ORUKA
THERAPEUTICS

Company Overview

May 2024

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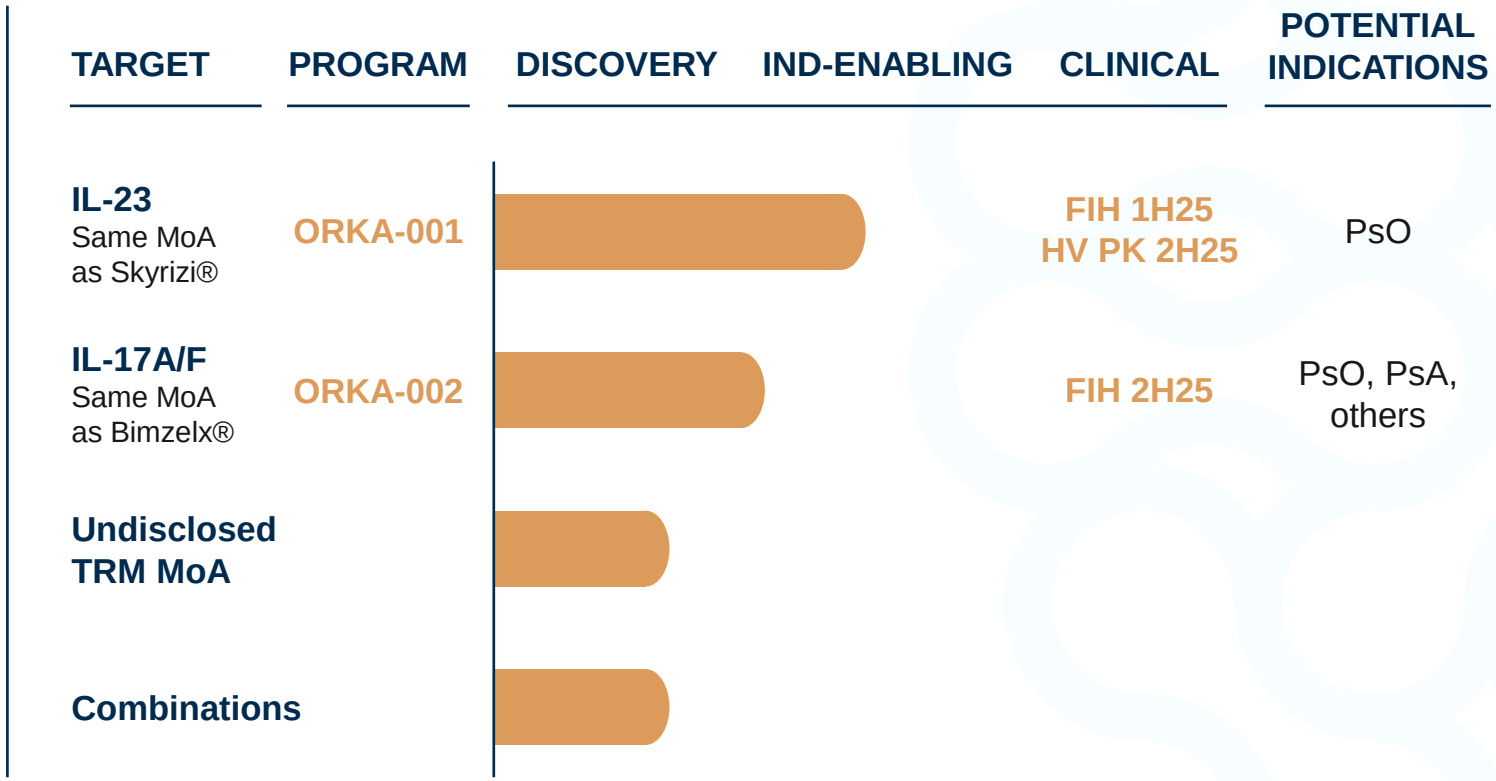
Market and industry data and forecasts used in this presentation have been obtained from independent industry sources as well as from research reports prepared for other purposes. Although we believe these third-party sources to be reliable, we have not independently verified the data obtained from these sources and we cannot assure you of the accuracy or completeness of the data. Forecasts and other forward-looking information obtained from these sources are subject to the same qualifications and uncertainties as the other forward-looking statements in this presentation. Statements as to our market and competitive position data are based on market data currently available to us, as well as management's internal analyses and assumptions regarding the Company, which involve certain assumptions and estimates. These internal analyses have not been verified by any independent sources and there can be no assurance that the assumptions or estimates are accurate. While we are not aware of any misstatements regarding our industry data presented herein, our estimates involve risks and uncertainties and are subject to change based on various factors. As a result, we cannot guarantee the accuracy or completeness of such information contained in this presentation.

Building best-in-class therapies for psoriasis and other diseases

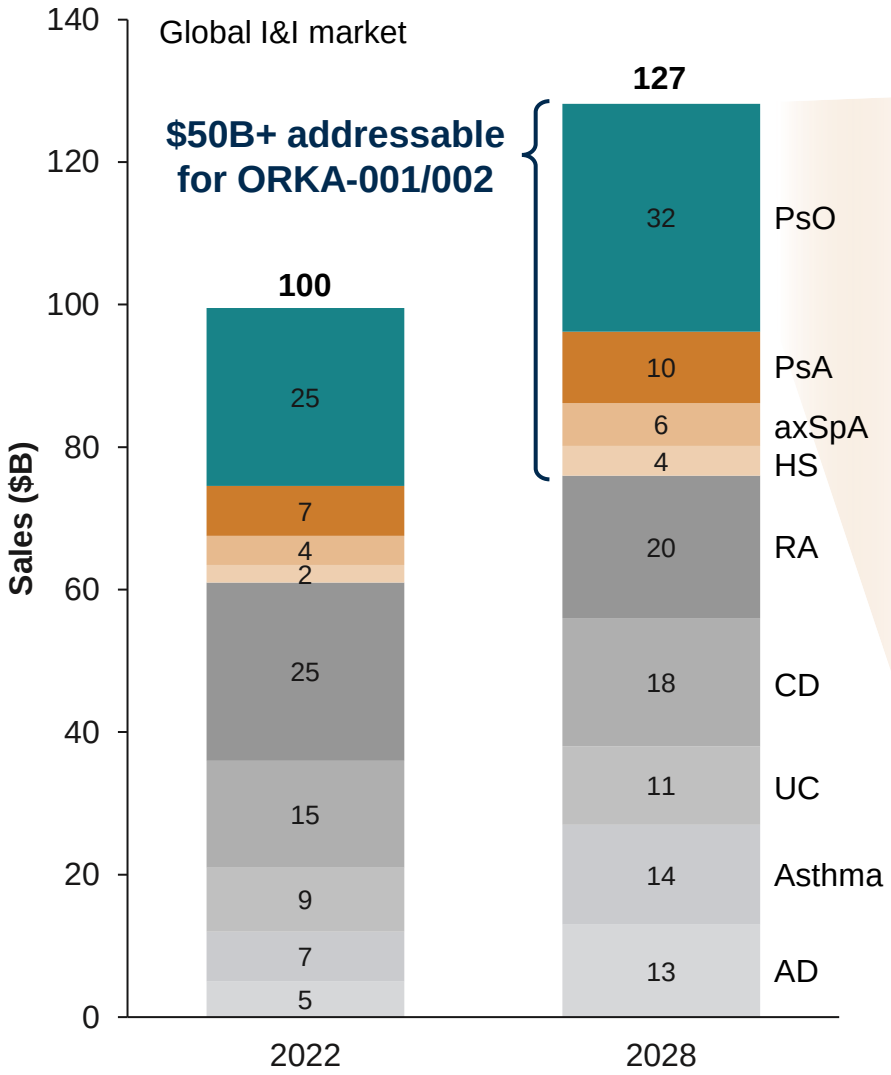
Our name – derived from ***or*, for "skin," and *arukah*, for "restoration"** – reflects our mission to deliver **best-in-class therapies for inflammatory skin diseases**

- Potentially **best-in-class half-life extended mAbs** designed to **maximize efficacy** with as little as **one dose per year**
- Targeting mechanisms with **proven efficacy and safety** involved in disease pathology and maintenance of tissue-resident memory T cells (TRM) **to treat and potentially cure disease**
- **Acquired rights to development candidates from Paragon Therapeutics,** an antibody discovery company founded by Fairmount, **following in the footsteps of Apogee and Spyre** which collectively raised >$700M in 2023

