ORUKA THERAPEUTICS

Corporate Overview

NASDAQ: ORKA

May 2025

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Fully funded through a potential psoriasis breakthrough

2024 was a year of superb execution...

- **Raised >$475M in two oversubscribed transactions** and went public via reverse merger
- **Lead program ORKA-001 entered the clinic in December 2024,** well ahead of schedule

…and continued external tailwinds

- **Better biologics overdeliver in PsO**
  - UCB's Bimzelx launch exceeding expectations **– $1.4B[1] 2025 and $5B+ peak sales consensus**
  - Skyrizi continues to exceed forecasts **– now projecting $12.5B 2027 sales in psoriatic disease**
- **Orals do not reach biologic efficacy –** e.g., JNJ-2113 (icotrokinra) Ph3 in Q4 2024

Clinical data catalysts coming every 6 months

- **Q3 2025 –** ORKA-001 HV PK
- **~YE 2025 –** ORKA-002 HV PK
- **2H 2026 –** ORKA-001 PsO Ph2a
- **Beyond –** ORKA-002 Ph2, ORKA-021: major additional sources of optionality and upside

Multiple "ways to win"

- Ultra-long dose interval (1-2x per year)
- Highest IL-23 PASI 100 (à la KNOCKOUT)
- Long-term "remissions" in some patients

Fully-funded through 2027

- **Funded well-beyond ORKA-001 PsO Ph2a readout, with cash through 2027 –** no need to raise on healthy volunteer data
- **55.1M total shares** of common stock and common stock equivalents

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(1) Bloomberg consensus sales estimate for Bimzelx as of 2/1/2025

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	POTENTIAL INDICATIONS
ORKA-001	IL-23p19	**HV PK 3Q25**	**Initiation 2H25**	Psoriasis
ORKA-002	IL-17A/F	**HV PK ~YE25**	**Initiation 1H26**	Psoriasis, psoriatic arthritis, others
ORKA-003	Undisclosed			
ORKA-021		Sequential combination regimen of ORKA-002 and -001		

Rights to development candidates acquired from Paragon Therapeutics

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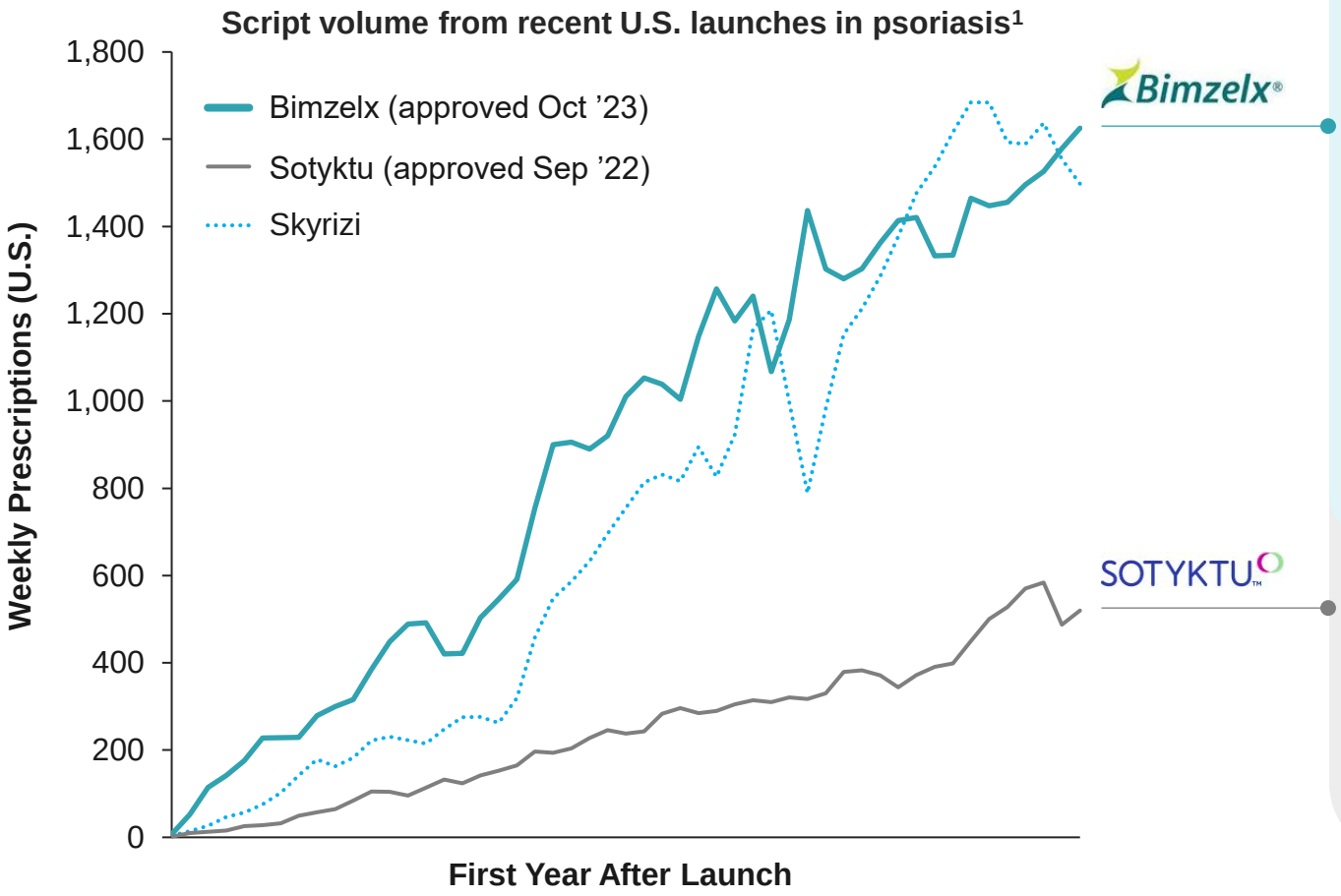
Notes: Oruka has exclusive worldwide rights to ORKA-001 (for all fields outside of IBD) and ORKA-002 (for all fields) from Paragon Therapeutics, Inc.
Abbreviations: FIH, first-in-human dosing; HV, healthy volunteer; PK, pharmacokinetics

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 –** consensus sales of $1.4B[2] in Year 2 and $5B+ peak
- **Market underestimated the opportunity –** UCB market cap $15B pre-launch vs. $35B one year later ($20B 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; (2) Bloomberg consensus sales estimate for Bimzelx as of 2/1/2025

The psoriasis market will continue to reward biologic innovation

Psoriasis is a massive, growing market where biologics are still underpenetrated

$30B+ **growing market today** with further potential in mild-to-moderate disease

Pharma believes in the future of this market

Shown by major investments in orals, which sacrifice efficacy in favor of perceived convenience

Takeda · Lilly · J&J · nimbus THERAPEUTICS · DICE Therapeutics · Protagonist Therapeutics

Dermatologists and patients want new and better biologics

Even a base-case profile of Q6M dosing with equal efficacy surveys at **~50%** **of new patient starts in 2030+**

Differentiated biologics have a proven ability to gain market access

Bimzelx forecasted to reach peak sales of **$5B+** Showing smaller, non-incumbent companies can achieve access

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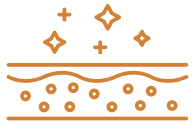
ORKA-001 & -002 complement each other to address all PsO/PsA

ORKA-001

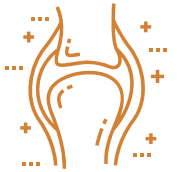
For patients with purely skin disease



Majority of dermatologists prefer an anti-IL-23p19

ORKA-002

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



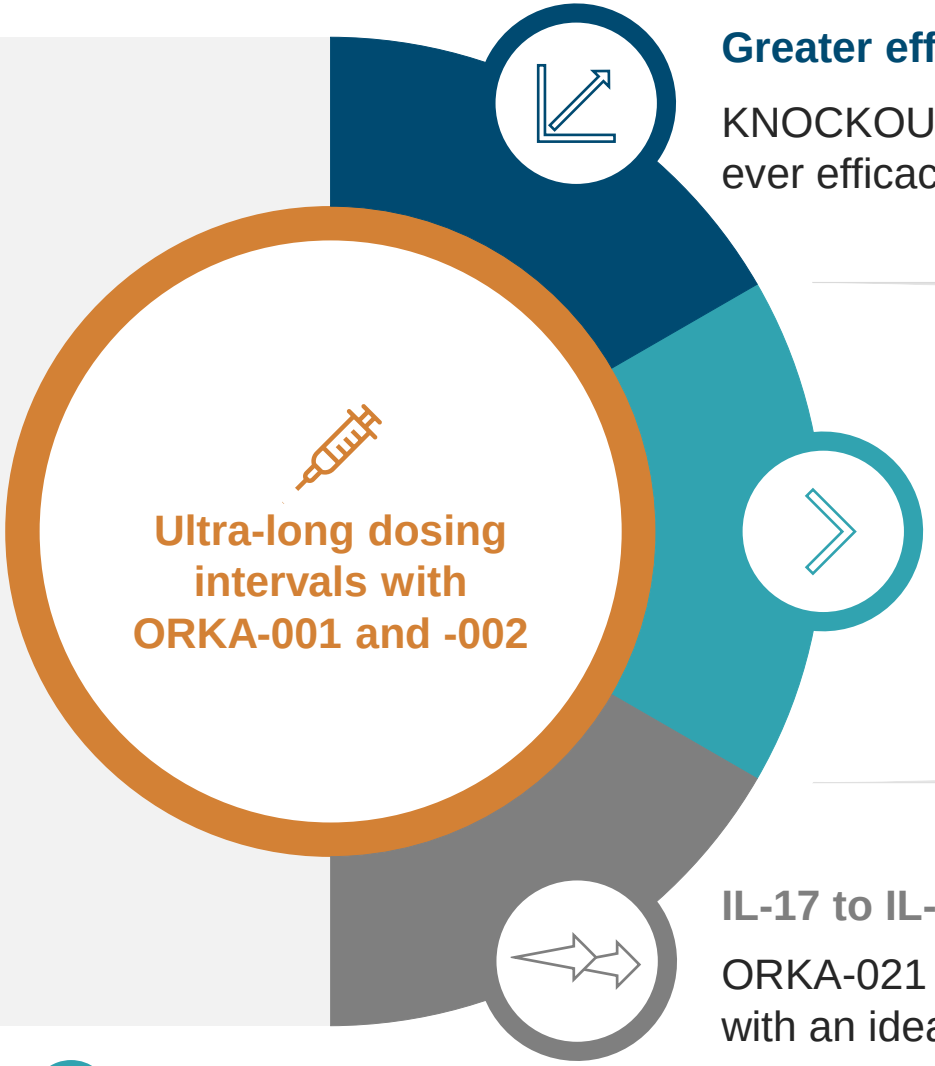
Anti-IL-17 preferred, and **IL-17A/F emerging as the best approach**

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

Multiple orthogonal paths for Oruka to maximize differentiation



Greater efficacy

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

Long-term “remissions”

