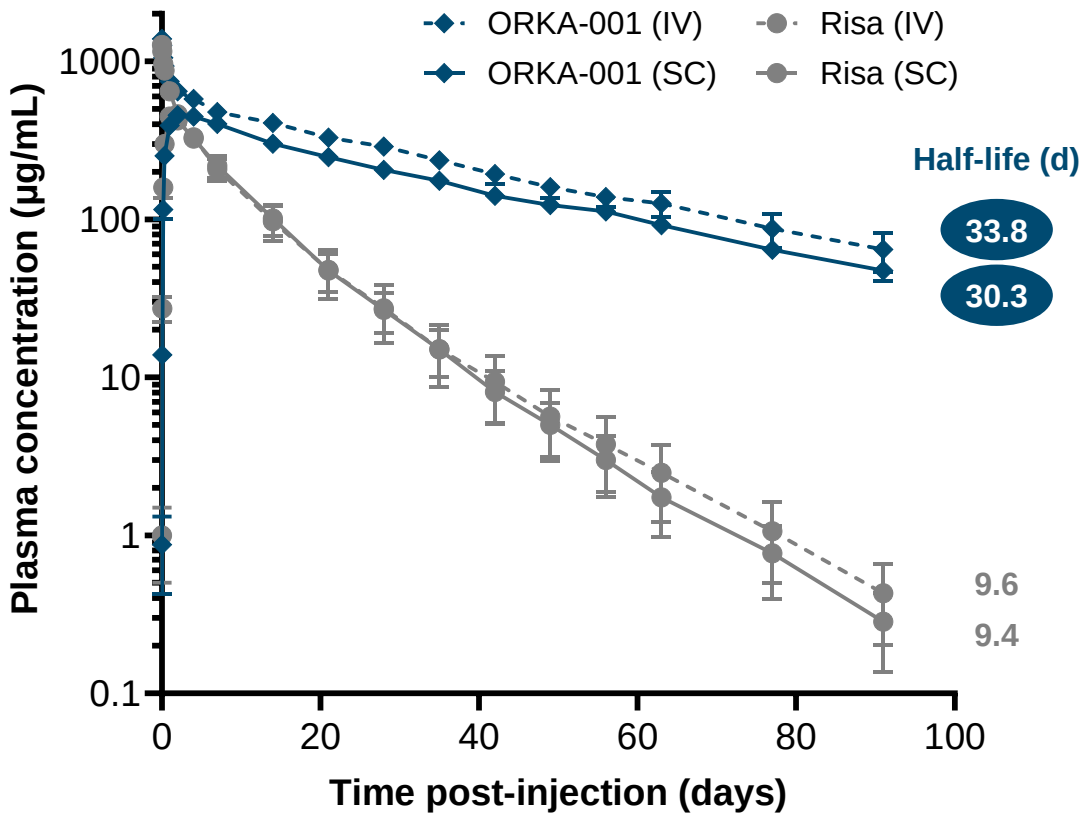
Similar results observed across a range of* in vitro *assays