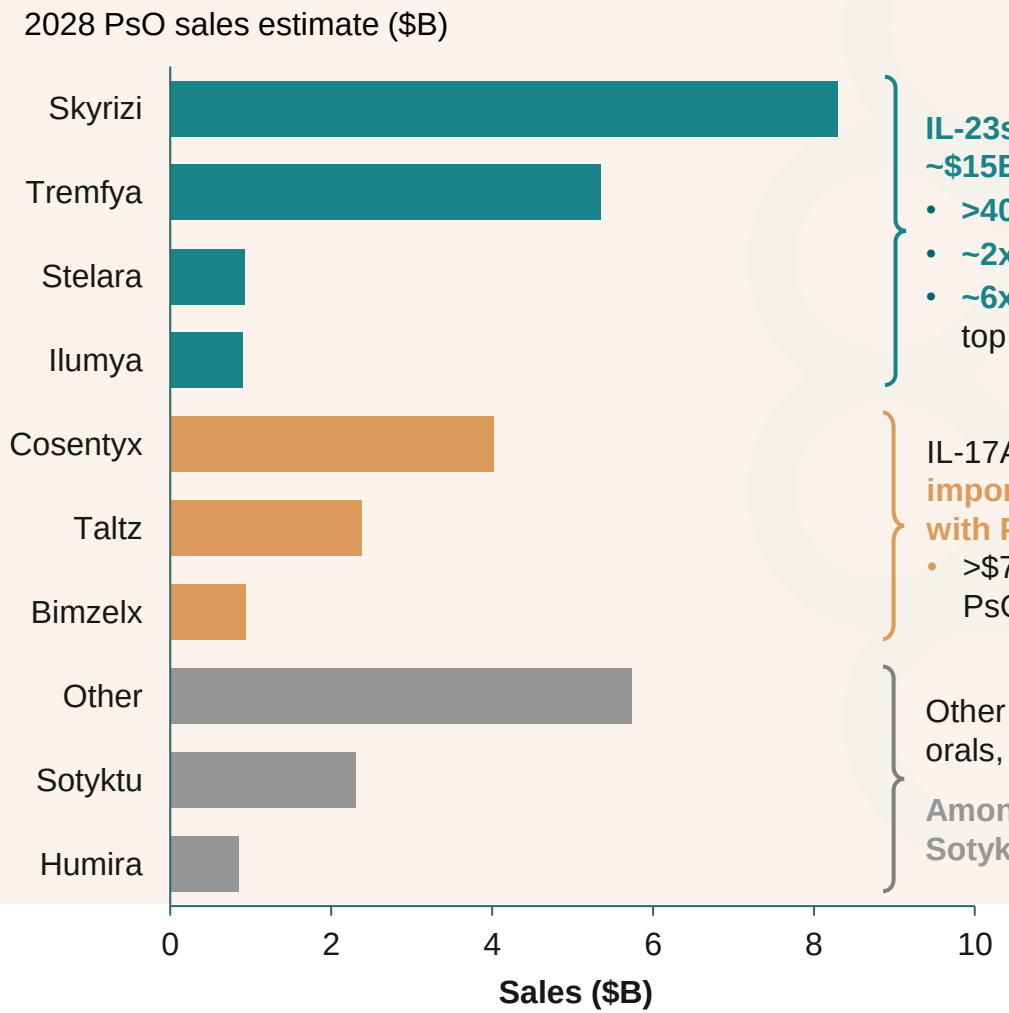


Notes: Oruka has an option to acquire exclusive worldwide rights from Paragon Therapeutics, Inc., for all programs, with IL-23 rights for all therapeutic indications outside of IBD. Abbreviations: FIH, first-in-human; HV, healthy volunteer; mAb, monoclonal antibody; MoA, mechanism of action; PK, pharmacokinetics; PsA, psoriatic arthritis; PsO, psoriasis

Co-lead programs target a $50B+ total market opportunity



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



IL-23s forecast to generate ~$15B in 2028 sales:

- **>40% of market**
- **~2x IL-17** sales
- **~6x TYK2** sales amongst top 10 therapies

IL-17A and IL-17A/F class **important for patients with PsA involvement**

- >$7.5B in 2028 sales in PsO alone

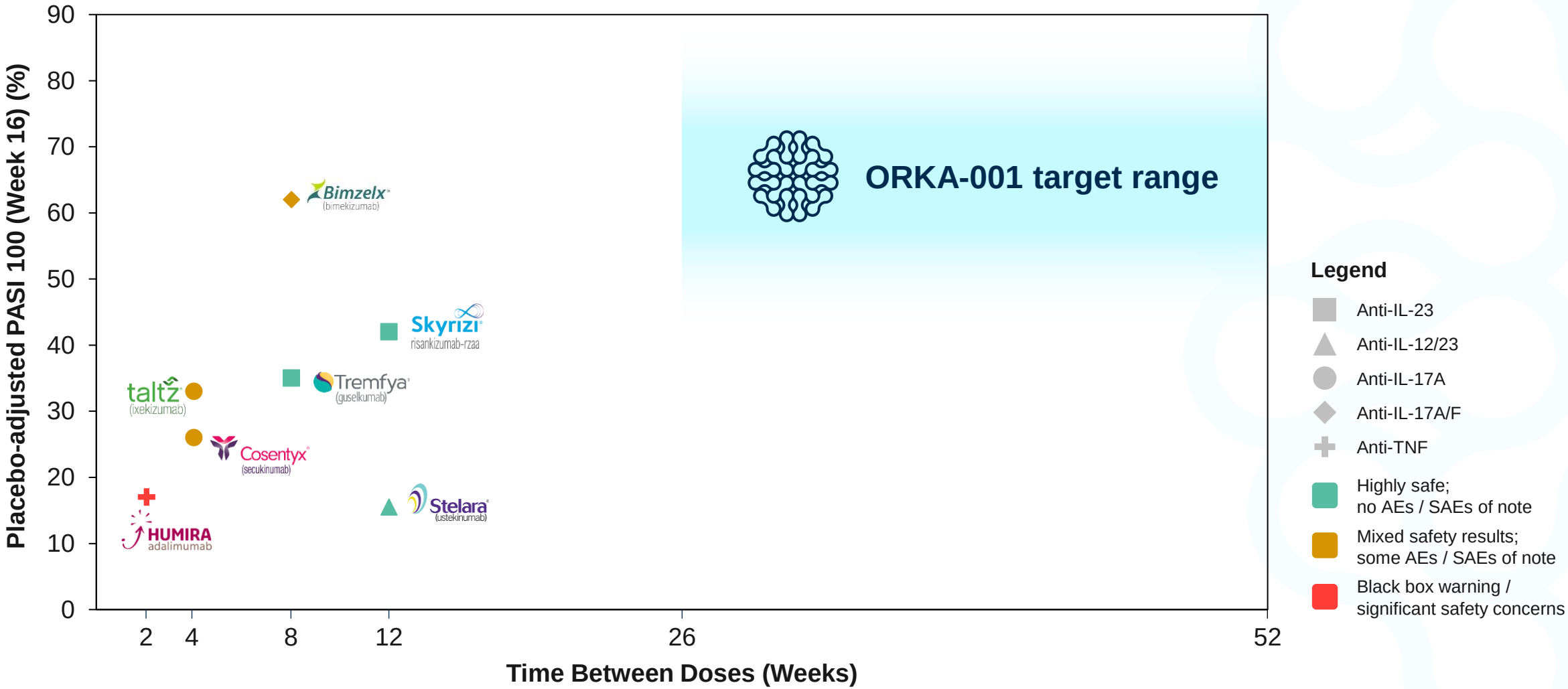
Other therapies, including orals, **are <20%** of market