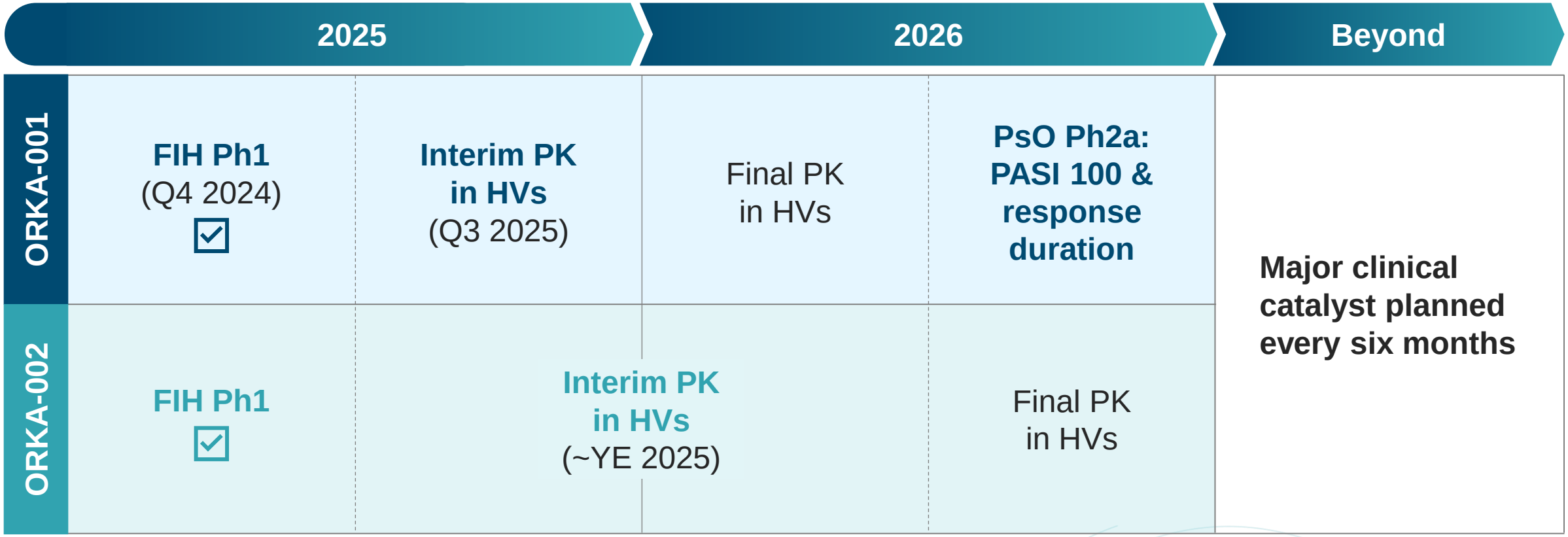
High exposures of anti-IL-23 could lead to long-lasting clearance in some patients

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

Clinical data catalysts coming every 6 months going forward



Fully funded through 2027, >1 year past ORKA-001 Ph2a readout in PsO

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

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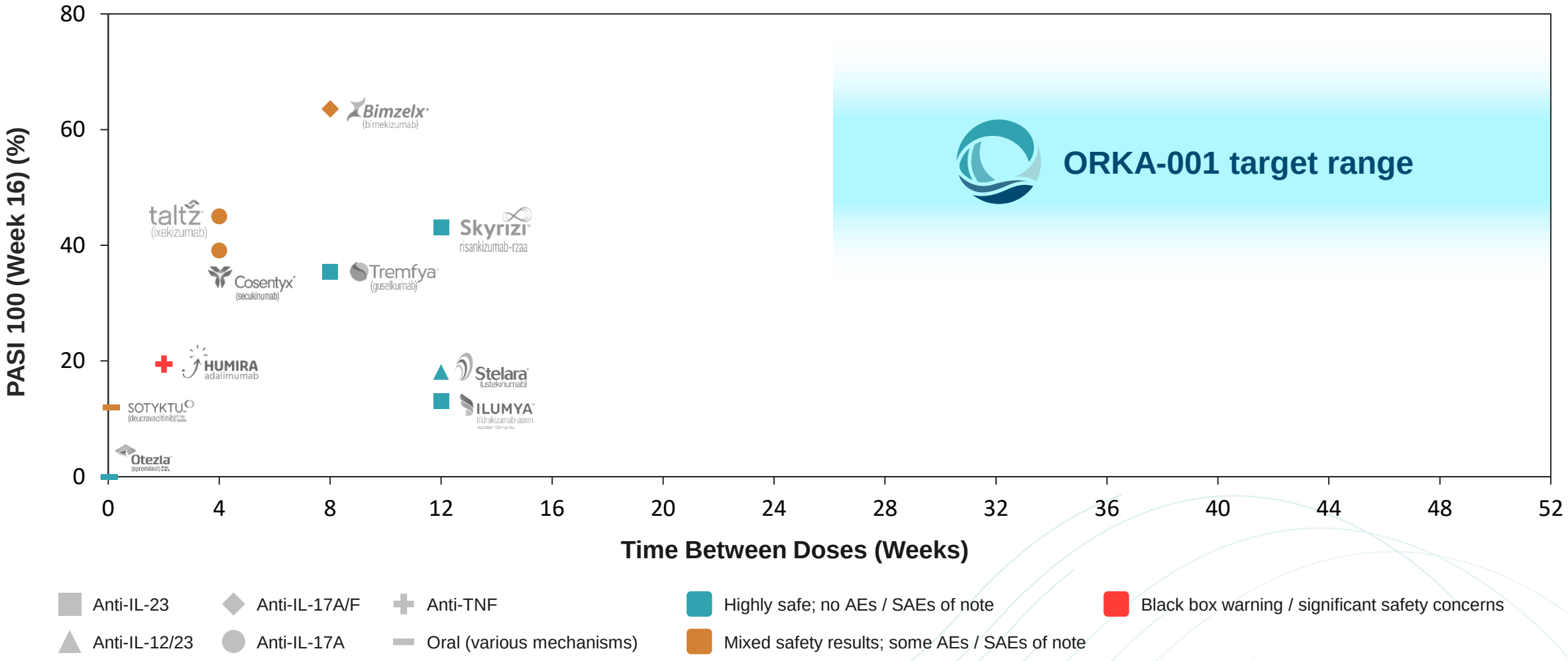
Biologics have raised the bar on standard of care in PsO, but there is ample room for improvement



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*

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

Binds similar epitope to Skyrizi (risankizumab) with similar potency

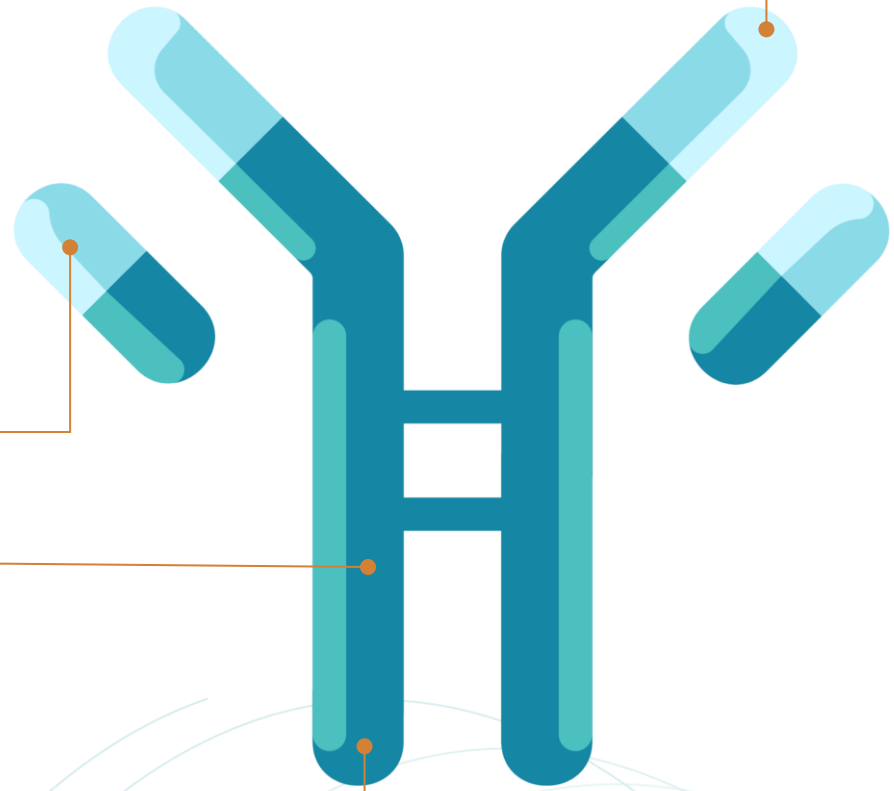
- Validated mechanism of action
- **Specific for IL-23p19** (not IL-12/23 p40)
- **K_D < 5 pM**
- Predicted **equivalent safety**
- Predicted to **meet or beat efficacy**

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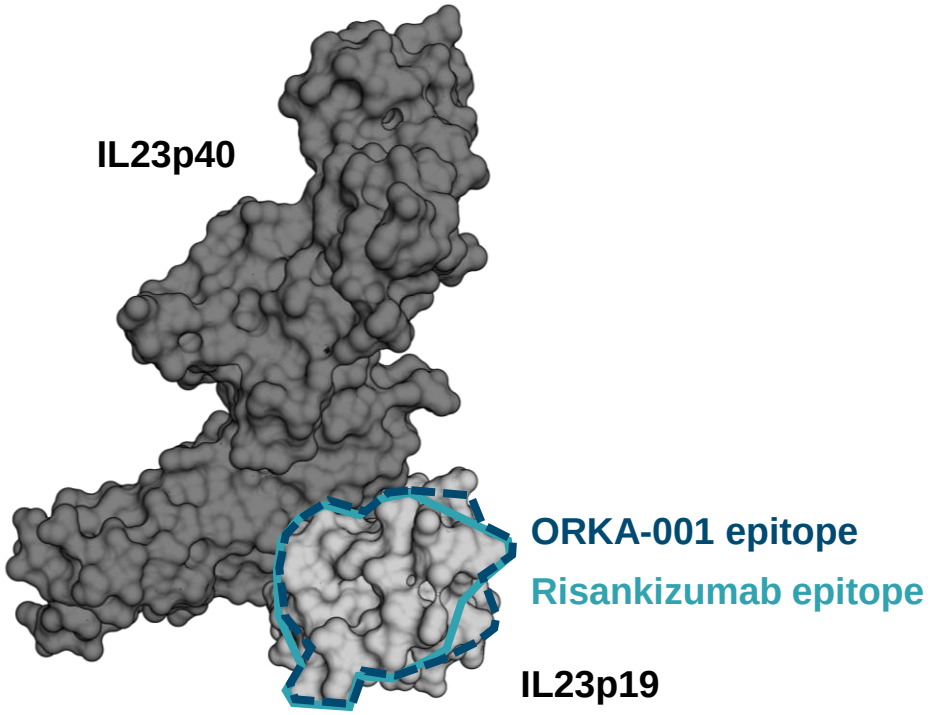
Notes: Oruka holds worldwide rights to all therapeutic indications outside of IBD