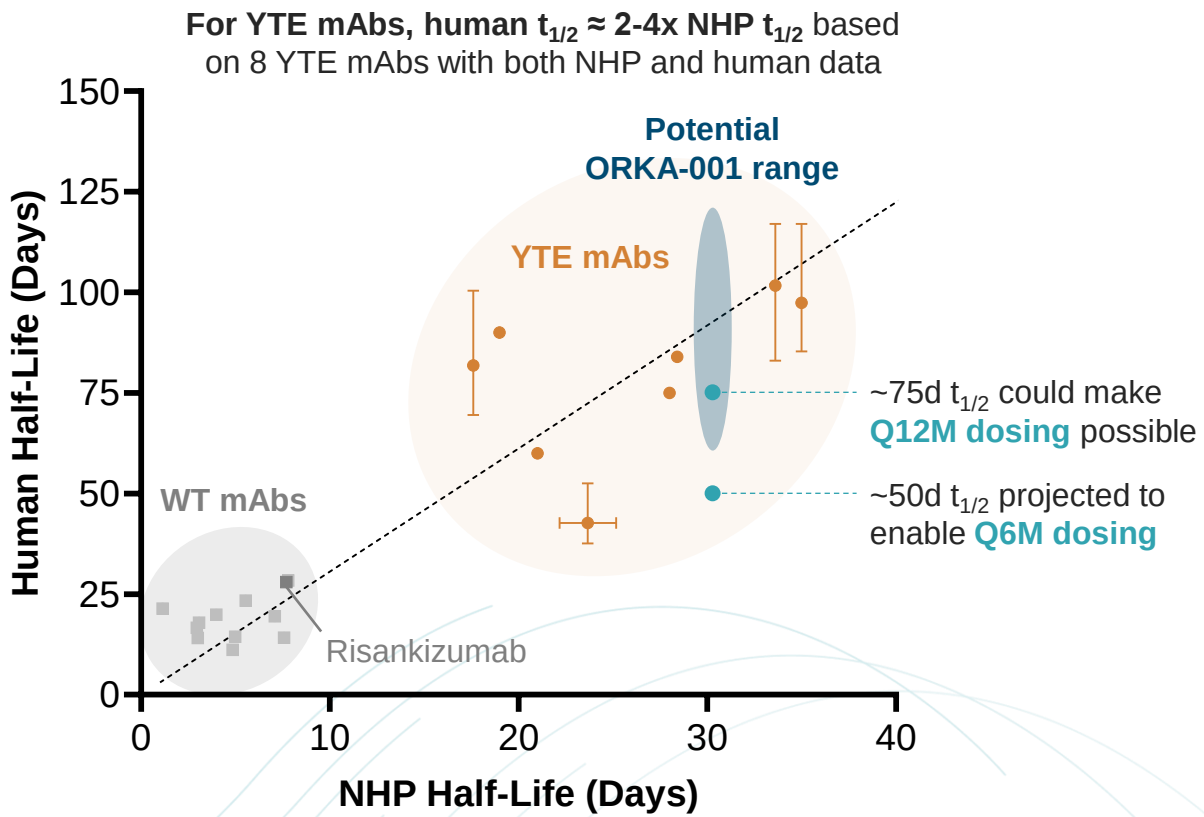
Notes: Presented at EADV 2024

Clinical experience with YTE predicts significant $t_{1/2}$ extension

ORKA-001 has a >3x longer half-life than risankizumab in NHPs

Implies ORKA-001 could have a significantly longer half-life in humans



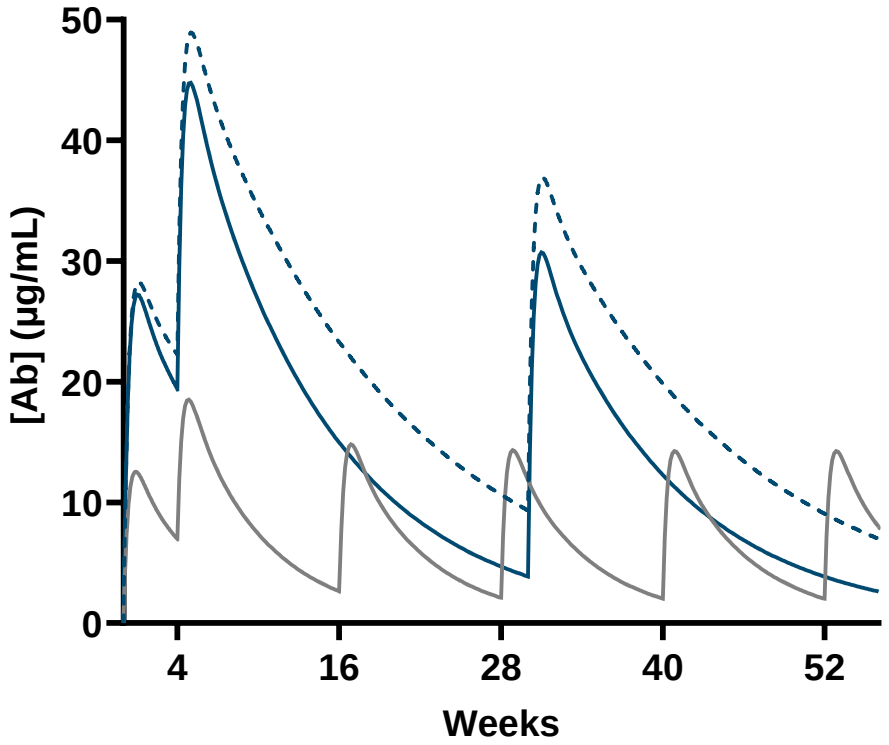


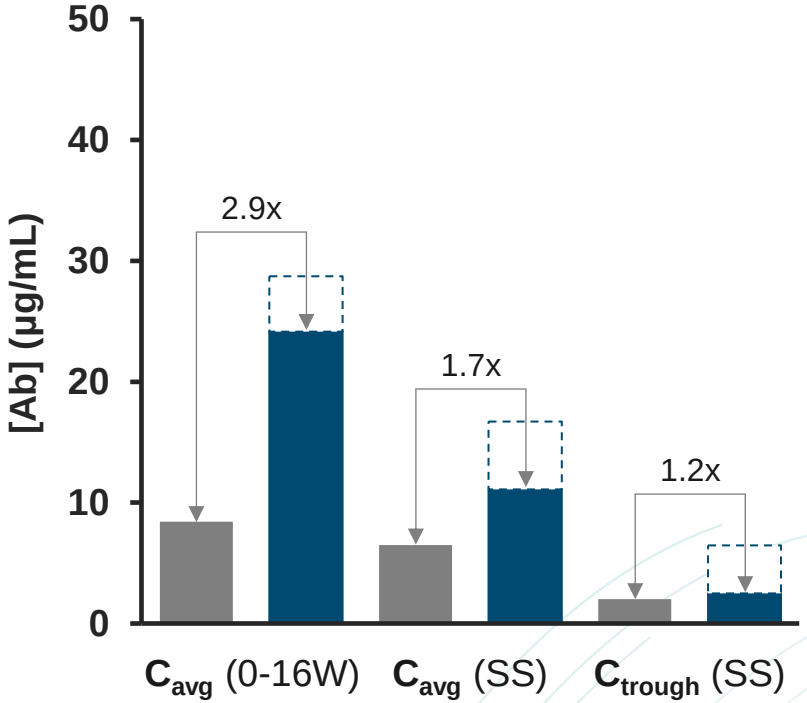
Notes & Sources: (left) Presented at EADV 2024; NHP datapoints associated with ADA excluded from analysis. (right) Sources on file for other wildtype (WT) and YTE mAbs; Skyrizi BLA review notes a ~7.2- to 7.7-day half-life in NHPs, which translated to ~28-day half-life in humans

Base case is achievable even at lower end of predicted half-life

ORKA-001 exposure could exceed SKYRIZI under a variety of half-life scenarios

— **ORKA-001 (~50d half-life):** 300 mg W0, 4, Q6M
--- **ORKA-001 (~75d half-life):** 300 mg W0, 4, Q6M
— **Skyrizi:** 150 mg W0, 4, Q12W (approved regimen)





Even at a 50-day half-life, Q6M dosing with ORKA-001 is projected to give a significantly higher C_{avg} and C_{trough} than Skyrizi

Notes & Sources: Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi; steady-state (SS) C_{avg} and C_{trough} projected using the dosing interval ending at W160

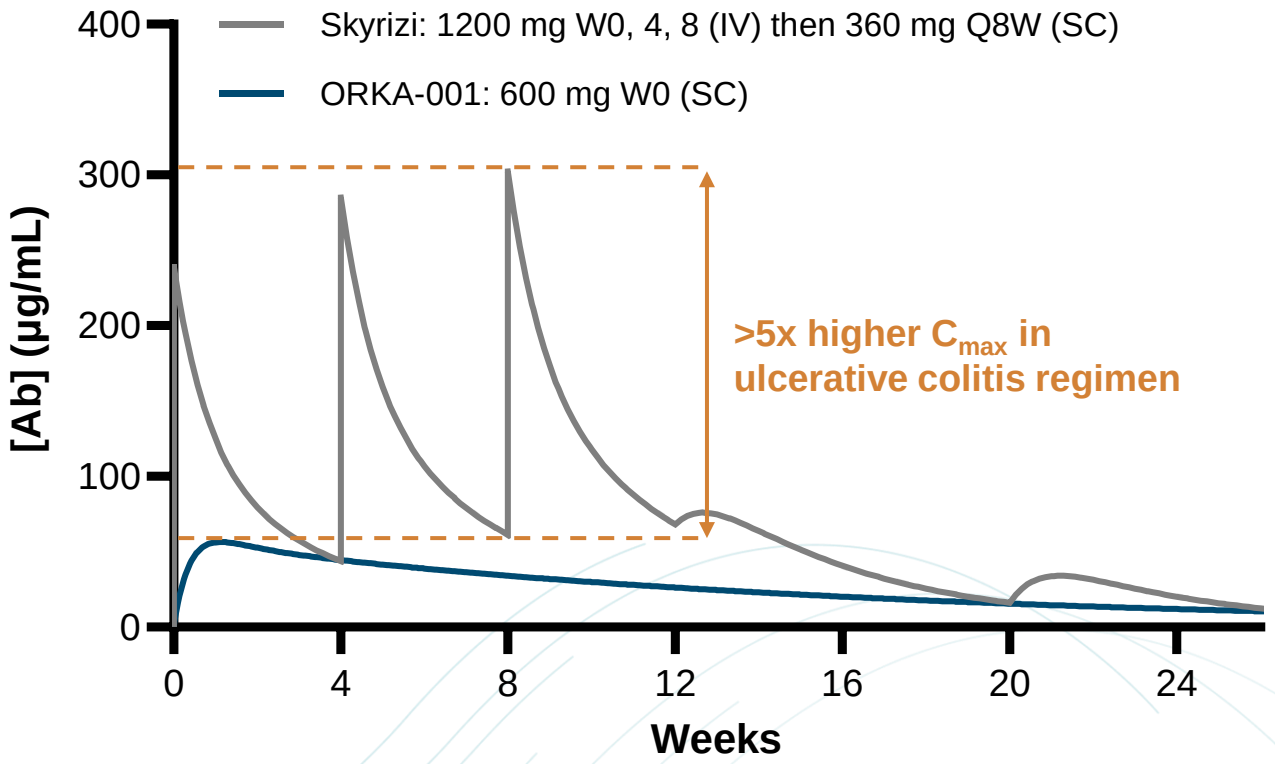
ORKA-001 benefits from a large body of clinical evidence with IL-23 inhibition

Very uncommon to have clinical precedent in large numbers of patients for the safety of higher exposures

- Peak and average exposures of ORKA-001 dosed at 600 mg are **multiples lower** than those with approved Skyrizi regimens in IBD
- No correlations observed at the patient level between exposure and safety signals **across >4,000 patients dosed** with Skyrizi in clinical trials

All five IL-23p19 inhibitors with published data in psoriasis have performed as expected based on their biophysical properties