Among TYK2s, only Sotyktu breaks into top 10

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

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

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



Sources: FDA and EMA Approval Labels

Perfecting the product profile in plaque psoriasis

1-2 doses per year

Enabled by half-life extension

Higher PASI 100

Higher exposure drives higher response

IL-23p19 safety profile

Strong safety precedent even at high peak exposures

Disease modifying

Evidence for disease modification via high exposure anti-IL-23

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

Similar epitope to Skyrizi (risankizumab) with equal or better potency

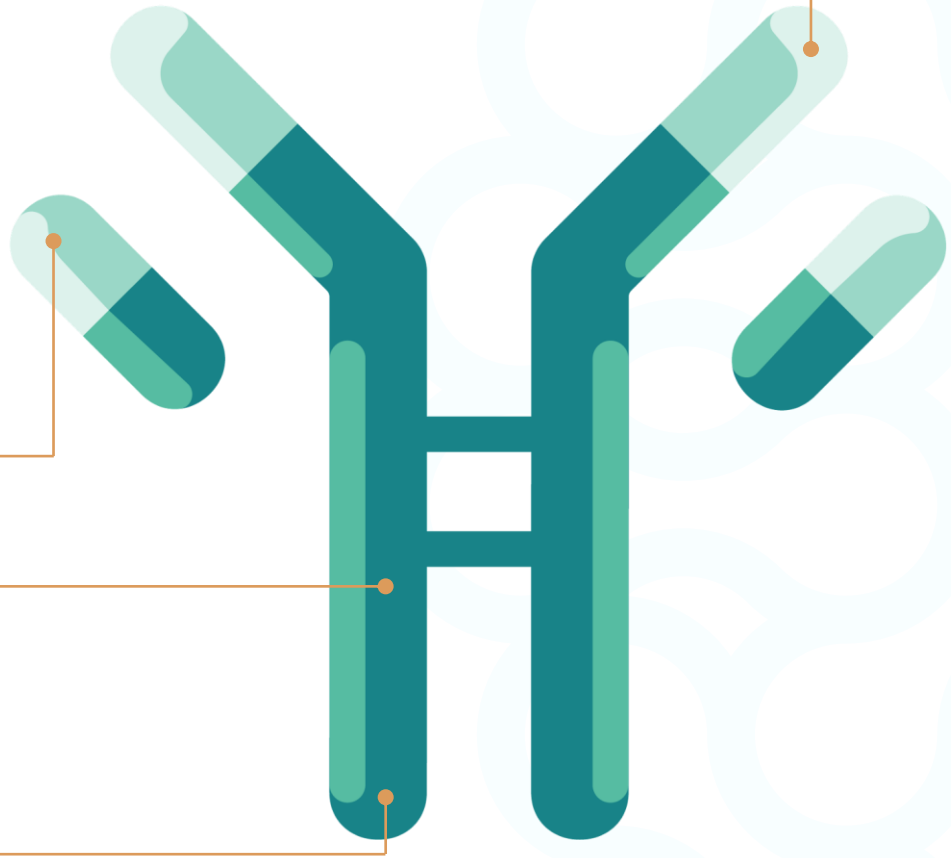
- Validated mechanism of action
- Binds **specifically to IL-23p19** (not IL-12/23 p40)
- **K_D < 20 pM**
- Predicted **equivalent safety**
- Predicted to **meet or beat efficacy**

Novel IP for composition of matter into 2040s

Half-life extension through validated Fc modification

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

Effector-null human IgG1 Fc



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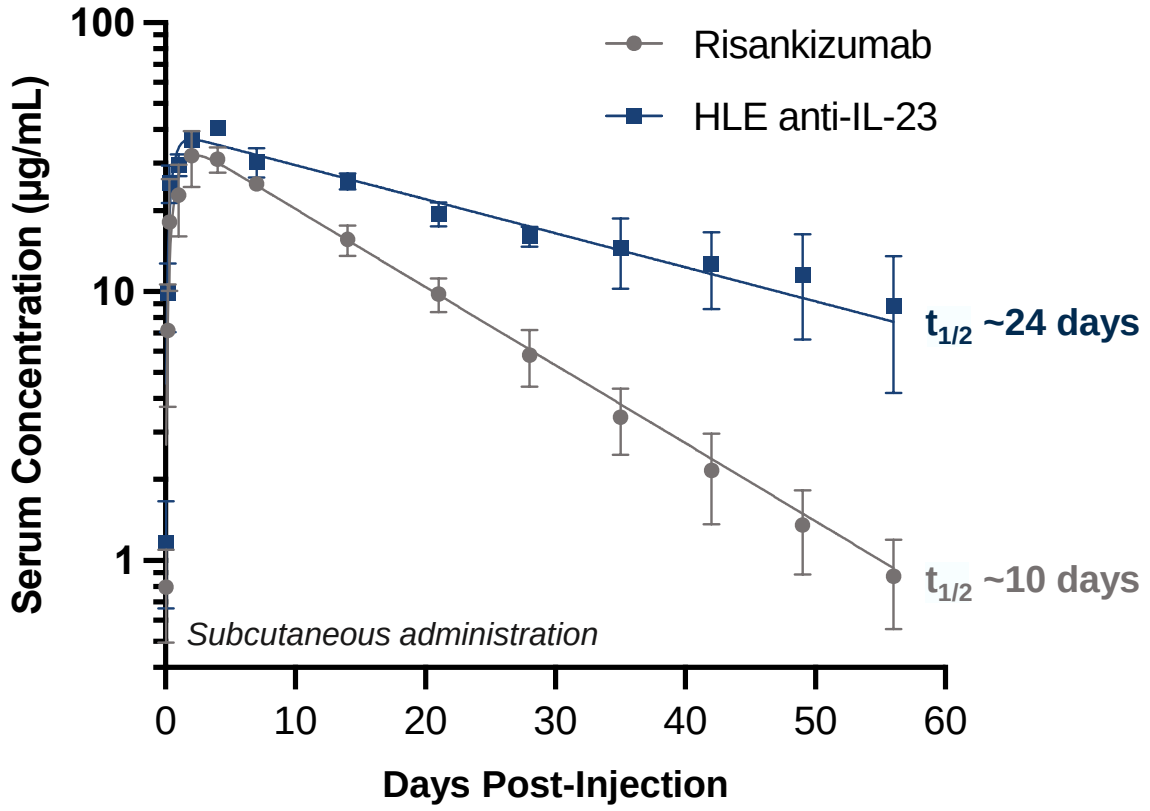
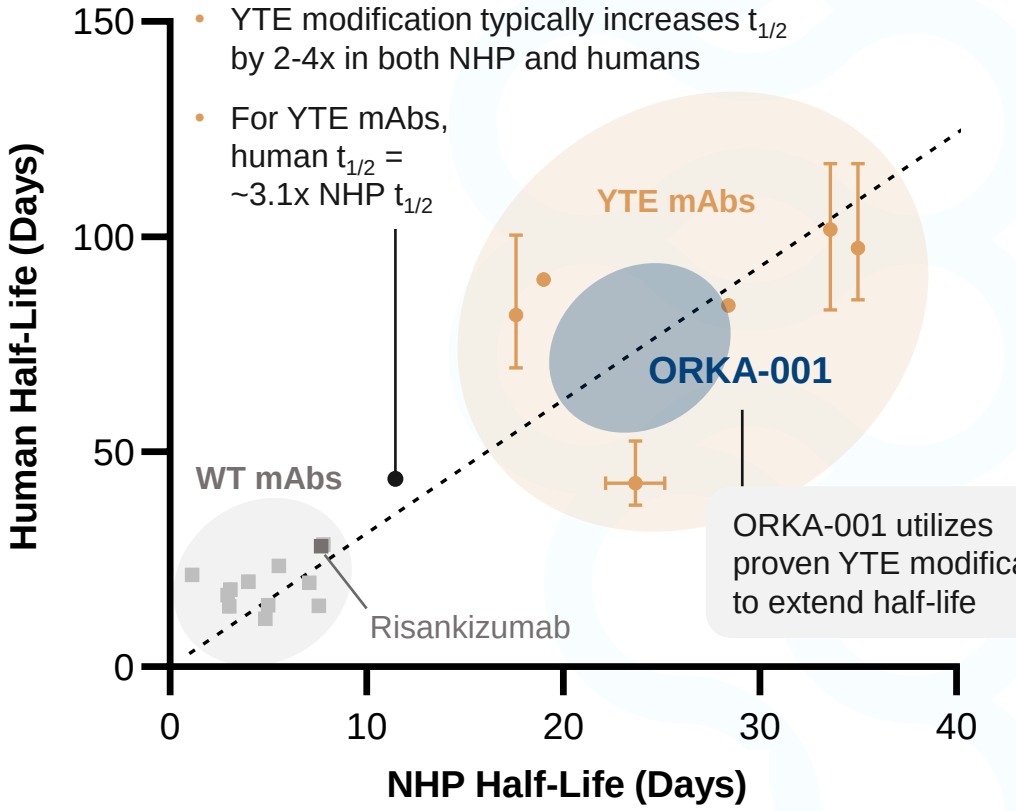
Notes: Oruka holds worldwide rights to all therapeutic indications outside of IBD