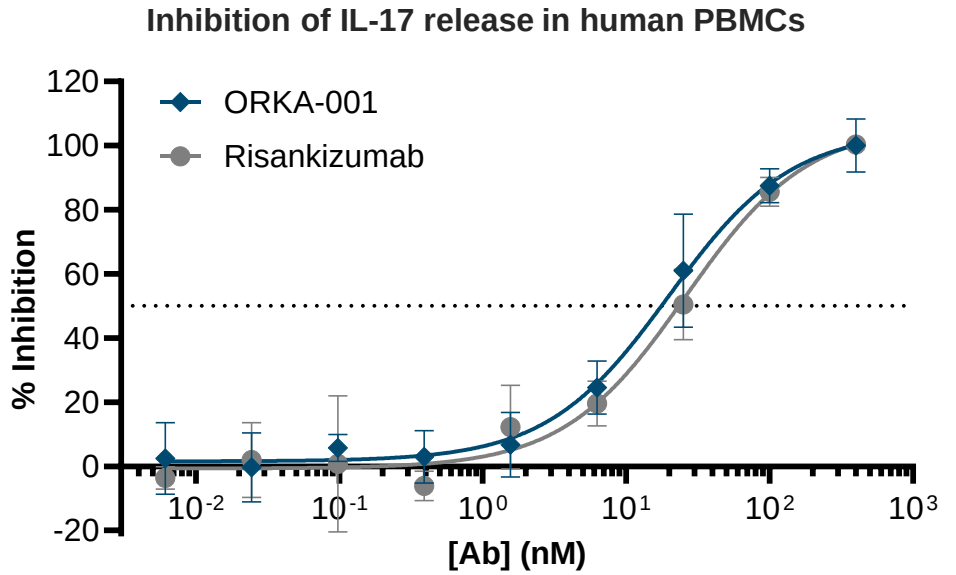
ORKA-001 binds a similar epitope as risa with similar potency

ORKA-001 binds a nearly identical epitope to risankizumab



Comparable affinity (<5 pM) as well

ORKA-001 shows comparable potency to risankizumab



	ORKA-001	Risankizumab	Guselkumab
Relative IC50	0.76	1.0	4.83

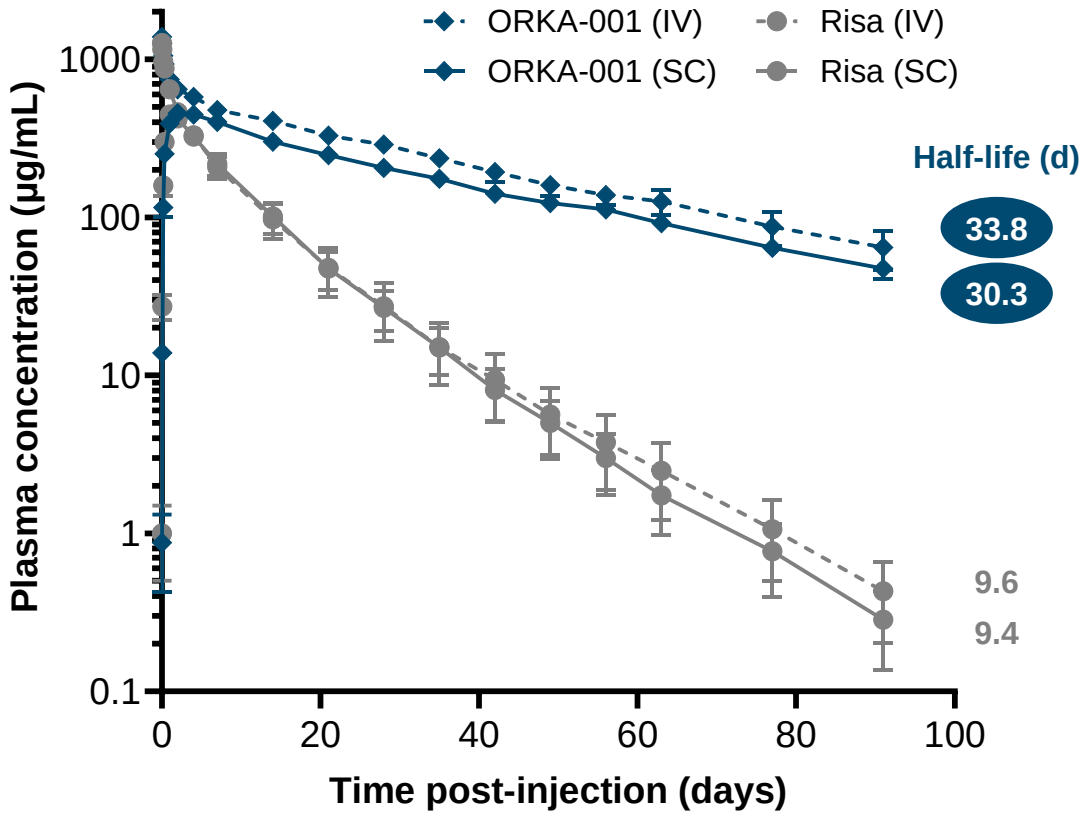
Similar results observed across a range of in vitro *assays*

Notes: Presented at EADV 2024

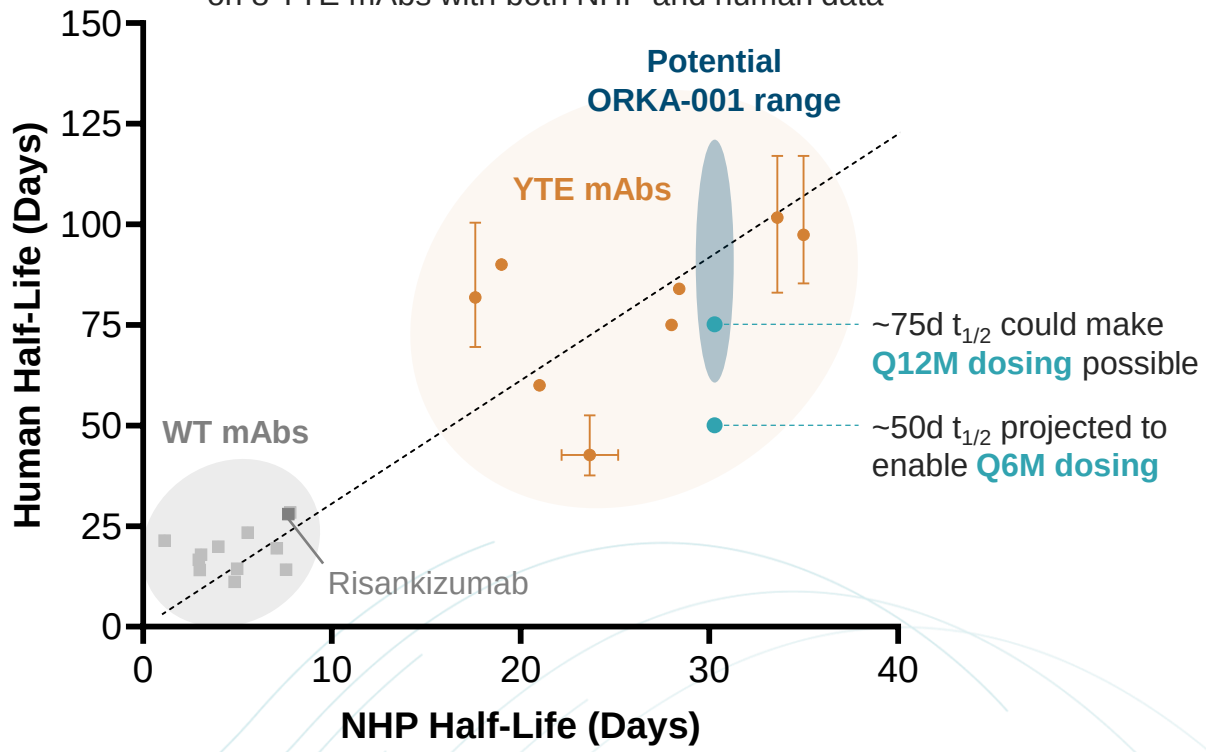
Clinical experience with YTE predicts significant $t_{1/2}$ extension

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

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



For YTE mAbs, human $t_{1/2}$ ≈ 2-4x NHP $t_{1/2}$ based on 8 YTE mAbs with both NHP and human data



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

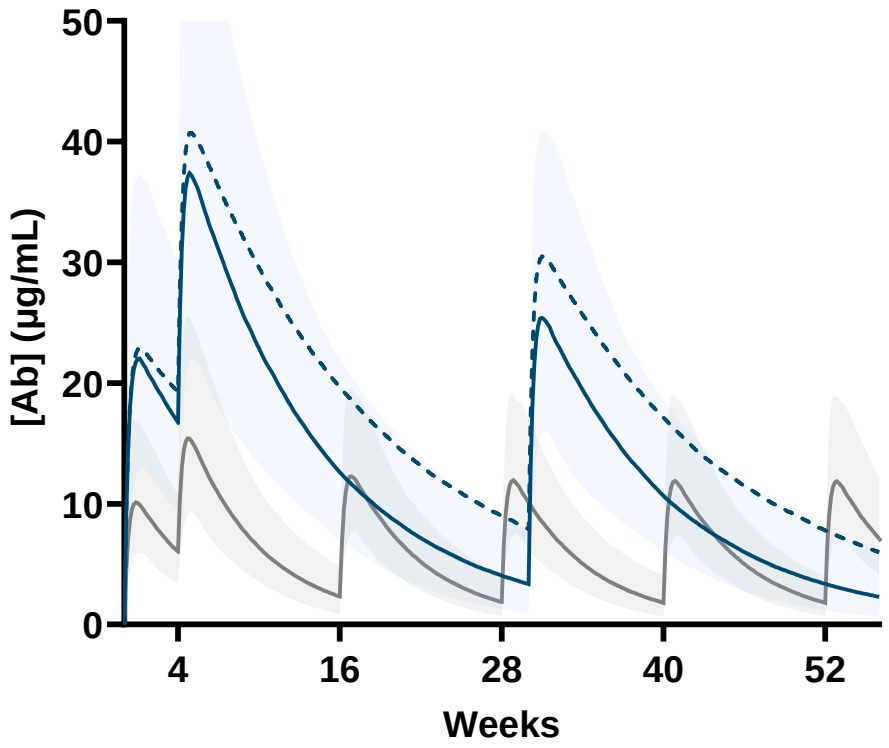
Base case is achievable even at lower end of predicted half-life