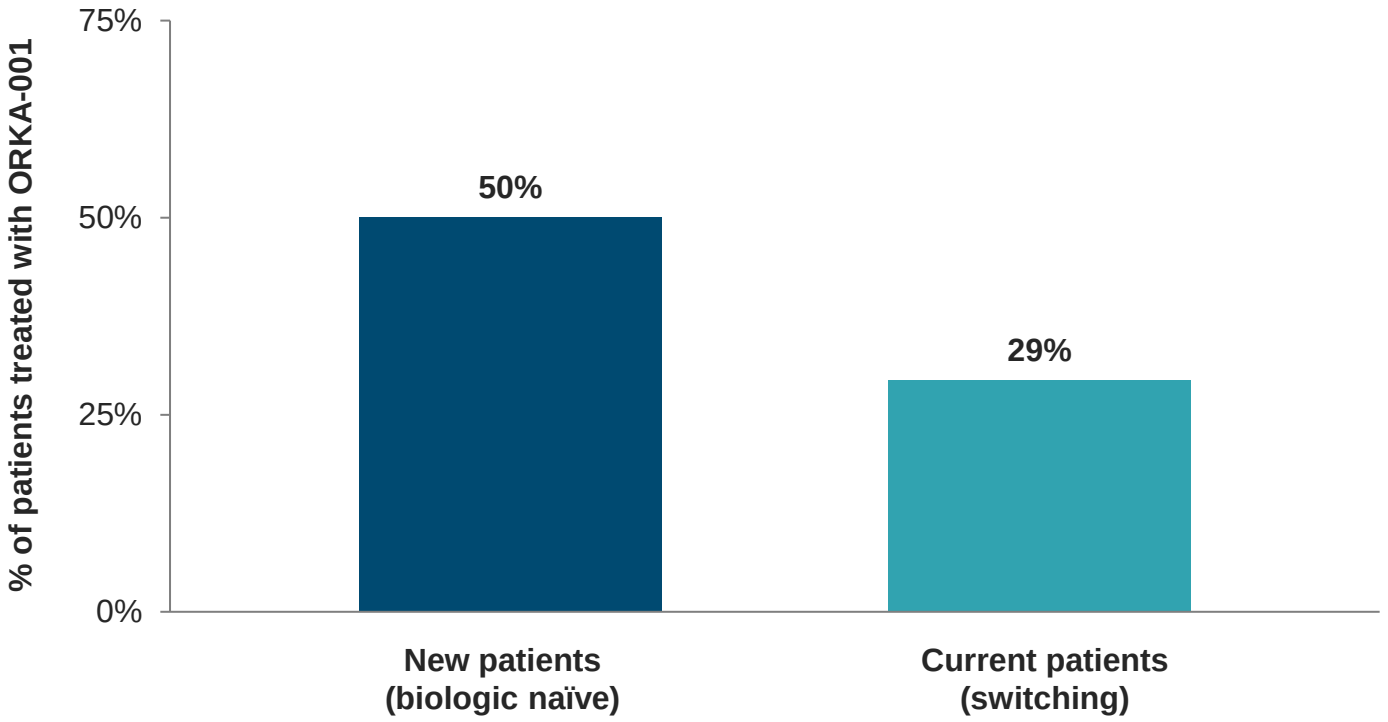
Skyrizi regimen in UC establishes the safety of very high exposures



Notes & Sources: Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi; modeled Skyrizi exposure reflects approved regimen in ulcerative colitis; 2019 Khatri (Clin Pharmacol Ther); 2022 Thrake (Rheumatol Ther); 2022 Suleiman (Clin Pharmacol Ther); 2024 Thrake (Clin Pharmacol Ther)

Dermatologists view the “base case” as highly attractive

In the “base case,” dermatologists would put half of new patients on ORKA-001 even when accounting for entry of new oral medicines



Multiple examples support dosing as a major commercial differentiator:

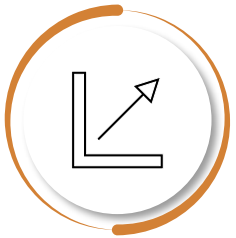
PsO	Skyrizi (risankizumab-rzaa) *Q12W*	**vs.**	Tremfya (guselkumab) *Q8W*
Asthma	Fasenra (benralizumab) *Q8W*	**vs.**	Nucala (mepolizumab) *Q4W*
wAMD	EYLEA (aflibercept) Injection *Q8W*	**vs.**	LUCENTIS RANIBIZUMAB *Q4W*

Increasing excitement about drugs with long dosing intervals:

- Positive Phase 3 results for depemokimab (GSK), ocrelizumab (Roche), lenacapavir (Gilead), all given twice-yearly
- GSK acquired Aiolos for a long-acting YTE mAb targeting TSLP

Sources: Weighted average of multiple independent surveys; N=32 practicing dermatologists for question on new patients; N=90 practicing dermatologists for question on current patients. Abbreviations: wAMD, wet age-related macular degeneration