Clinical experience with YTE predicts significant half-life extension for ORKA-001

2.4x longer half-life with PoC mAb vs. Skyrizi in NHPs



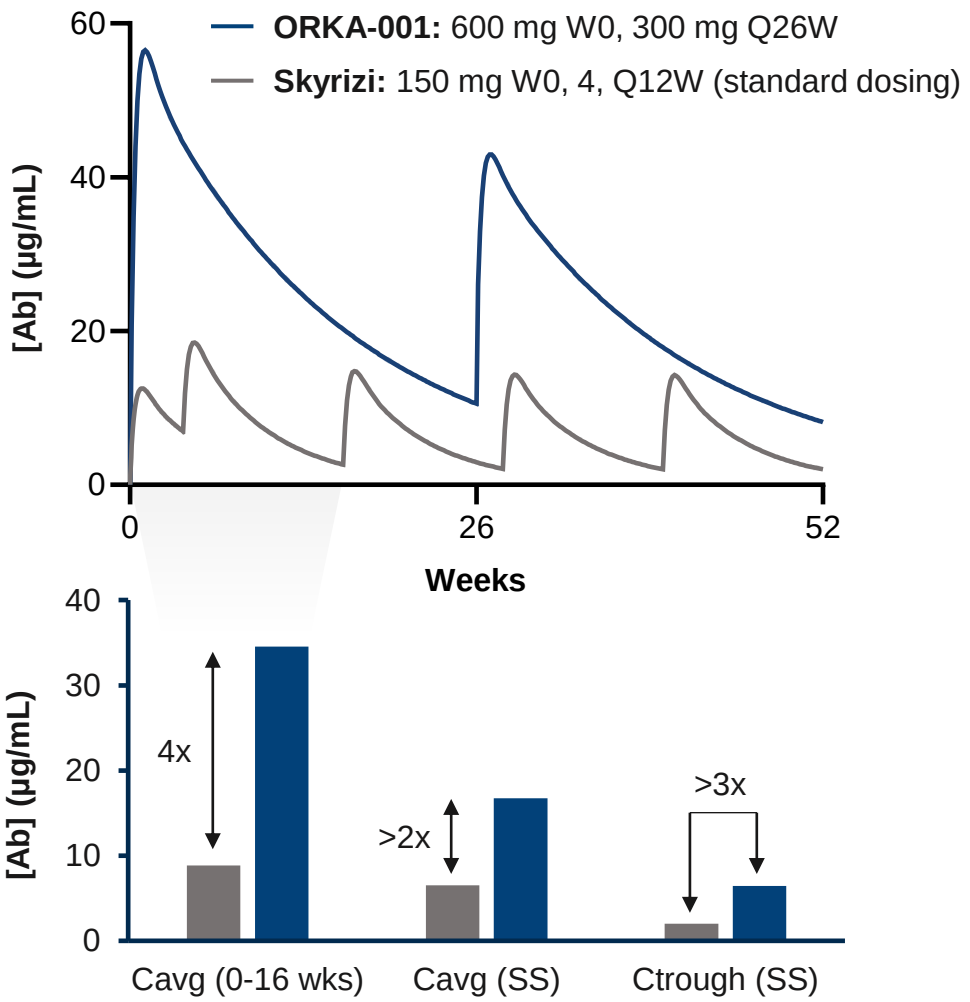
Implies ORKA-001 could have a half-life of ~74 days in humans



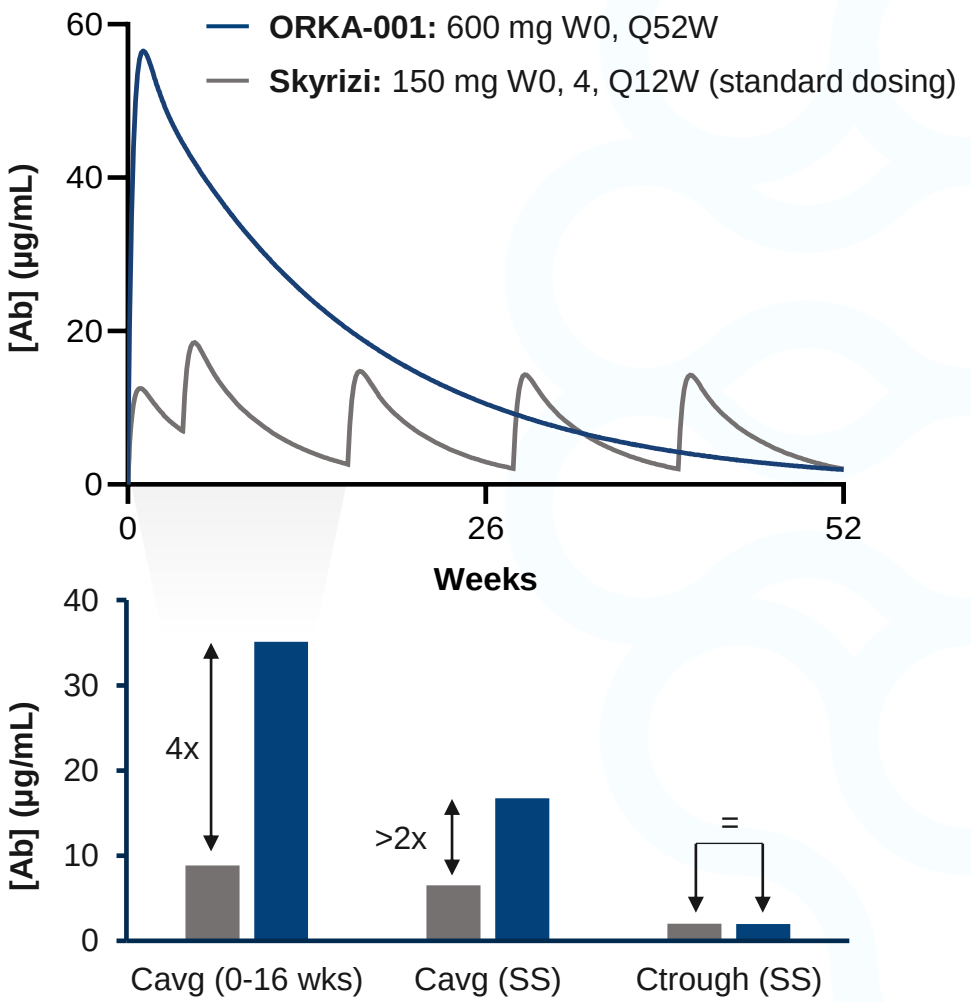
Notes & Sources: Internal data (left); NHP datapoints associated with ADA excluded from analysis; HLE indicates extended half-life; sources on file for other wildtype (WT) and YTE mAbs (right); Skyrizi BLA review notes a ~7.2- to 7.7-day half-life in NHPs, which translated to ~28-day half-life in humans