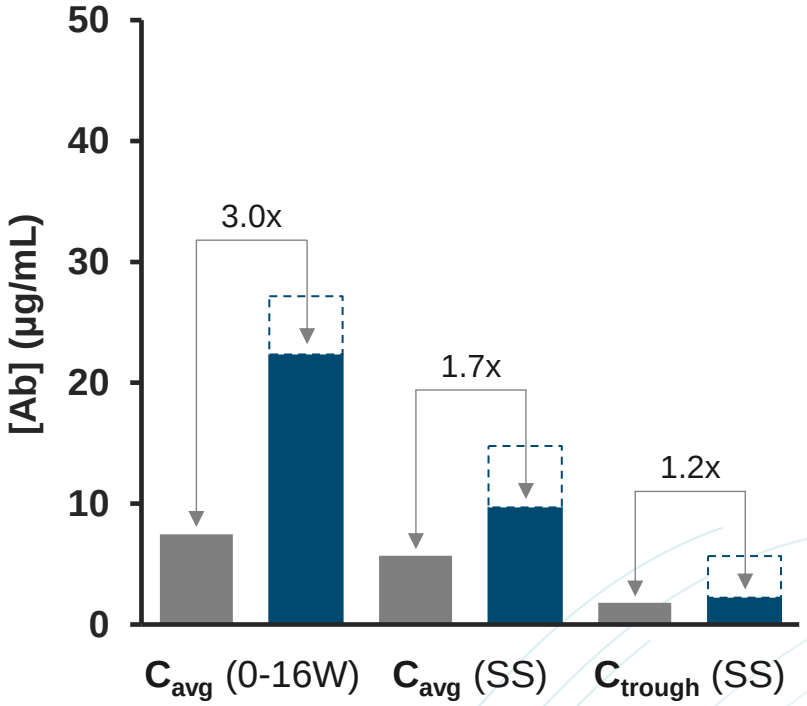
ORKA-001 exposure could exceed Skyrizi under a variety of half-life scenarios

— **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 population pharmacokinetic model for Skyrizi; error bars reflect 5th and 95th percentiles (not shown for ORKA-001 at ~75d half-life)

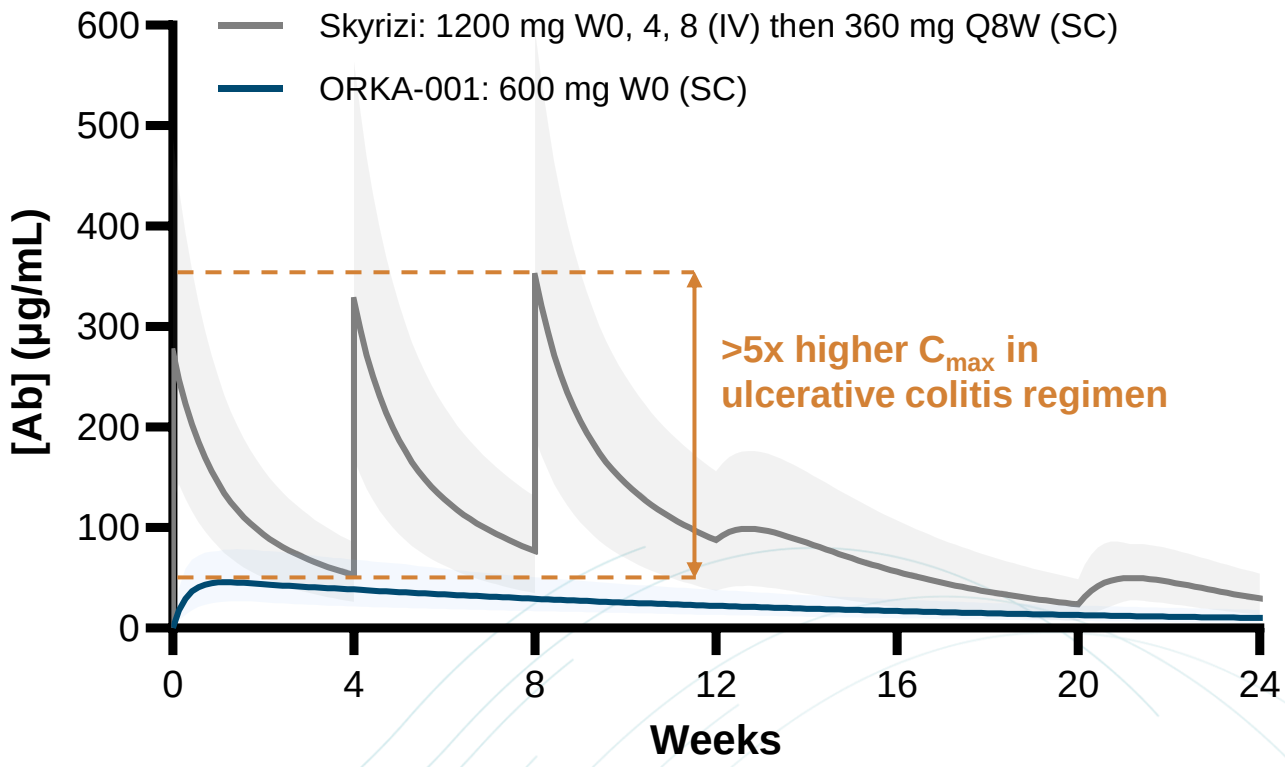
ORKA-001 benefits from a large body of clinical evidence with IL-23 inhibition

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

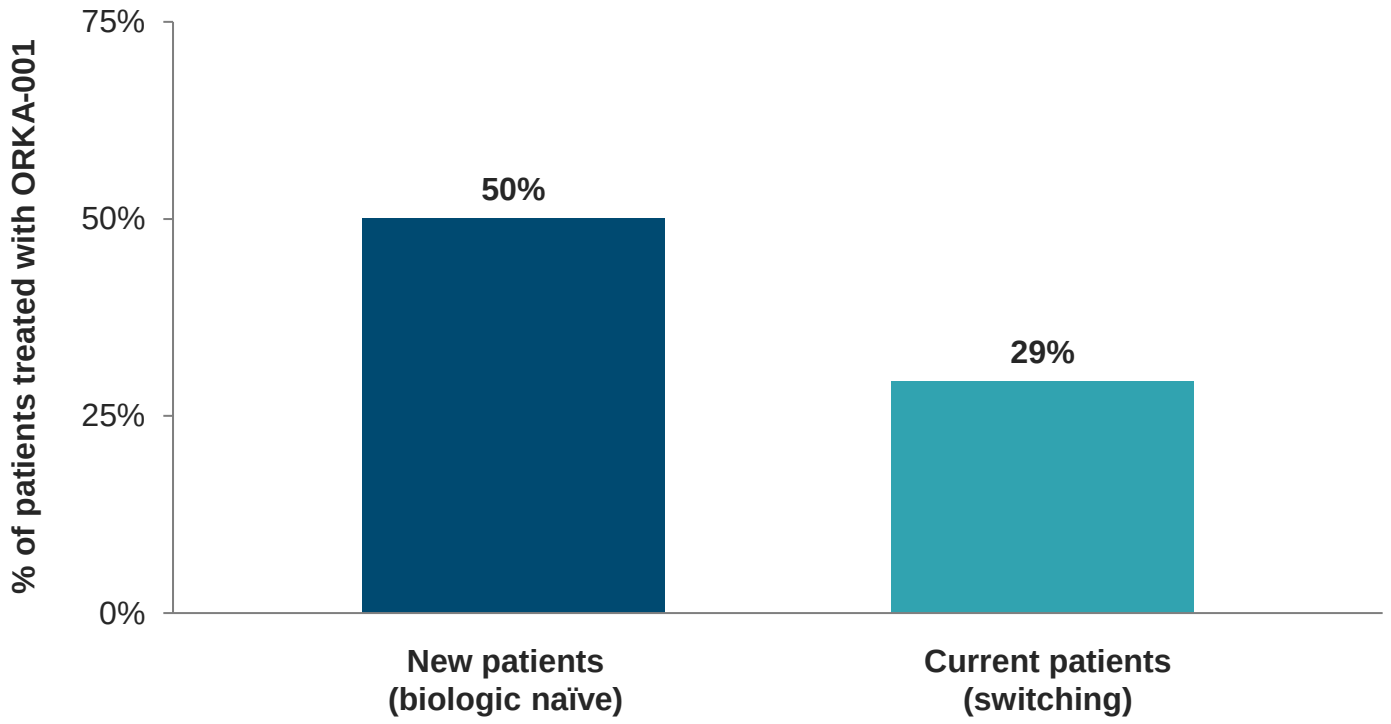
Skyrizi regimen in UC establishes the safety of very high exposures



Notes & Sources: Oruka modeling based on internal data and published population pharmacokinetic model for Skyrizi; error bars reflect 5th and 9th percentiles; 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