Three potential upside scenarios for ORKA-001

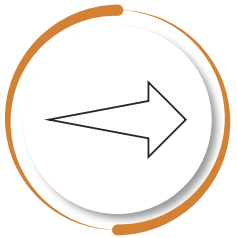


Superior efficacy

Higher exposure could drive higher PASI 100

1-year dosing interval

Enabled by half-life extension



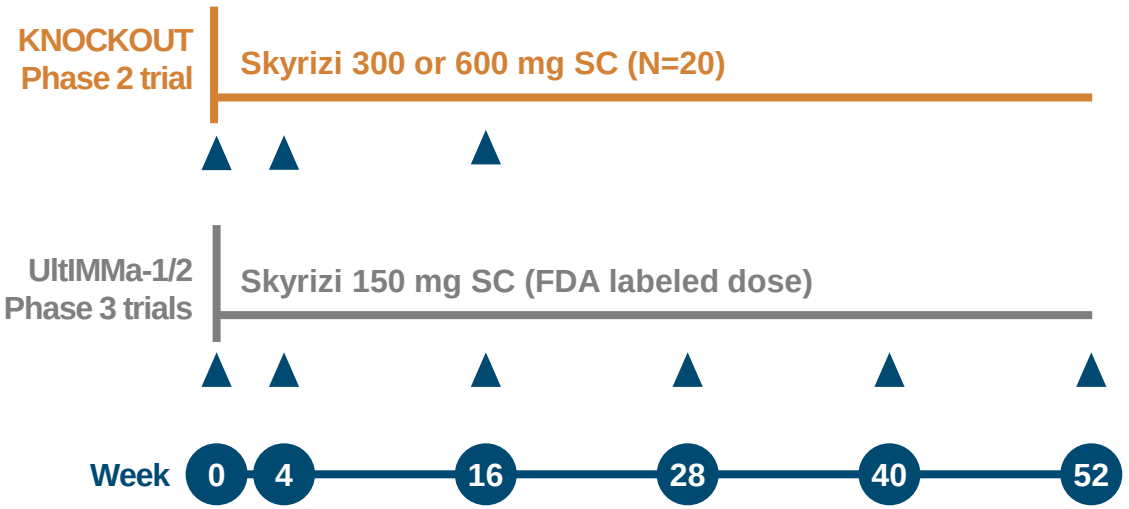
Disease modification

Patient-specific dosing to allow for treatment-free remissions

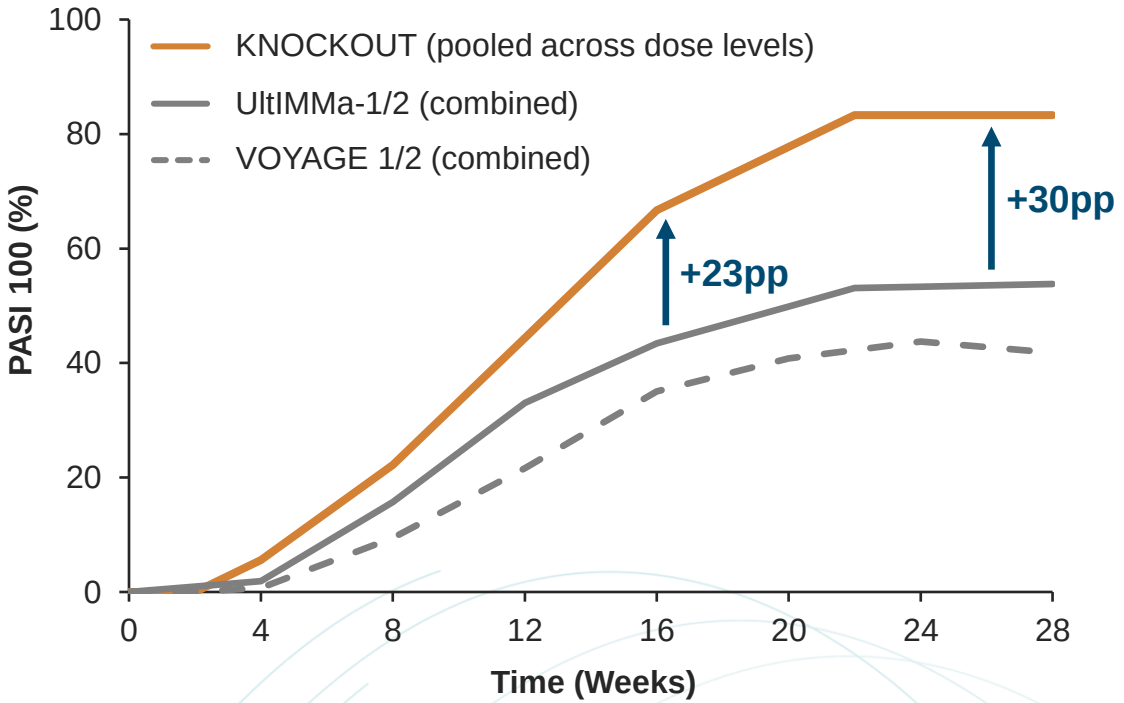
Higher exposures drove higher efficacy in KNOCKOUT study

KNOCKOUT evaluated 2-4x the approved Skyrizi dose…

Screening	Double-blind dosing (W0-16)	Double-blind follow-up (W16-52)



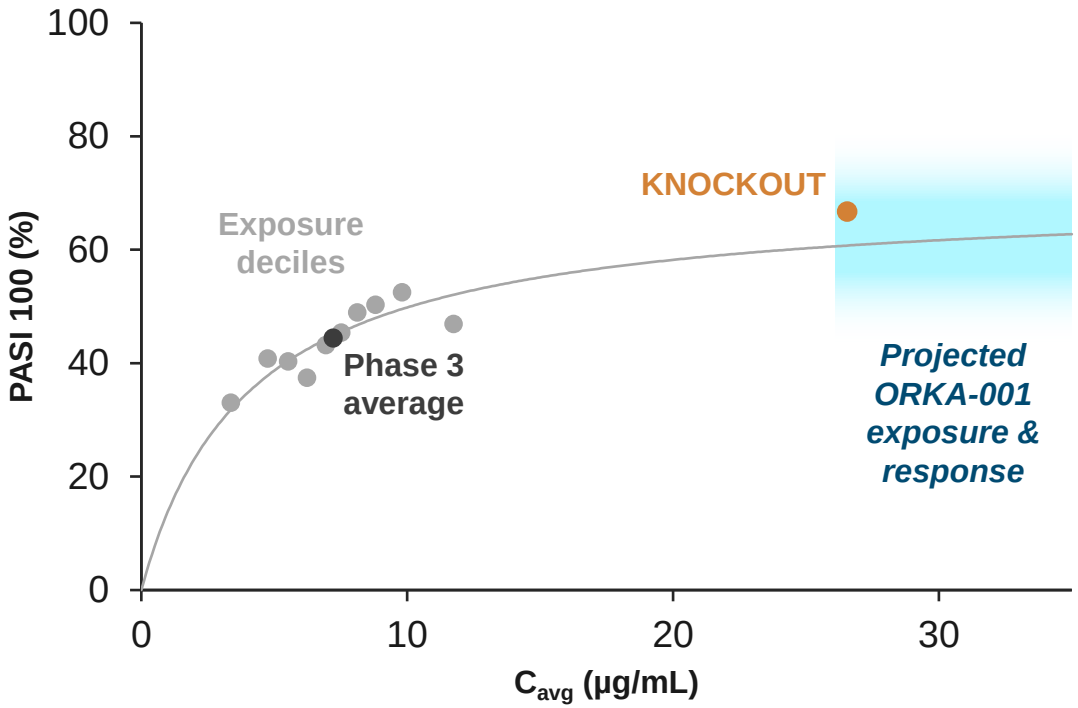
…and resulted in the highest PASI 100 rates observed to date



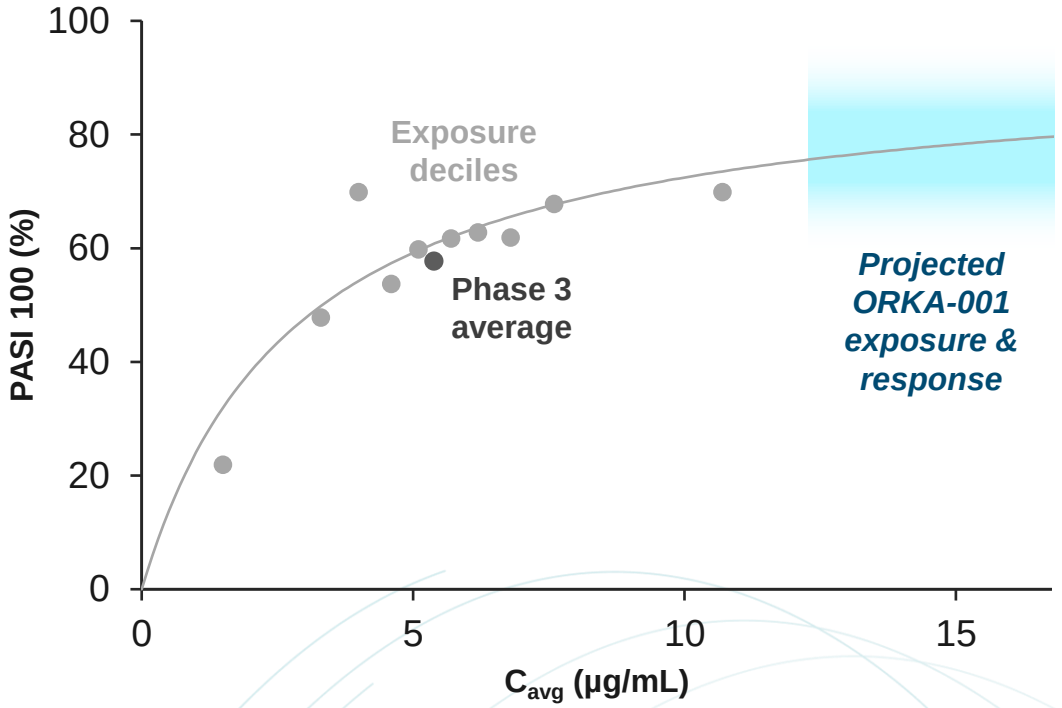
Notes: Cross-trial comparisons. Not placebo controlled. VOYAGE 1/2 Phase 3 trials tested Tremfya at 100 mg SC (W0, 4, Q8W) (FDA labeled dose)
Sources: 2017 Blauvelt (JAAD); 2017 Reich (JAAD); 2018 Gordon (Lancet); 2023 Blauvelt (WCD presentation)