ORKA-001 could exceed Skyrizi exposures at 1-2 doses per year

Base case – 2 maintenance doses per year



Upside case – 1 maintenance dose per year

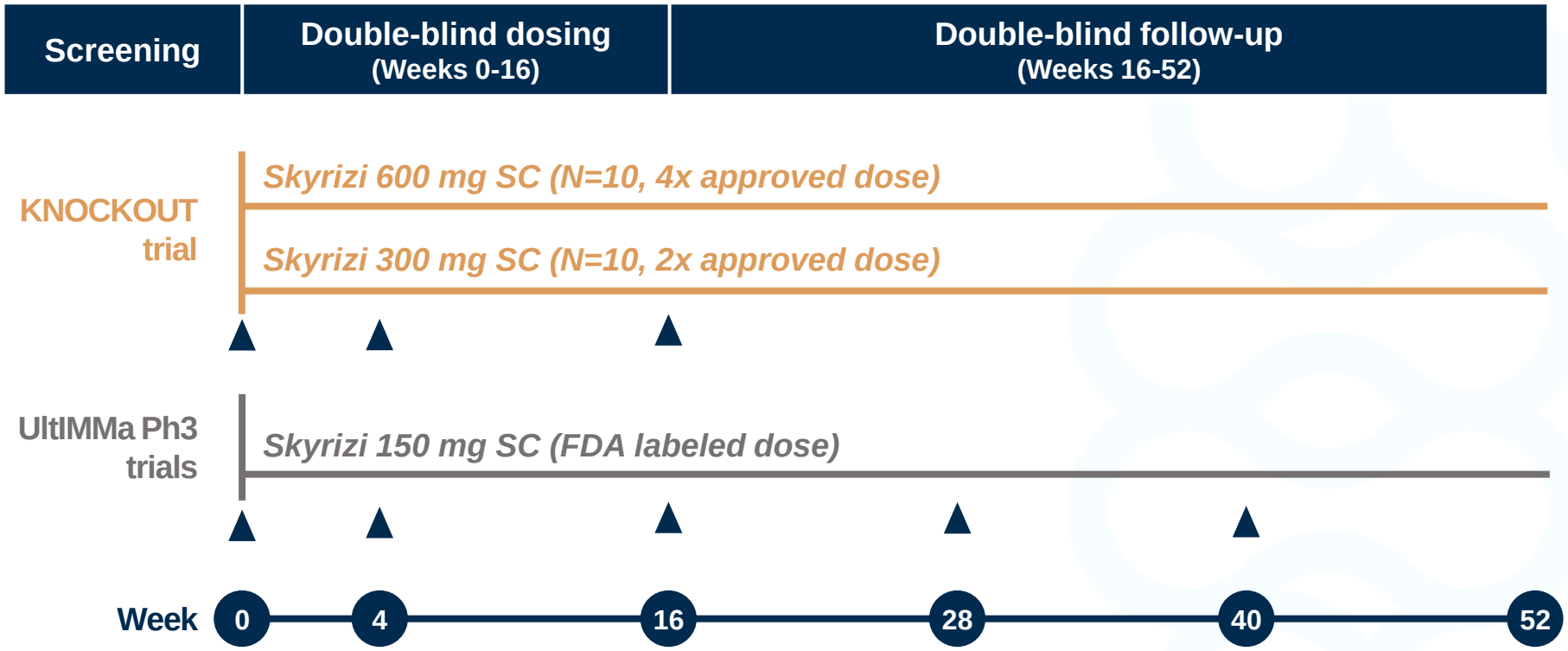


Sources: Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi

KNOCKOUT study tested higher anti-IL-23 exposures in PsO

KNOCKOUT inclusion criteria

- Adults
- Chronic, stable plaque psoriasis
  - ≥ 6 months
  - PASI ≥ 12
  - ≥ 10% BSA
- No prior Skyrizi use



Goal to determine if **high-dose IL-23 inhibition at 2-4x the approved Skyrizi dose could result in higher PASI 100 rates and long-term remissions by eliminating TRMs**

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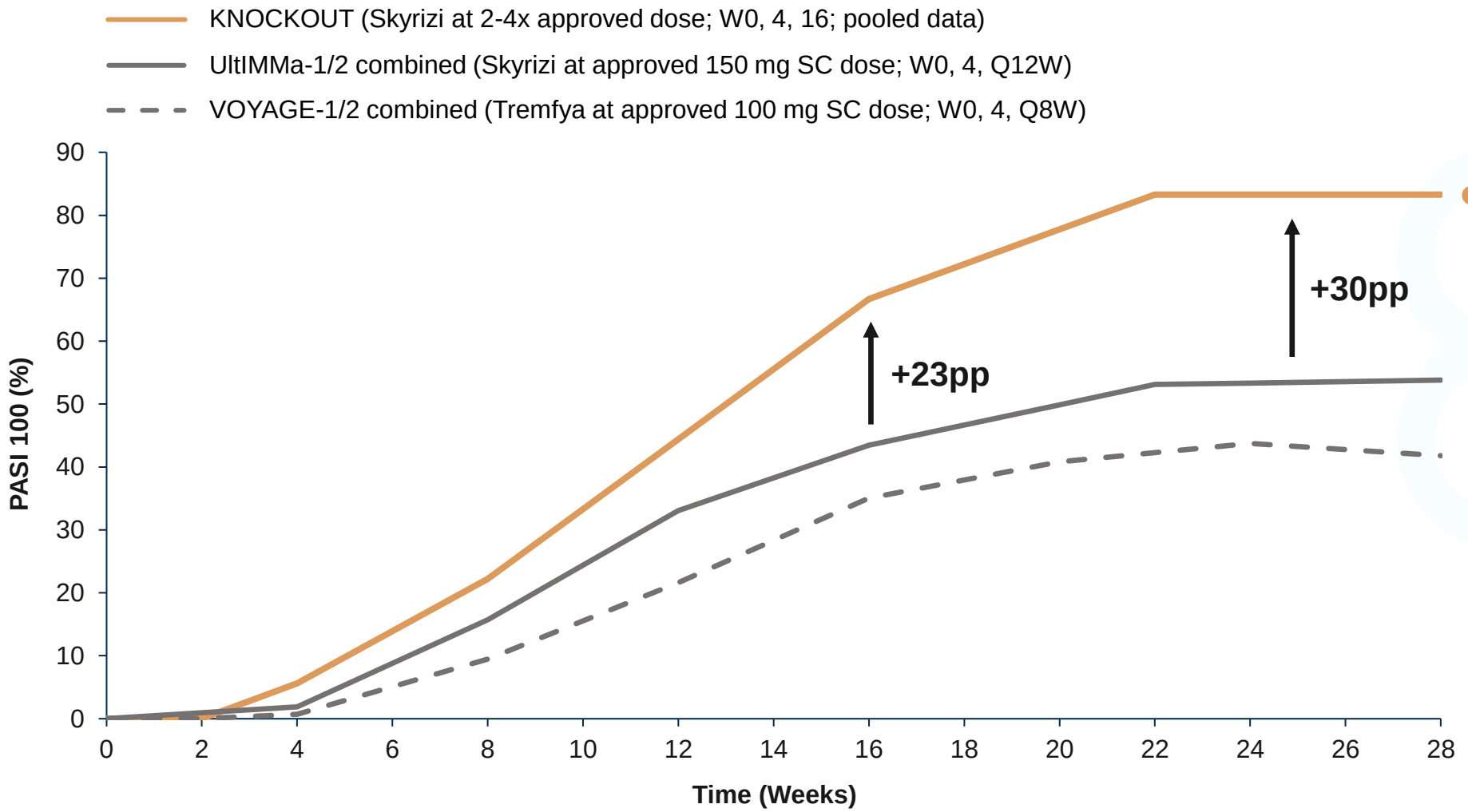
Sources: 2018 Gordon (Lancet); 2023 Blauvelt (WCD presentation)

KNOCKOUT extended exposure-response relationship – higher exposures drove higher PASI 100

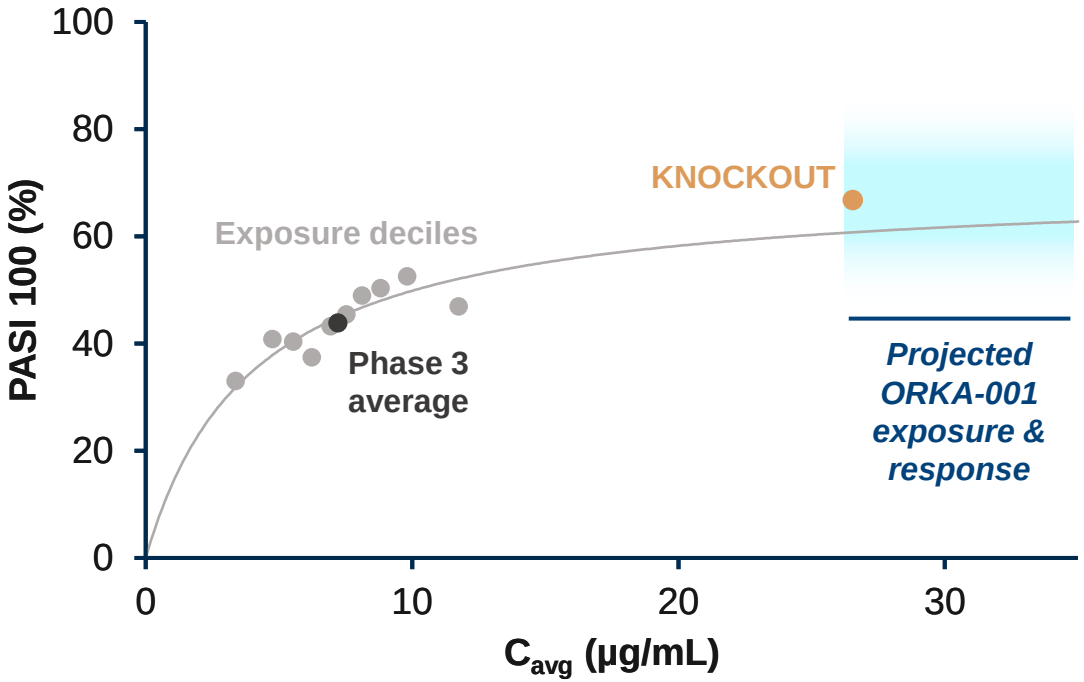


Ongoing follow-up to test whether **higher exposures can drive durable remissions** by eliminating TRM cells from the tissue