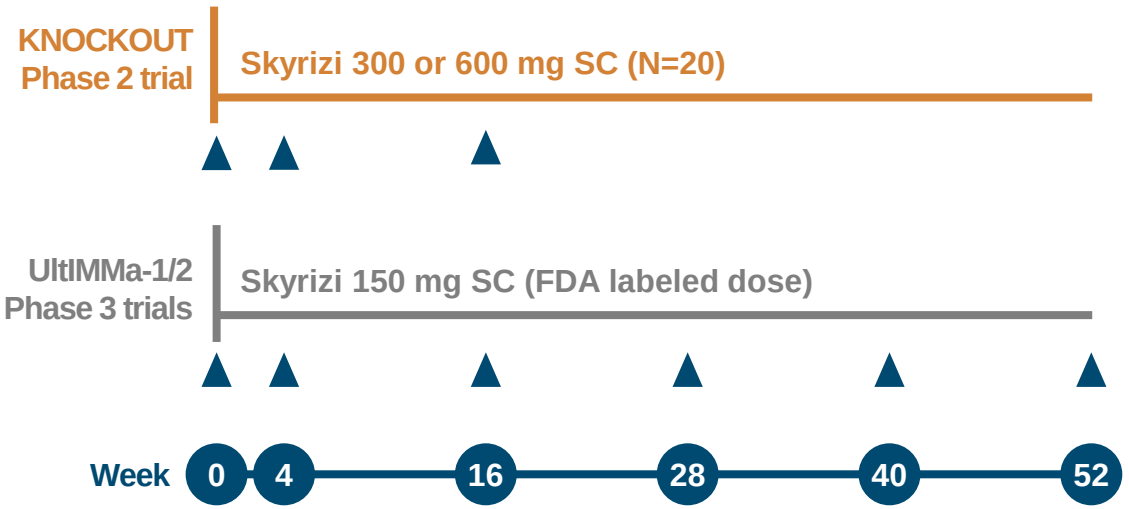
Disease modification

Patient-specific dosing to allow for treatment-free remissions

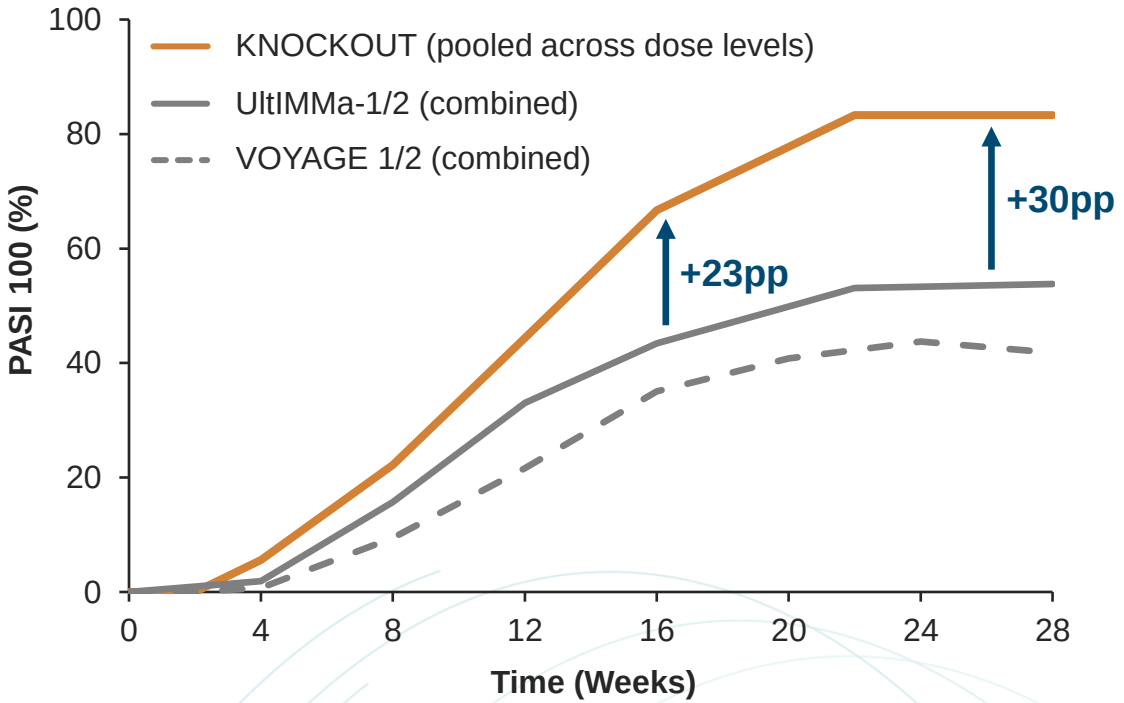
Higher exposures drove higher efficacy in KNOCKOUT study

KNOCKOUT evaluated 2-4x the approved Skyrizi dose…

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



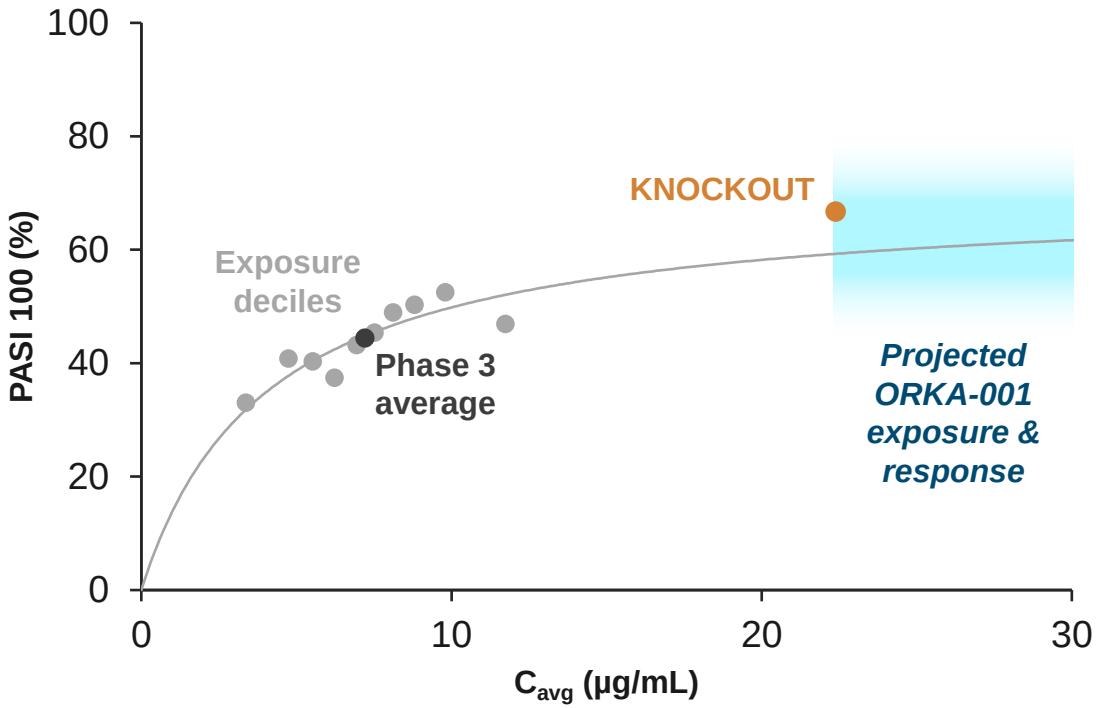
…and resulted in the highest PASI 100 rates observed to date



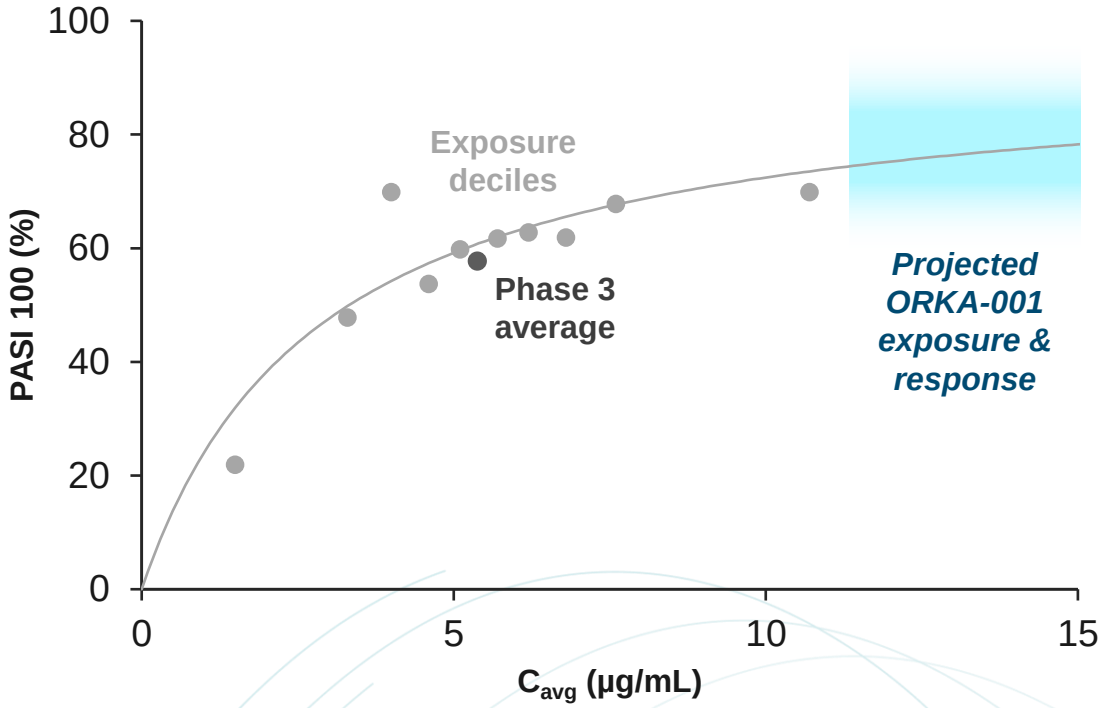
Notes: Cross-trial comparisons. Not placebo controlled. VOYAGE 1/2 Phase 3 trials tested Tremfya at 100 mg SC (W0, 4, Q8W) (FDA labeled dose)
Sources: 2017 Blauvelt (JAAD); 2017 Reich (JAAD); 2018 Gordon (Lancet); 2023 Blauvelt (WCD presentation)

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

Risankizumab induction phase (0-16 weeks)

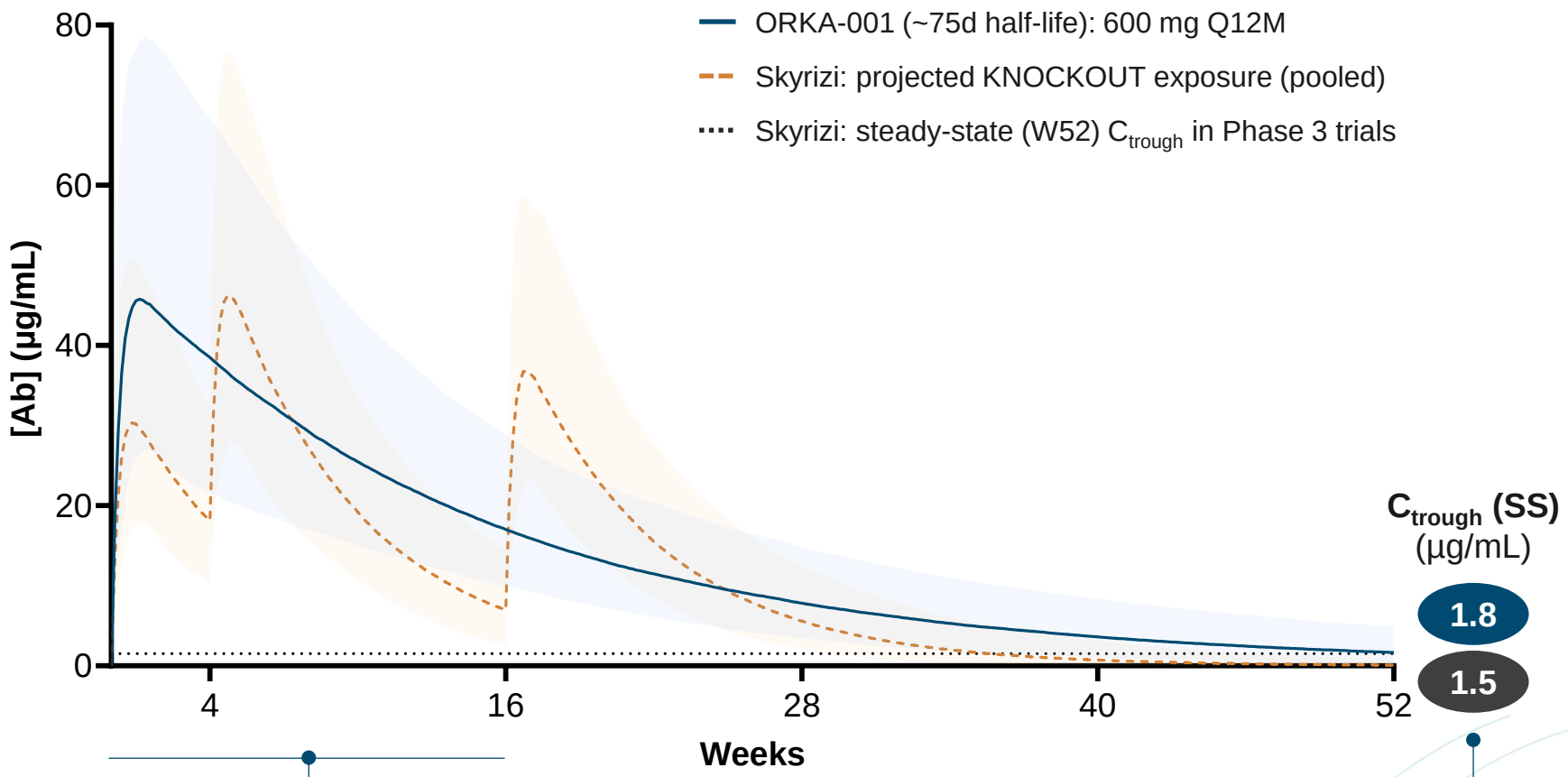


Risankizumab steady-state phase (40-52 weeks)