ORKA-001 could drive higher efficacy based on KNOCKOUT and a consistent exposure-response trend across trials

Induction phase (0-16 weeks)

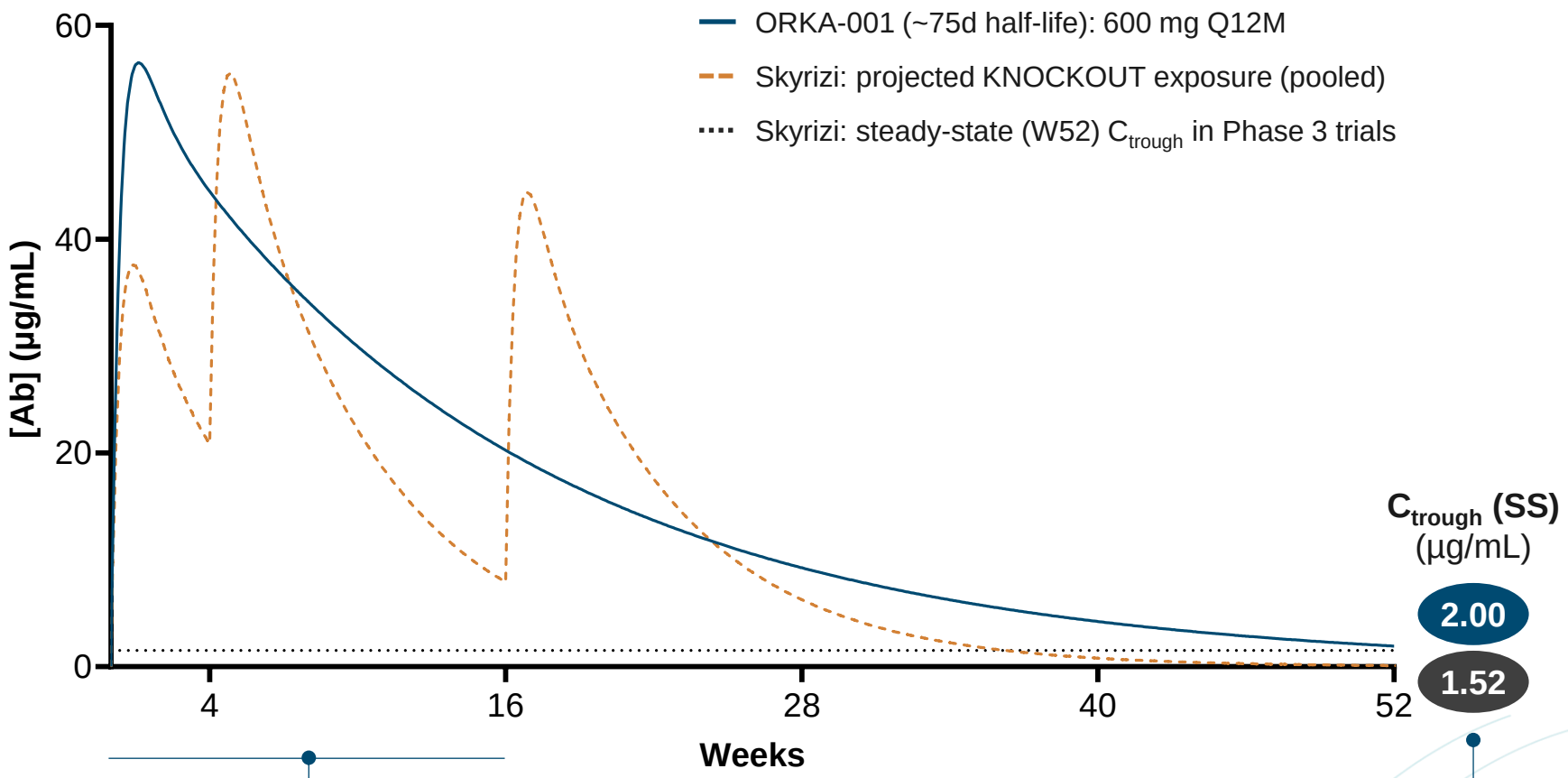


Steady-state phase (40-52 weeks)



Notes & Sources: Adapted from 2019 Khatri (Clin Pharmacol Ther) and Skyrizi BLA Multi-disciplinary Review (Fig. 20); KNOCKOUT pooled PASI 100 from 2023 Blauvelt (WCD presentation); gray dots represent observed PASI 100 rates within each C_{avg} decile for Skyrizi; gray lines represent model-estimated probabilities for PASI 100 for Skyrizi derived from Khatri; for induction phase (0-16 weeks), model-estimated probabilities reflect all patients, and do not exclude Asian ethnicity

KNOCKOUT-like exposures are possible with one dose per year



With a ~75-day half-life, ORKA-001 at one dose per year could match or exceed both KNOCKOUT early exposures and steady-state trough levels of standard Skyrizi dosing

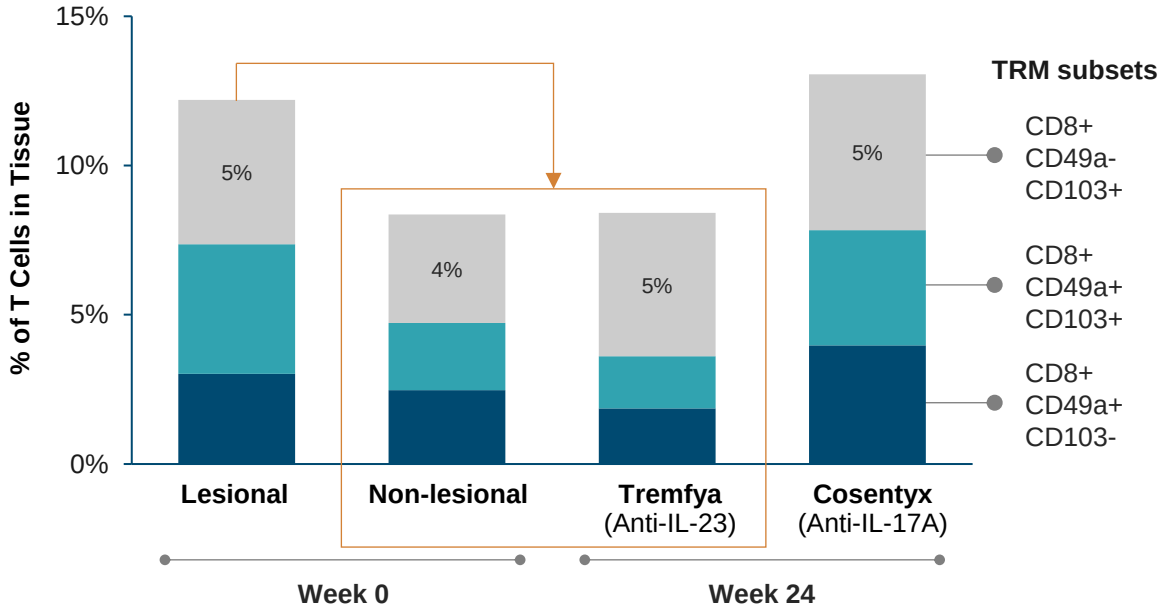
Comparable or greater early exposure vs. KNOCKOUT