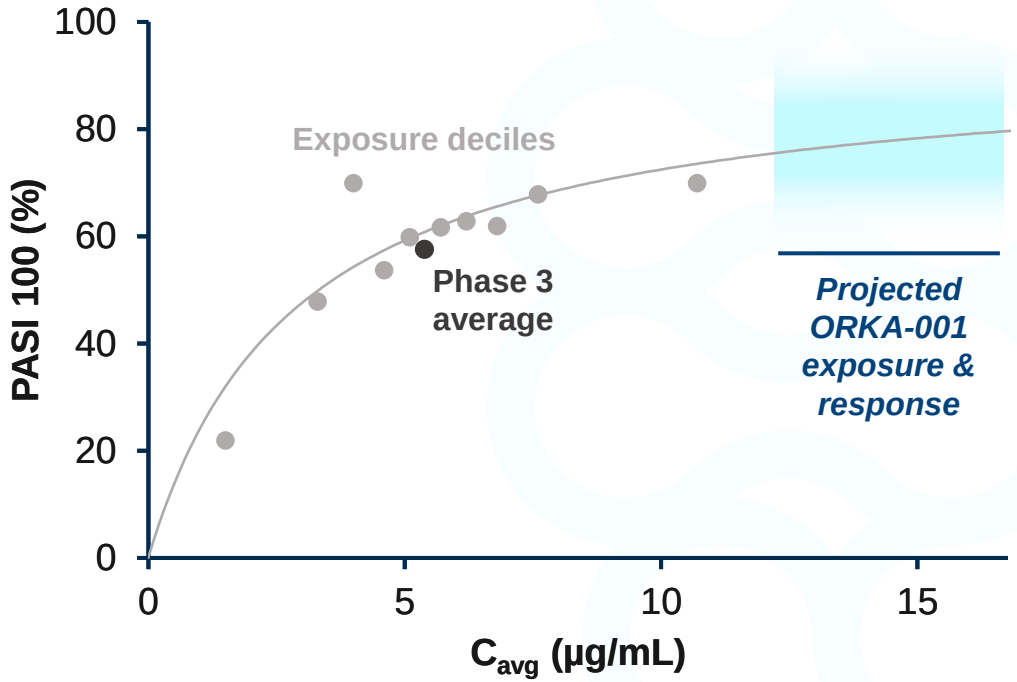
Notes: Cross-trial comparisons. Not placebo controlled. KNOCKOUT data consists of pooled analysis of 300 and 600 mg dose levels
Sources: 2017 Blauvelt (JAAD); 2017 Reich (JAAD); 2018 Gordon (Lancet); 2023 Blauvelt (WCD presentation)

ORKA-001 projected to extend exposure-response relationship established by Skyrizi Phase III and KNOCKOUT

Induction phase (0-16 weeks)



Steady-state phase (40-52 weeks)



Skyrizi exposure-response data indicates that **projected ORKA-001 exposures could result in 10-20% higher PASI 100 rates than Skyrizi**

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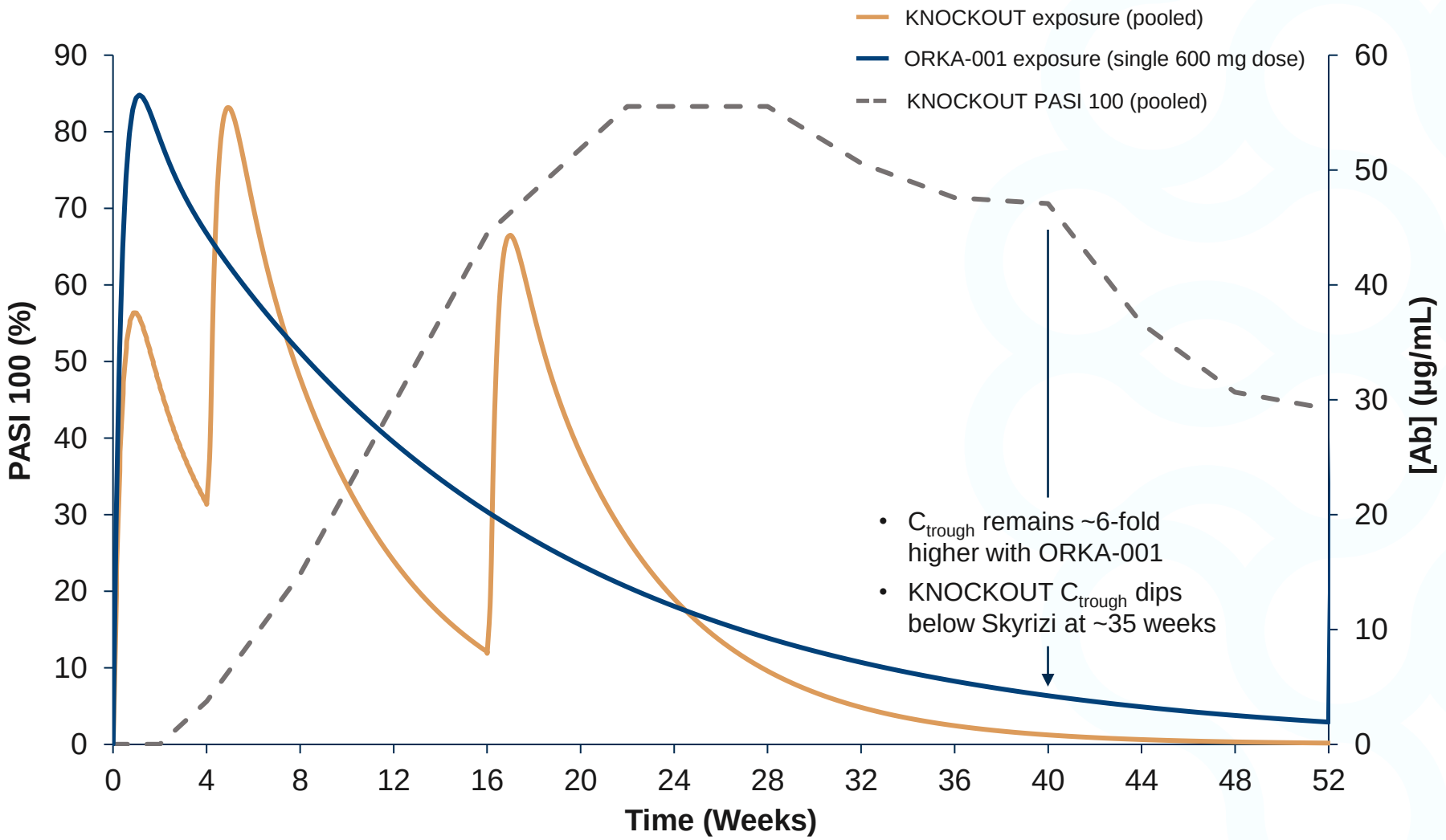
Notes & Sources: Adapted from 2019 Khatri (Clin Pharmacol Ther) and Skyrizi BLA Multi-disciplinary Review (Fig. 20); KNOCKOUT pooled PASI 100 from 2023 Blauvelt (WCD presentation); gray dots represent observed PASI 100 rates within each C_{avg} decile for Skyrizi; gray lines represent model-estimated 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

ORKA-001 at one dose per year could match KNOCKOUT early exposures and greatly exceed trough levels