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

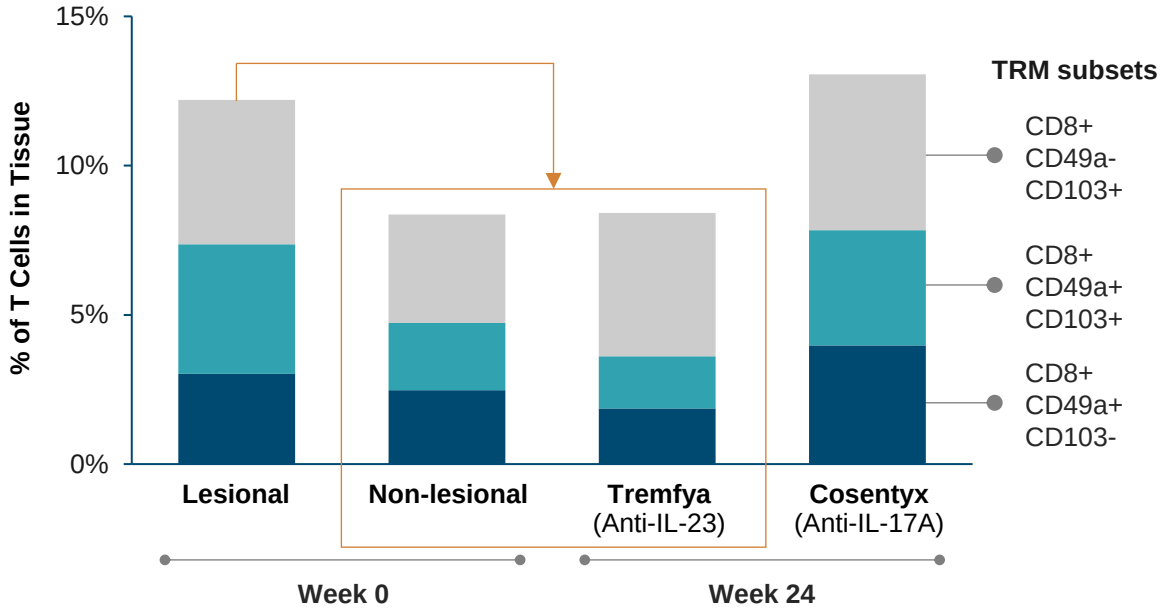
Comparable or greater early exposure vs. KNOCKOUT

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

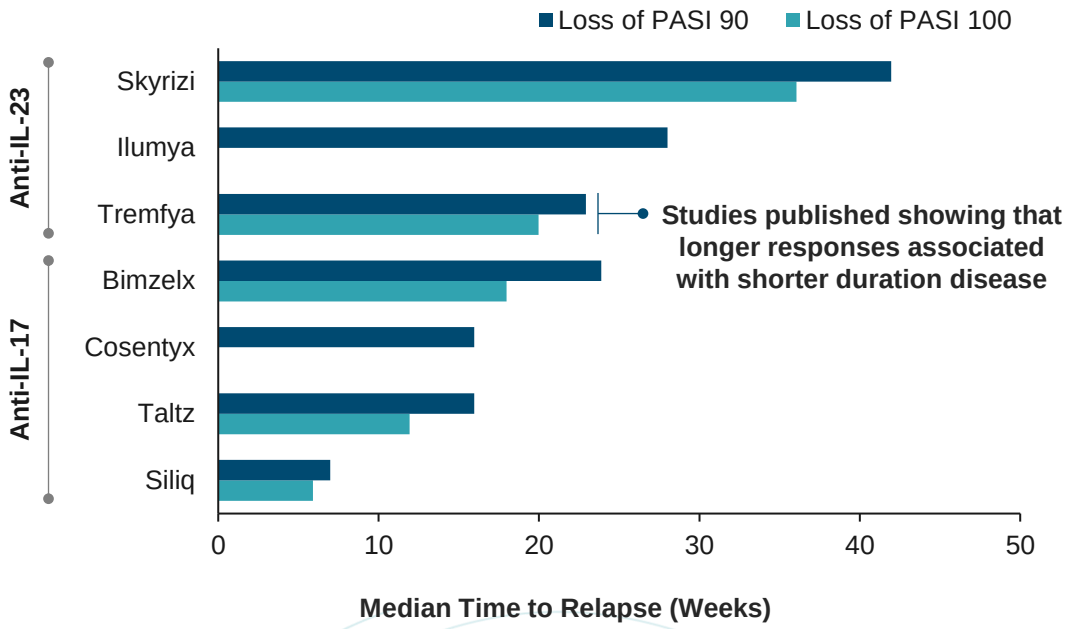
Notes & Sources: KNOCKOUT and ORKA-001 exposure from Oruka modeling based on internal data and published population pharmacokinetic model for Skyrizi; ; error bars represent 5th and 95th percentiles; ORKA-001 steady-state (SS) C_{trough} projected using the dosing interval ending at W104; Skyrizi C_{trough} 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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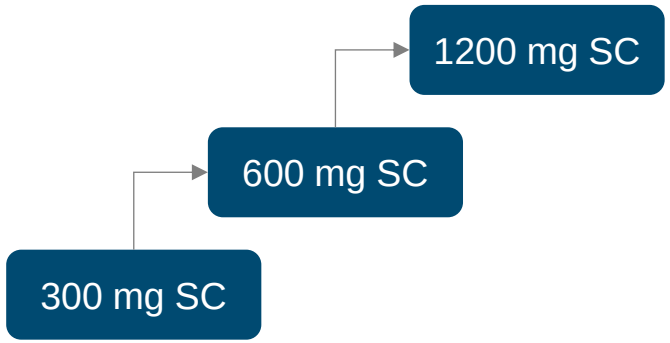
Notes & Sources: Charts adapted from 2021 Mehta (J Invest Derm) (Fig. 5b) and 2022 Regnault (Am J Clin Dermatol) (Fig. 2b); 2022 Blauvelt (J Psoriasis Psoriatic Arthritis); 2023 Chiu (J Am Acad Dermatol). Abbreviations: TRM, tissue-resident memory T cell

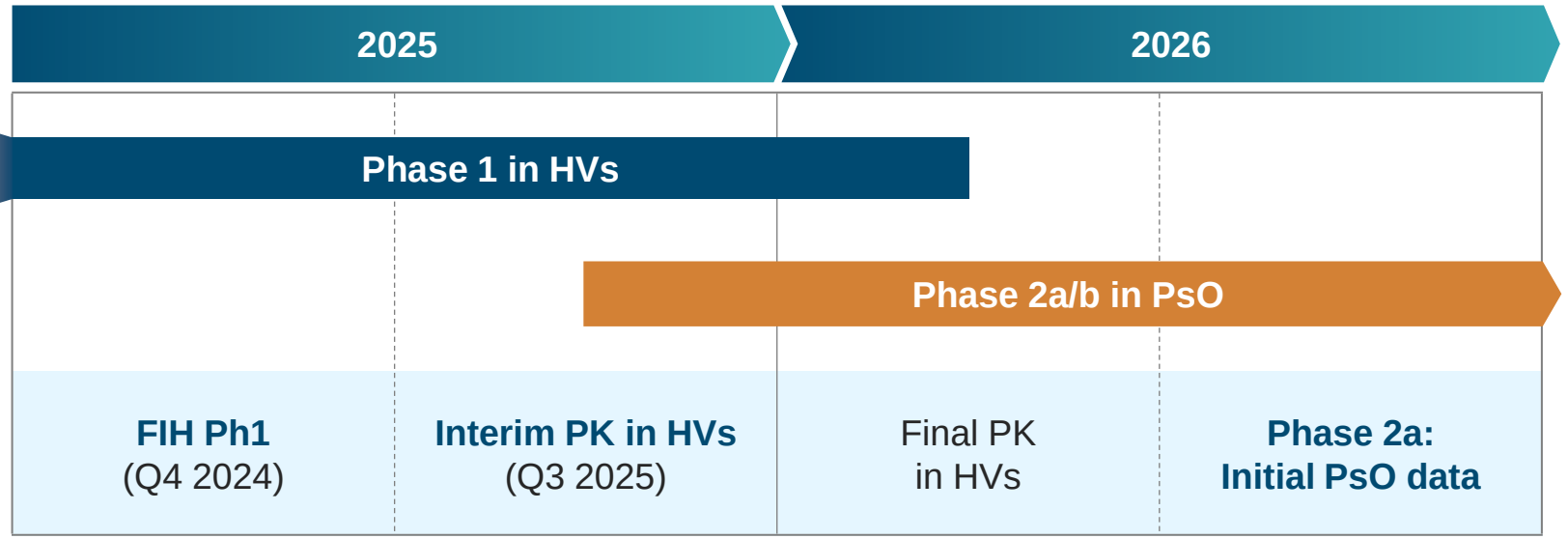
ORKA-001 development path sets up a catalyst-rich next 2 years

Phase 1 study to evaluate the safety, tolerability, and PK of ORKA-001 in healthy participants

- Placebo-controlled, single ascending dose study (NCT06698939)



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



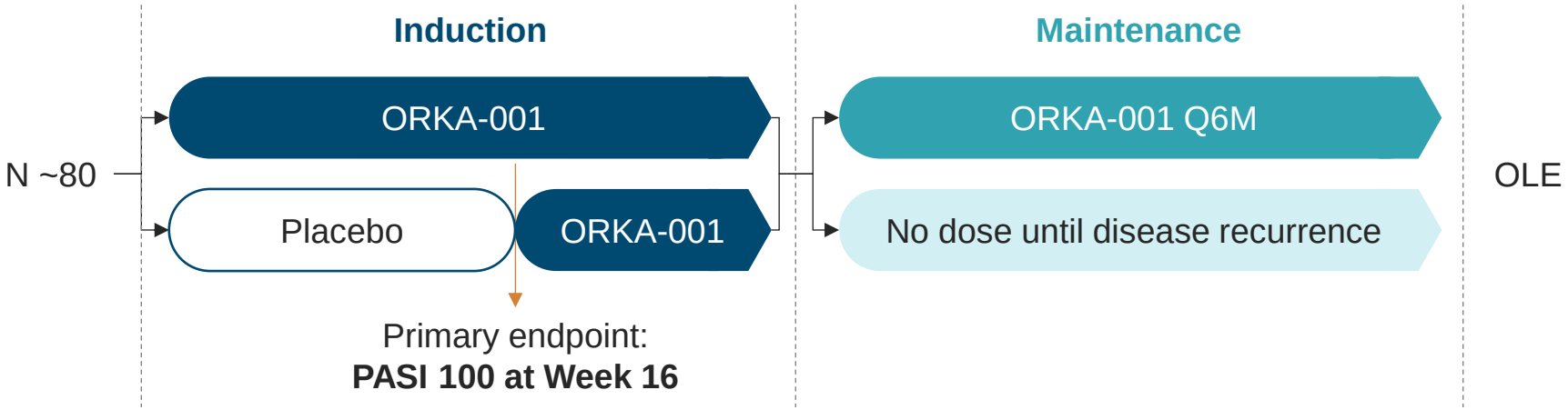
Potential for rapid de-risking, value recognition, and path to BLA