Comparable or greater steady-state C_{trough} vs. Skyrizi

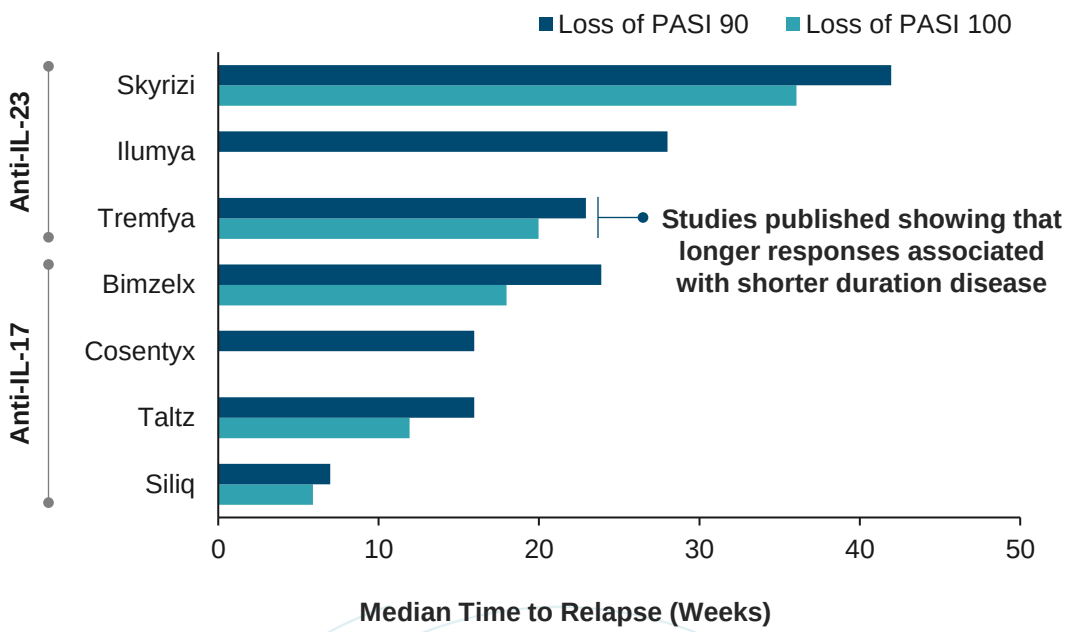
Notes & Sources: KNOCKOUT and ORKA-001 exposure from Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi; ORKA-001 steady-state (SS) C_{trough} projected using the dosing interval ending at W156; Skyrizi C_{trough} at W52 from BLA Multi-disciplinary Review

Potential for disease modification or cure by depleting TRMs

Anti-IL-23 acts upstream of disease-causing TRMs, and has a unique ability to deplete them from tissue



Leading to long-lasting remissions after treatment withdrawal – pointing to possibility of disease modification



Excitement growing in dermatology community to **test disease modification potential of high anti-IL-23** exposures early in disease – **a perfect opportunity for ORKA-001**

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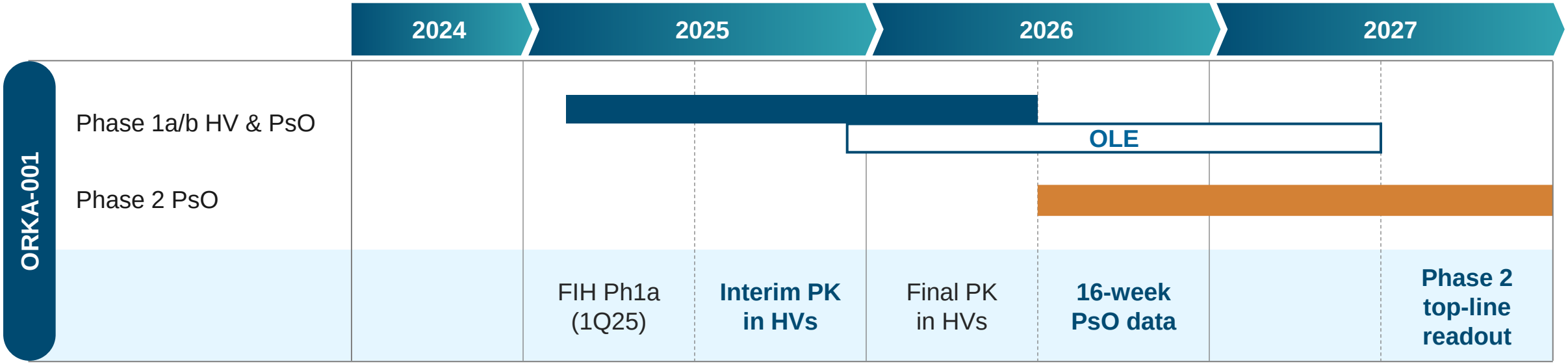
Notes & Sources: Charts adapted from 2021 Mehta (J Invest Derm) (Fig. 5b) and 2022 Regnault (Am J Clin Dermatol) (Fig. 2b); 2022 Blauvelt (J Psoriasis Psoriatic Arthritis); 2023 Chiu (J Am Acad Dermatol). Abbreviations: TRM, tissue-resident memory T cell

ORKA-001 development path sets up a catalyst-rich next 3 years



Potential for rapid de-risking, value recognition, and path to BLA

- **Interim PK data is highly validating,** showing both basis for differentiation and early safety
- Validated clinical endpoints (e.g., PASI 100) show **highly robust correlation between Phase 2 and 3**
- Rapid timelines possible in PsO – **average time from FIH to BLA/NDA is 6.5 years**

Notes: Average time from FIH to BLA/NDA reflects average of Skyrizi, Tremfya, Bimzelx, and Sotyktu
Abbreviations: OLE, open-label extension