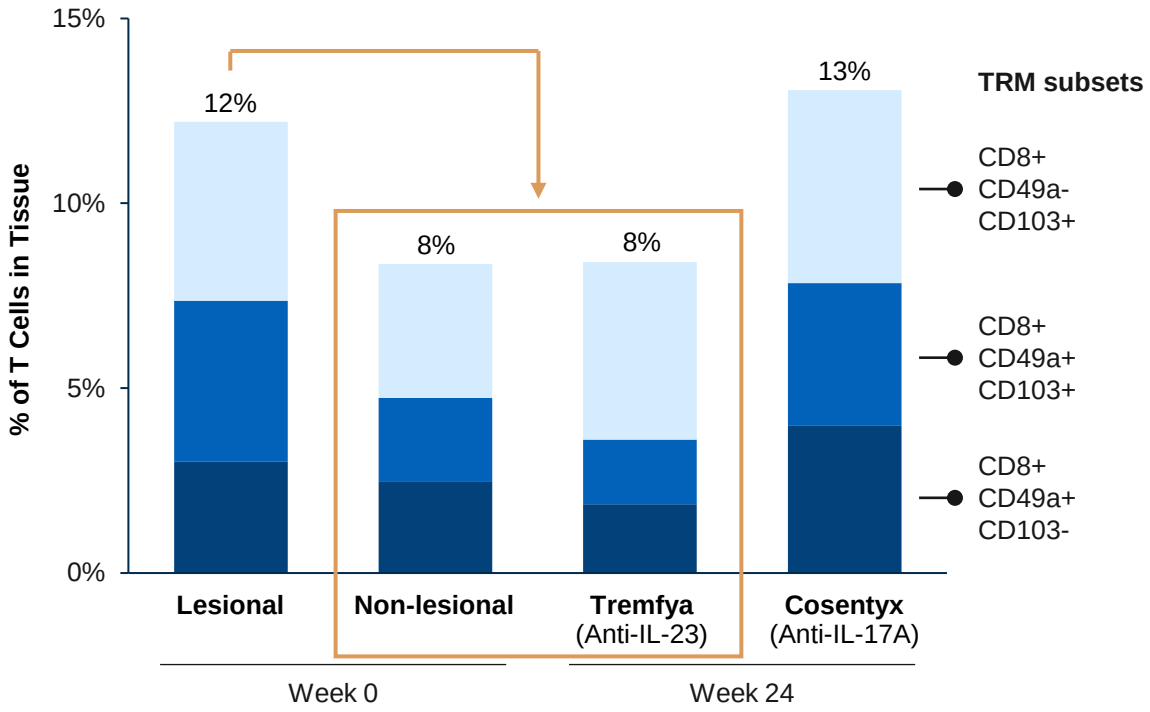
- Patients in KNOCKOUT received **2-4x approved Skyrizi** dose at 0, 4, and 16 weeks
- ORKA-001 could exceed these exposures **at an achievable dose for a Q1Y regimen**
- ORKA-001 could have **superior maintenance of response** late in the dosing interval via higher C_{trough} levels



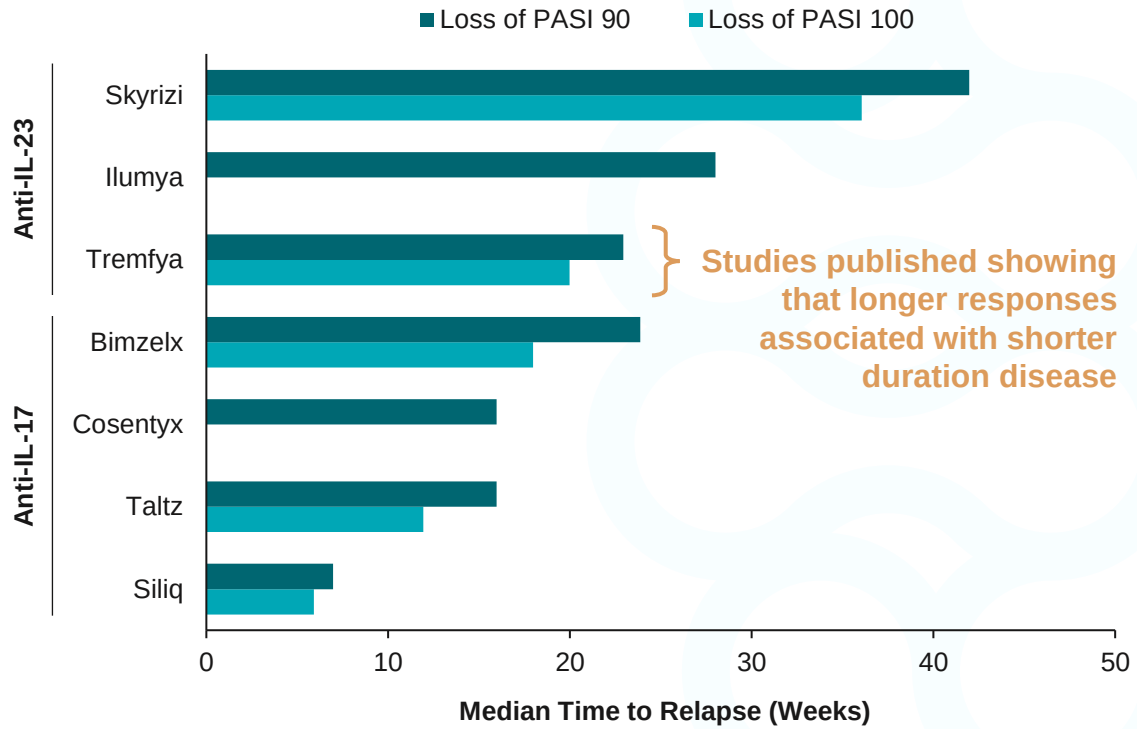
Notes & Sources: KNOCKOUT efficacy data from 2023 Blauvelt (WCD presentation); KNOCKOUT and ORKA-001 exposure from Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi

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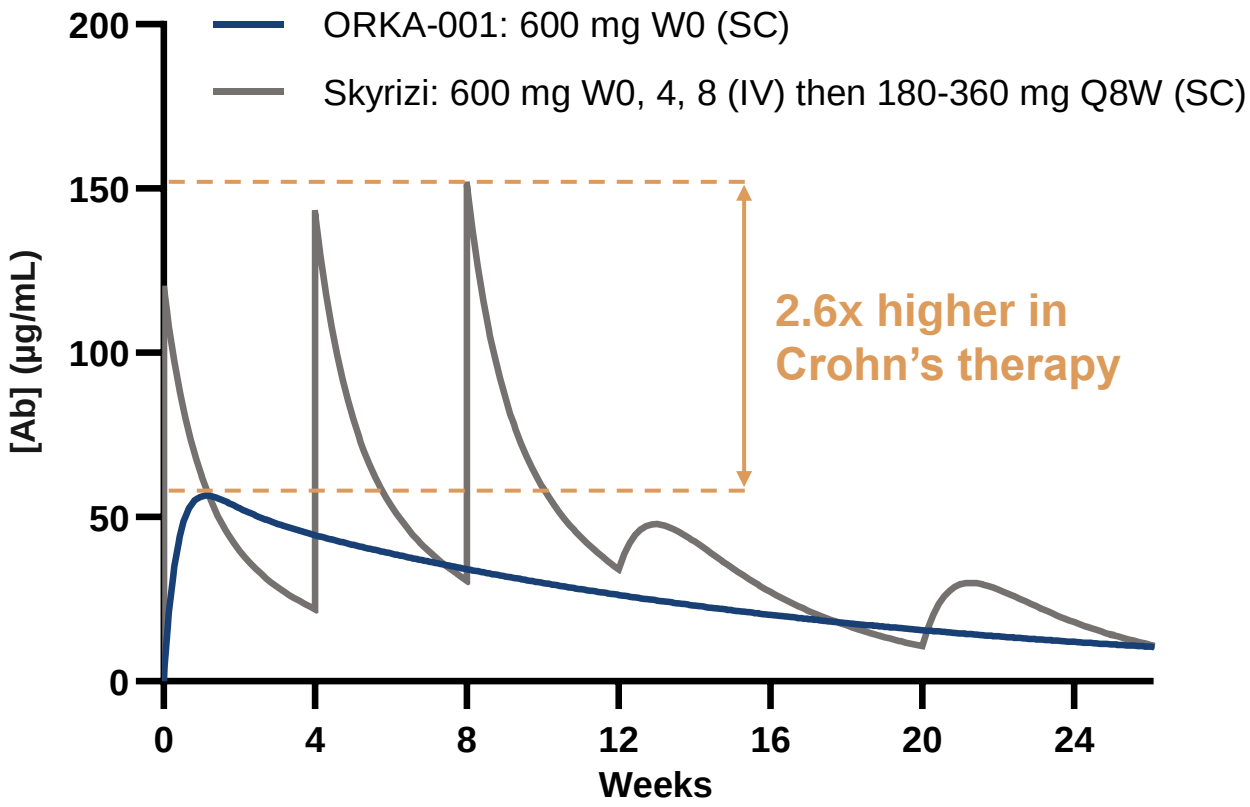
Notes & Sources: Charts adapted from 2021 Mehta (J Invest Derm) (Fig. 5b) and 2022 Regnault (Am J Clin Dermatol) (Fig. 2b); 2022 Blauvelt (J Psoriasis Psoriatic Arthritis); 2023 Chiu (J Am Acad Dermatol). Abbreviations: TRM, tissue-resident memory T cell