- **Interim PK is highly validating,** showing both basis for differentiation and early safety
- Validated clinical endpoints 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: SC, subcutaneous

Phase 2a to test KNOCKOUT-like exposures of ORKA-001

Phase 2a proof-of-concept study of ORKA-001 in moderate-to-severe psoriasis



Initial data readout has potential to inform all "upside" scenarios:

- Efficacy at W16 for all patients (as well as later timepoints for some patients)
- Preliminary durability, indicating the potential for extended dosing intervals and longer-term remissions

- Phase 2a expected to start in 2H 2025
- **Initial efficacy data expected in 2H 2026**
- Phase 2a/b trial enables **efficient transition to Phase 2b dose-ranging study** following Phase 2a

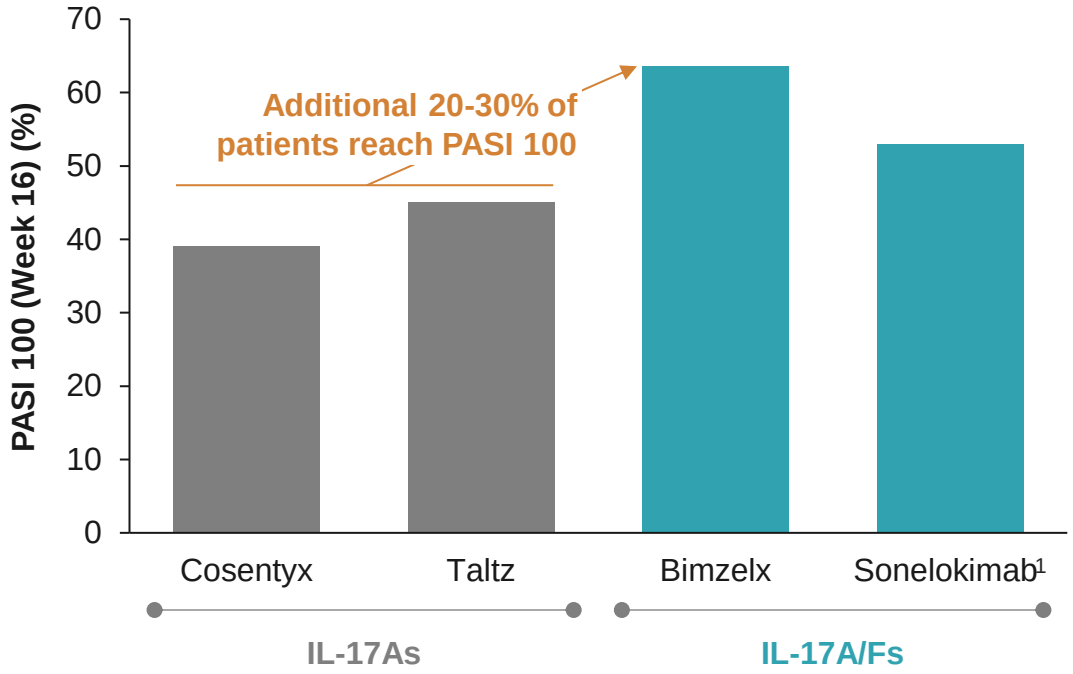
Abbreviations: OLE, open-label extension

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

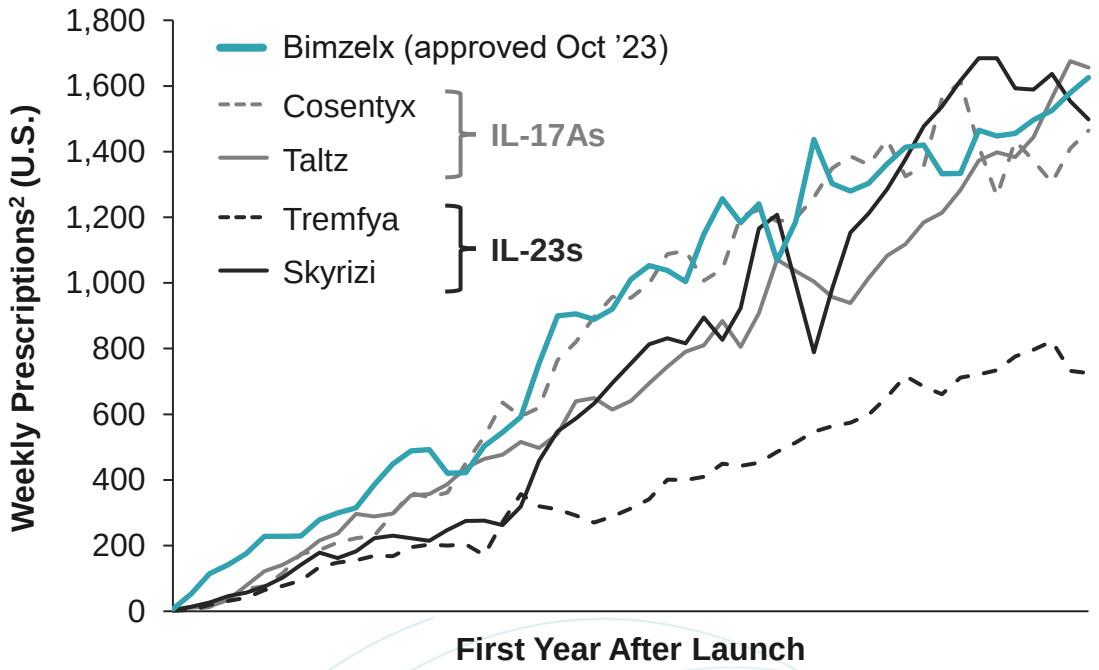
ORUKA THERAPEUTICS

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



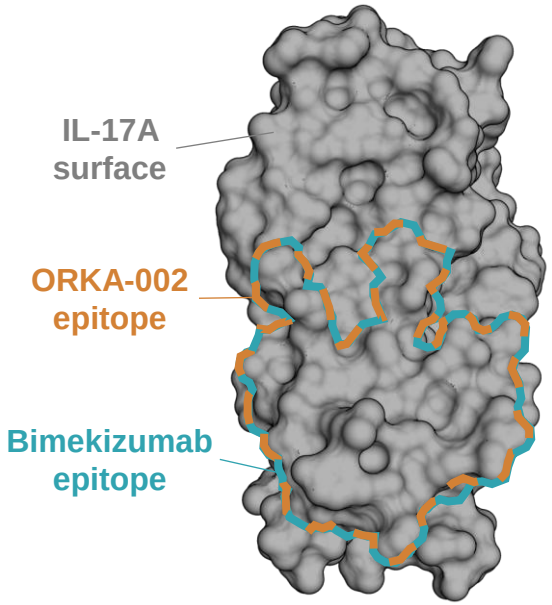
Superior efficacy in other indications as well

Bimzelx consensus peak sales estimate of >$5B

Notes: (1) Development not continued in PsO; (2) shown as 2-week moving average
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); Visible Alpha

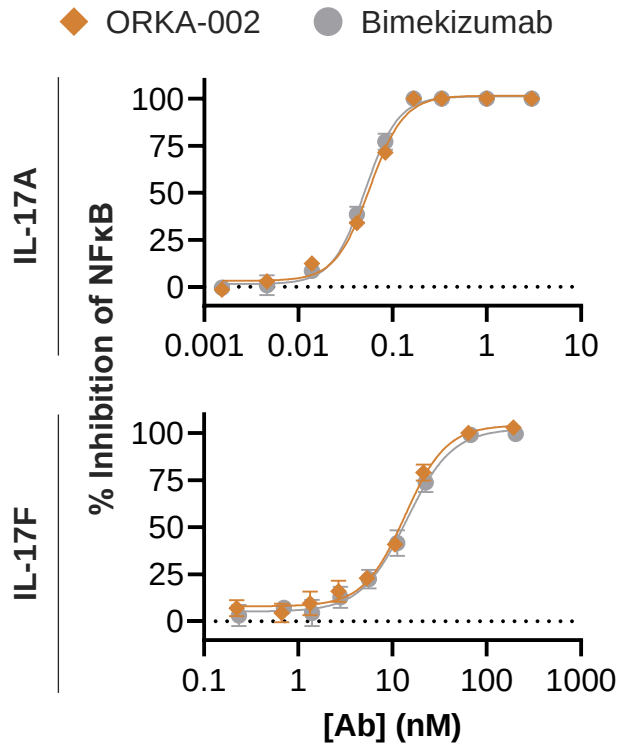
ORKA-002 has a dramatically extended half-life vs. bimekizumab