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

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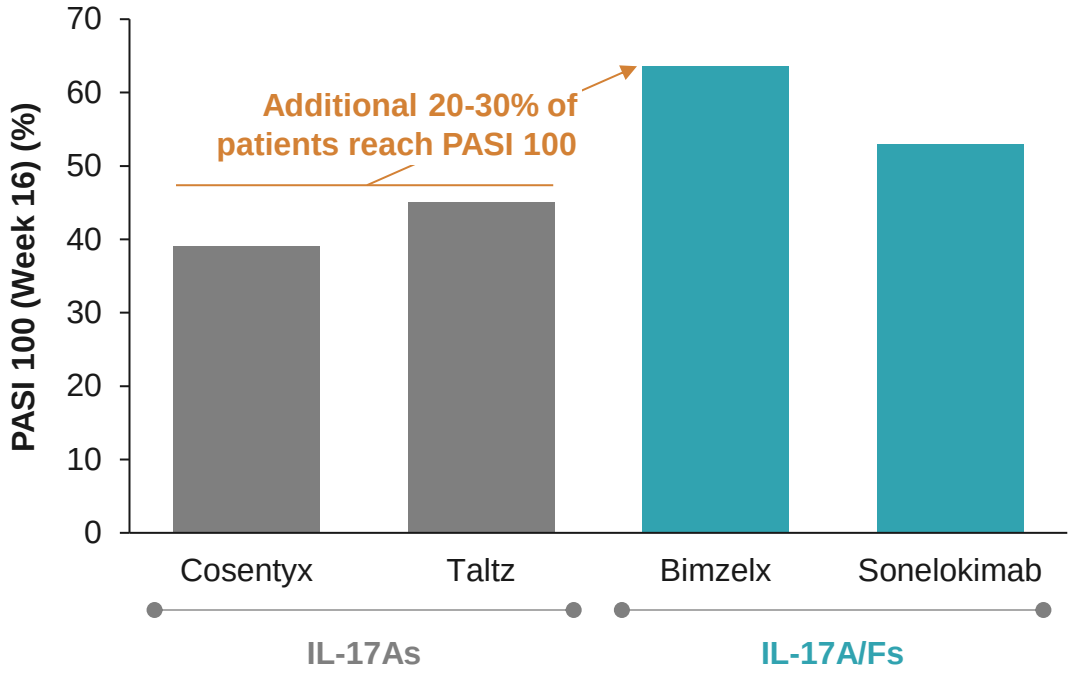
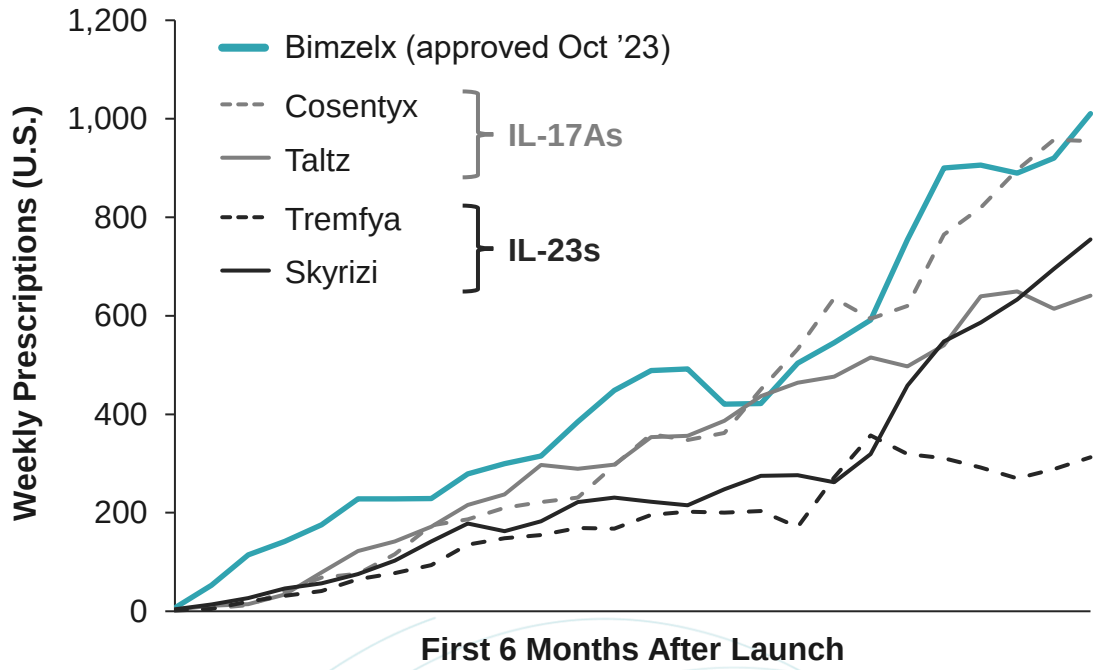
IL-17A/F dual blockade has emerged as the superior strategy

IL-17A/F shows superior efficacy to IL-17A in PsO



Bimzelx has had a very strong launch, validating both IL-17A/F and the ability to differentiate in PsO



Superior efficacy in other indications as well

Bimzelx consensus peak sales estimate of $4.5B

Notes & Sources: (left) Cosentyx: Ph3 trials in 2014 Langley (NEJM), Taltz: UNCOVER-3 Ph3 trial in 2016 Gordon (NEJM), Bimzelx: FDA Approval Label; sonelokimab: best-performing group in Ph2b trial in 2021 Papp (Lancet). (right) Jefferies (based on IQVIA data); shown as 2-week moving average; Bloomberg

ORKA-002 could be the best-in-class IL-17A/F inhibitor

Similar epitope to Bimzelx (bimekizumab) with equal or better potency

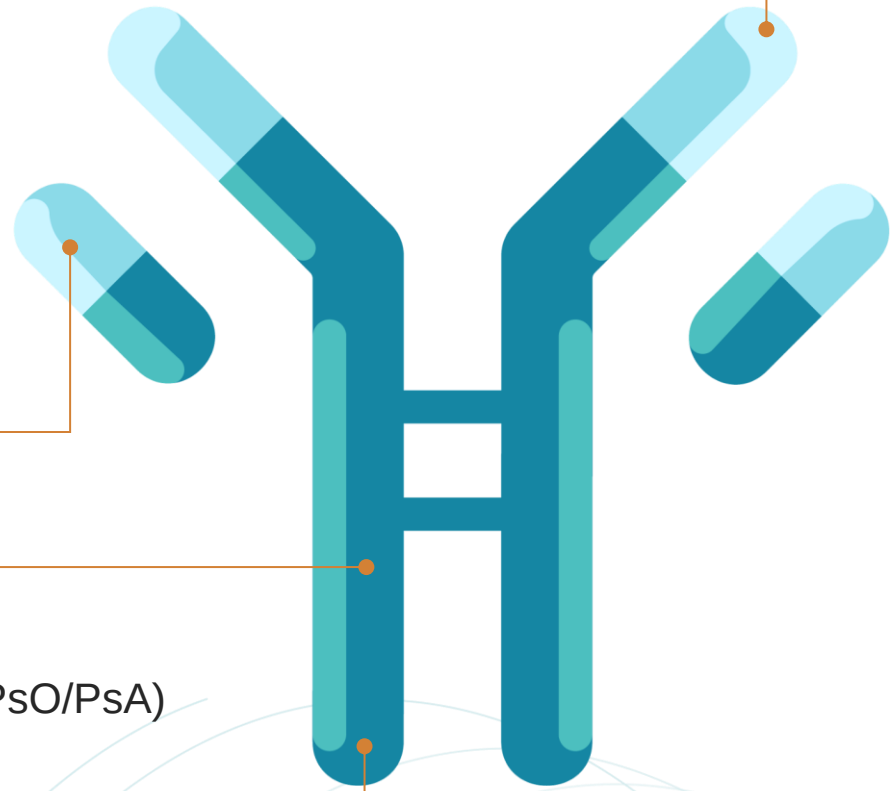
- Validated mechanism of action
- Binds **IL-17A and IL-17F** to prevent homodimer and heterodimer signaling
- **Equal or greater affinity** vs. bimekizumab
- Predicted **equivalent safety**
- Predicted to **meet or beat efficacy**

Novel IP for composition of matter into 2040s

Half-life extension through validated Fc modification

- **Higher exposure** to increase efficacy
- **Longer exposure** to reduce dosing frequency (targeting 2-3 doses/year in PsO/PsA)