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



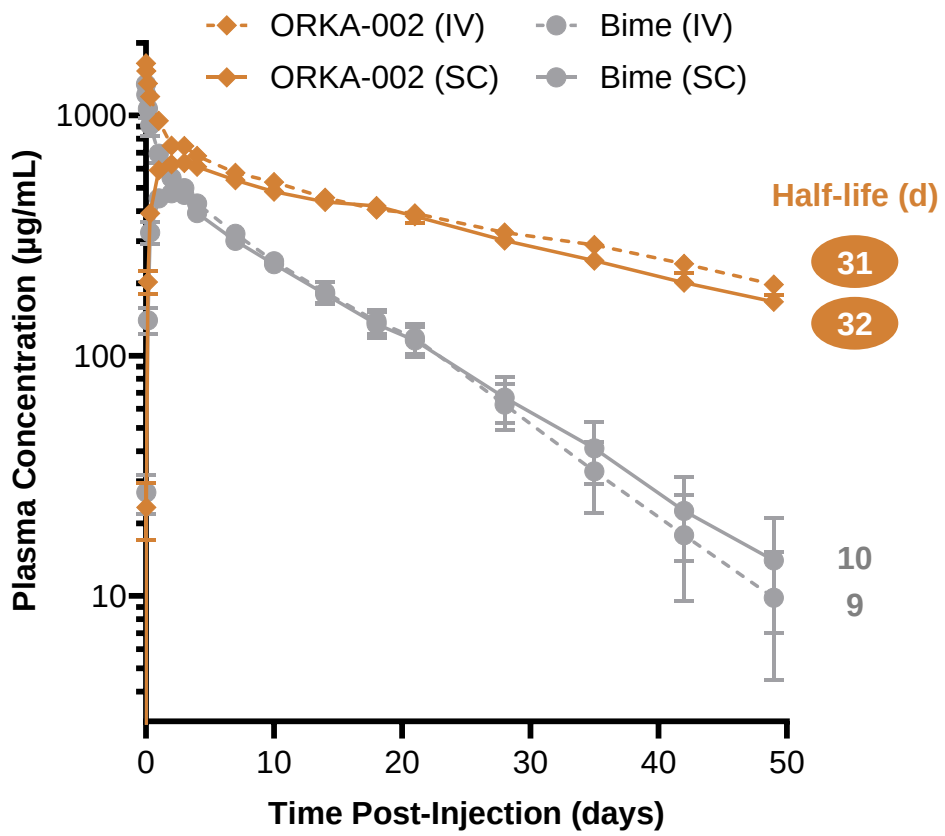
Similar epitope for IL-17F as well

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



Similar results observed across multiple in vitro *assays*

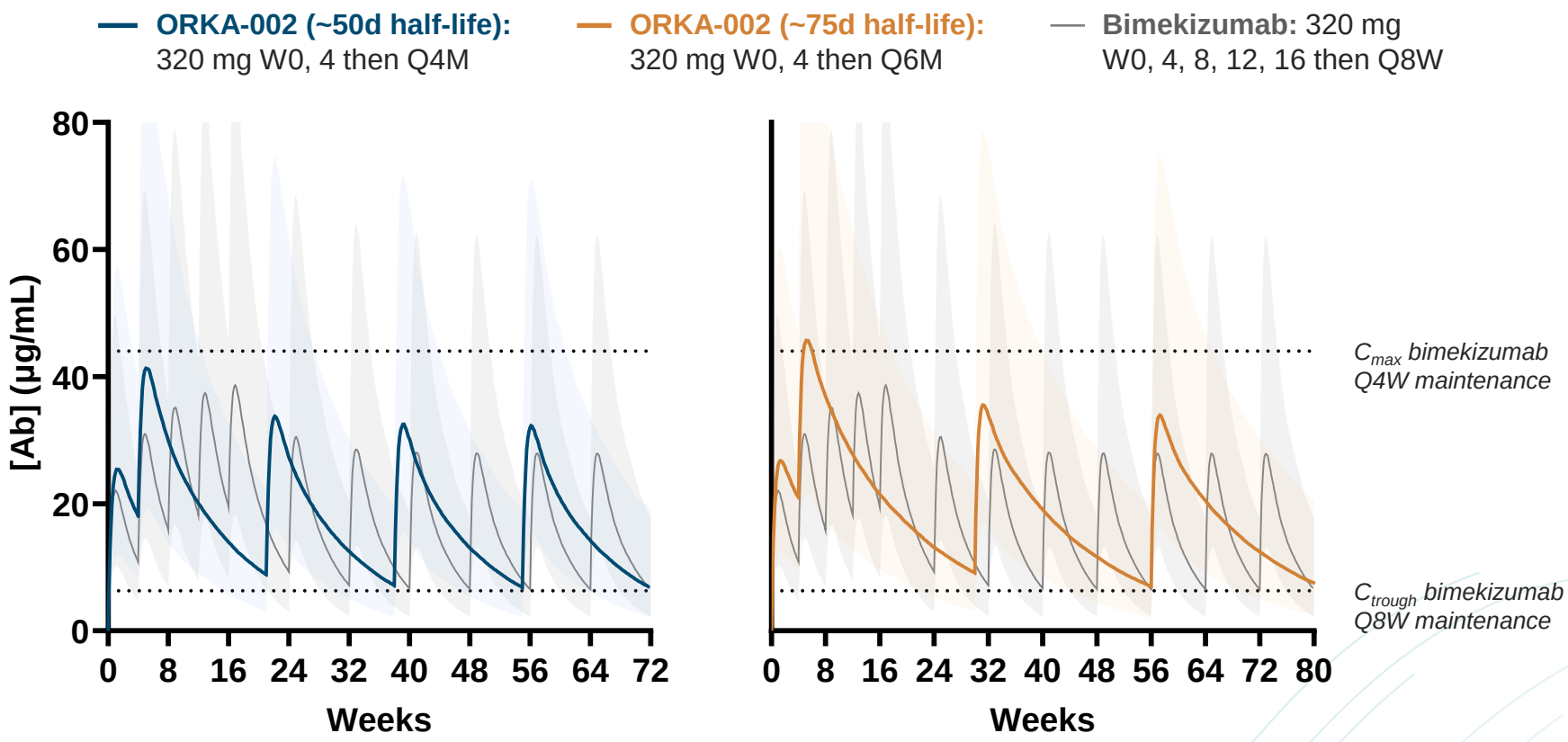
ORKA-002 has a >3x longer half-life than bimekizumab in NHPs



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



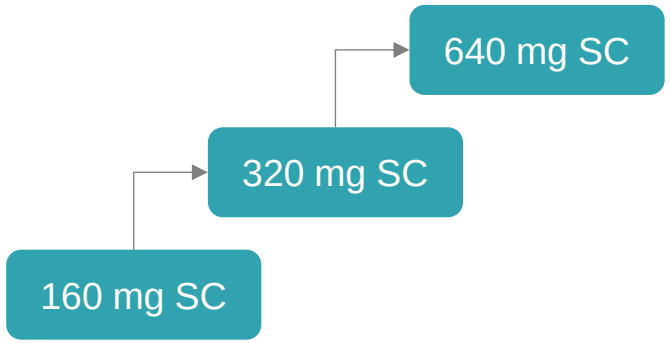
A ~50-day half-life could enable Q4M dosing and **~75-day half-life could enable Q6M dosing** while maintaining trough antibody levels above bimekizumab

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

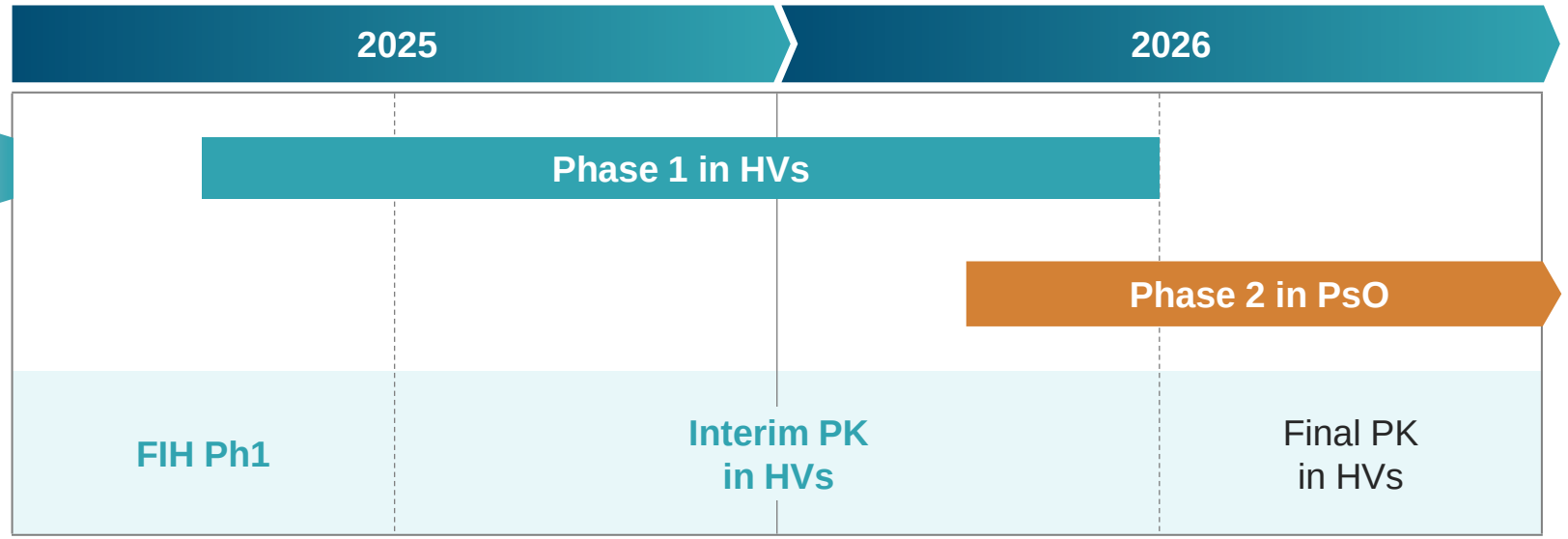
ORKA-002 is advancing just ~6 months behind ORKA-001

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

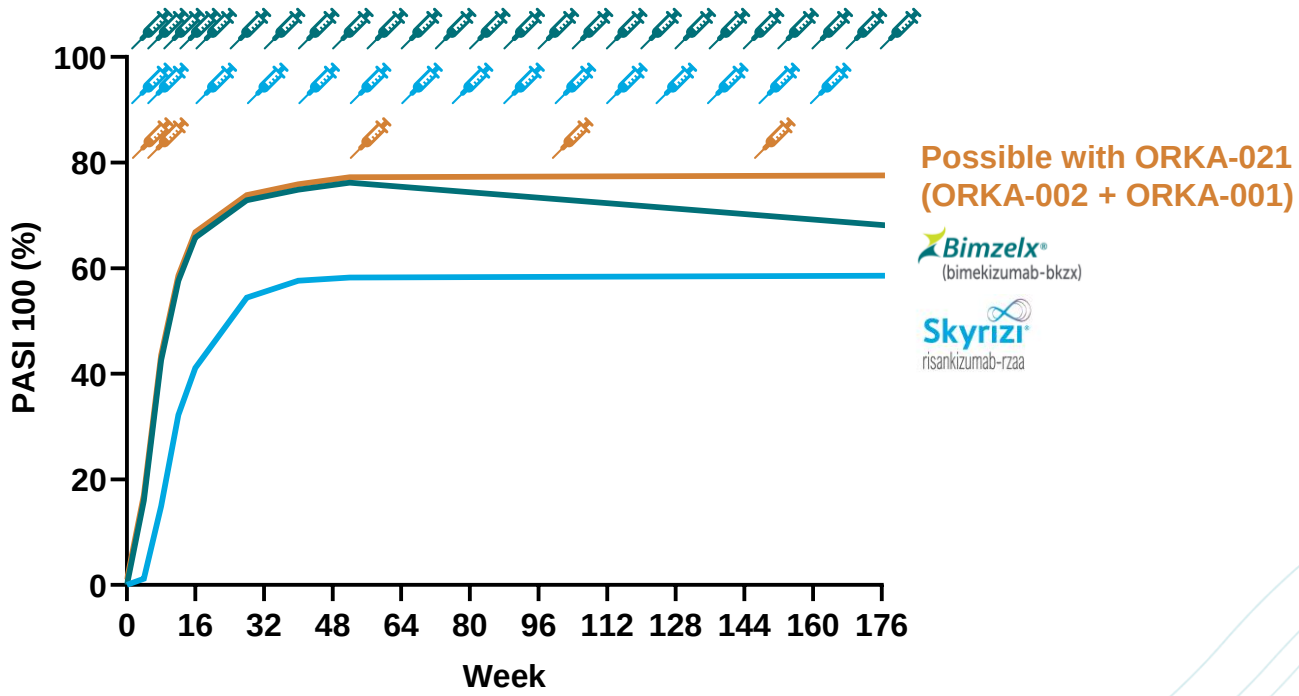
ORKA-021

ORUKA THERAPEUTICS

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"



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


ORUKA
THERAPEUTICS

Shares outstanding

As of Mar 31, 2025		Number of shares[1]
Common stock	• Shares outstanding	37.4M
Common stock equivalents	• Preferred stock (as-converted to common stock)	11.4M
	• Pre-funded warrants	6.2M
Common stock and common stock equivalents	• **Total outstanding[2]**	**55.1M**

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