Effector-null human IgG1 Fc



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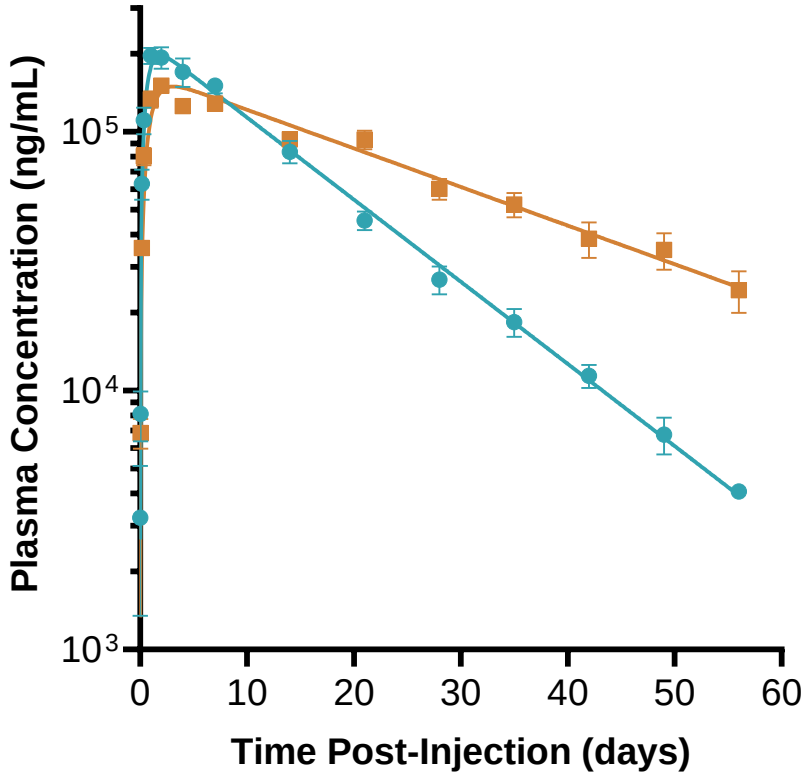
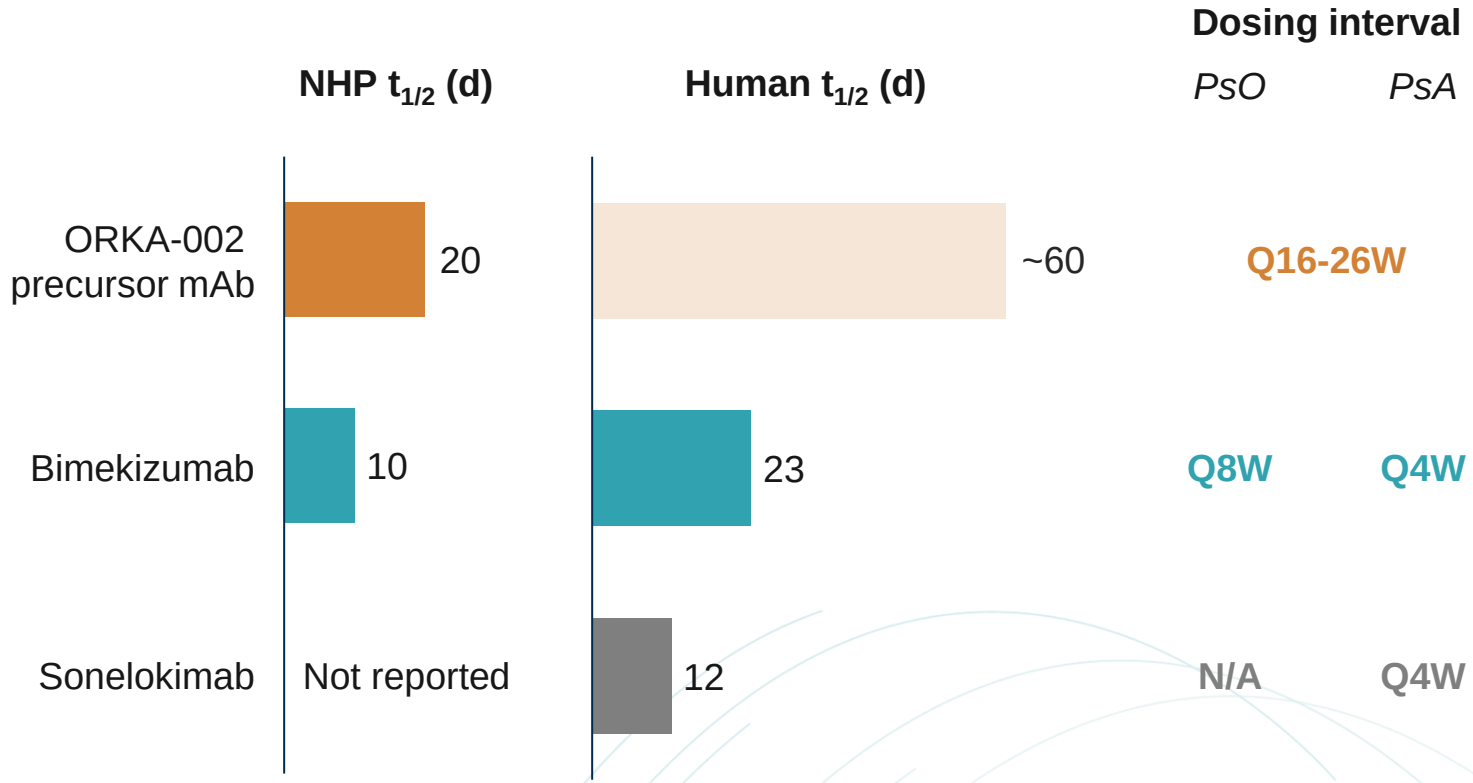
Potential for 2-3 doses per year in PsO/PsA via half-life extension

~2x longer half-life than bimekizumab with precursor mAb in NHPs

Implies ORKA-002 could have a significantly longer half-life in humans





Note: Potential human half-life for ORKA-002 derived from ~3x the half-life observed in NHPs for precursor mAb
Source: Internal data; Bimzelx FDA and EMA Approval Labels; 2019 Svecova (JAAD)

ORKA-002 could be best-in-class in a $15B market

Best target

- **Dual IL-17A/F inhibition has shown superior efficacy** vs. IL-17A
- **$15B+ in future market potential**

Best profile

- **Potential for Q16W dosing interval or longer**
- Reduced biological risk by pursuing Bimzelx MoA

Limited competition

- **Few other IL-17A/F inhibitors**
- Lengthy timeline to biosimilar entry

Rapid development path

- **Phase 1 HV study de-risks PK and dosing interval**
- Potential for **rapid development path** (Bimzelx took ~6 years from IND to BLA)

ORUKA THERAPEUTICS

Corporate

ORUKA THERAPEUTICS

Multiple inflection points across the pipeline over the next 2+ years

	2024	2025		2026	
ORKA-001		FIH Ph1a (1Q25)	**Interim PK in HVs**	Final PK in HVs	**16-week PsO data**
ORKA-002			FIH Ph1 (3Q25)	**Interim PK in HVs**	
ORKA-003		Target disclosure			

Building rapidly with backing from Paragon

Lawrence Klein
CEO

Joana Goncalves
CMO

Paul Quinlan
General Counsel

Laura Sandler
SVP, Operations

Arjun Agarwal
SVP, Finance

Christopher Finch
VP, Corp Dev & Strategy

Alan Lada
VP, Investor Relations

Rajiv Panwar
VP, Head of CMC

Joe Senn
SVP, Nonclinical R&D

Andrew Blauvelt
Chair, SAB

Board of Directors

Sam Kulkarni
CEO & Chairman, CRISPR Therapeutics

Kristine Ball
CEO, Antiva Biosciences

Carl Dambkowski
CMO, Apogee Therapeutics

Peter Harwin
Managing Member, Fairmount

Cameron Turtle
CEO, Spyre Therapeutics

Lawrence Klein
CEO, Oruka Therapeutics

ORUKA THERAPEUTICS

Capitalization following close of merger with ARCA and financings

As of September 12, 2024		Number of shares[1]
Common stock	• Shares outstanding	35.0M
Common stock equivalents	• Preferred stock (as-converted to common stock)	13.9M
	• Pre-funded warrants	6.2M
Common stock and common stock equivalents	• **Total outstanding[2]**	**55.1M**

Notes: Please refer to ORKA and ABIO SEC filings for additional information. (1) Shown on an as-converted-to-common basis and after the 12:1 reverse stock split carried out in connection with the merger with ARCA biopharma; (2) Excludes stock options and warrants held by employees, directors, and service providers


ORUKA
THERAPEUTICS