Safety of peak exposures established by Crohn's dose regimen



- **Peak exposures** with highest ORKA-001 proposed dosing are **less than ½ what is routinely used in Crohn's**
- **No correlations at patient level between exposure and safety** signals for Skyrizi across 1,000s of patients dosed in derm and IBD
- **Very uncommon to have clinical precedent** in large numbers of patients for safety of higher exposures

*"**You literally can't overdose this drug**…patients take two shots on accident and they're fine"* – U.S. KOL

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Notes & Sources: Oruka modeling based on internal data and published pharmacokinetic model for Skyrizi; modeled Skyrizi exposure reflects approved regimen in Crohn's disease

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

	Base case scenario	Upside scenario
Maintenance dosing	**Twice yearly**	**Once yearly**
PASI 100	**Match or exceed Skyrizi**	**Highest observed to date** (as in KNOCKOUT study)
Added benefit	Potential for **patient-specific dosing to extend interval**	**Modify and potentially cure disease** in some patients
	Best-in-class profile	*Paradigm-changing*

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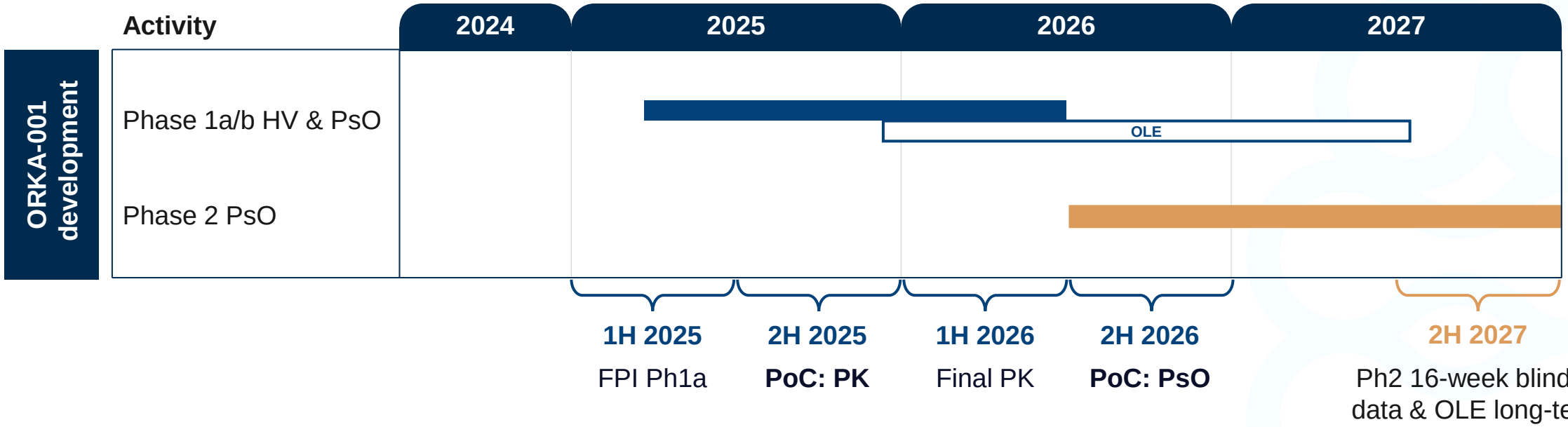
Development path sets up a catalyst-rich next 3 years



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

- **PoC 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**

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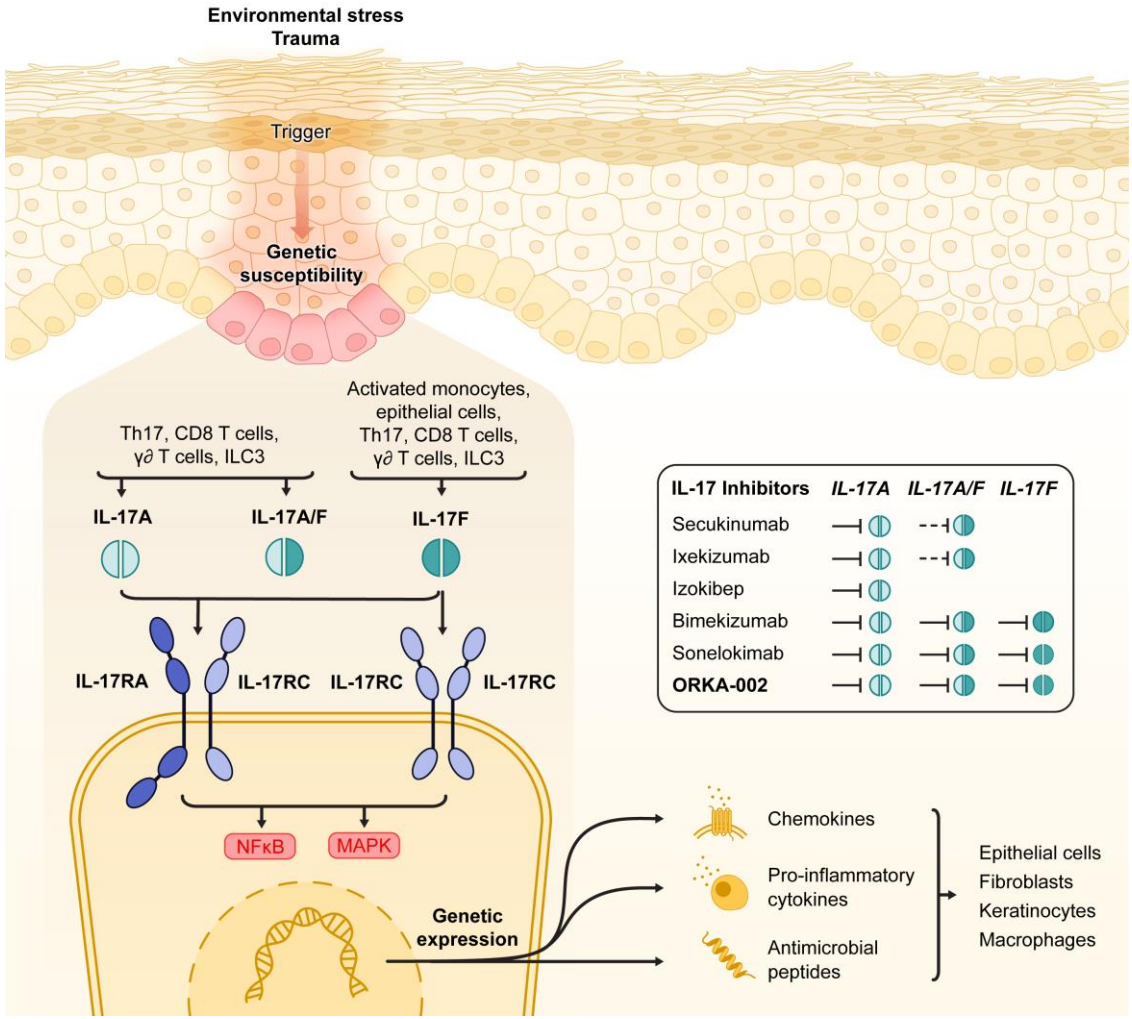
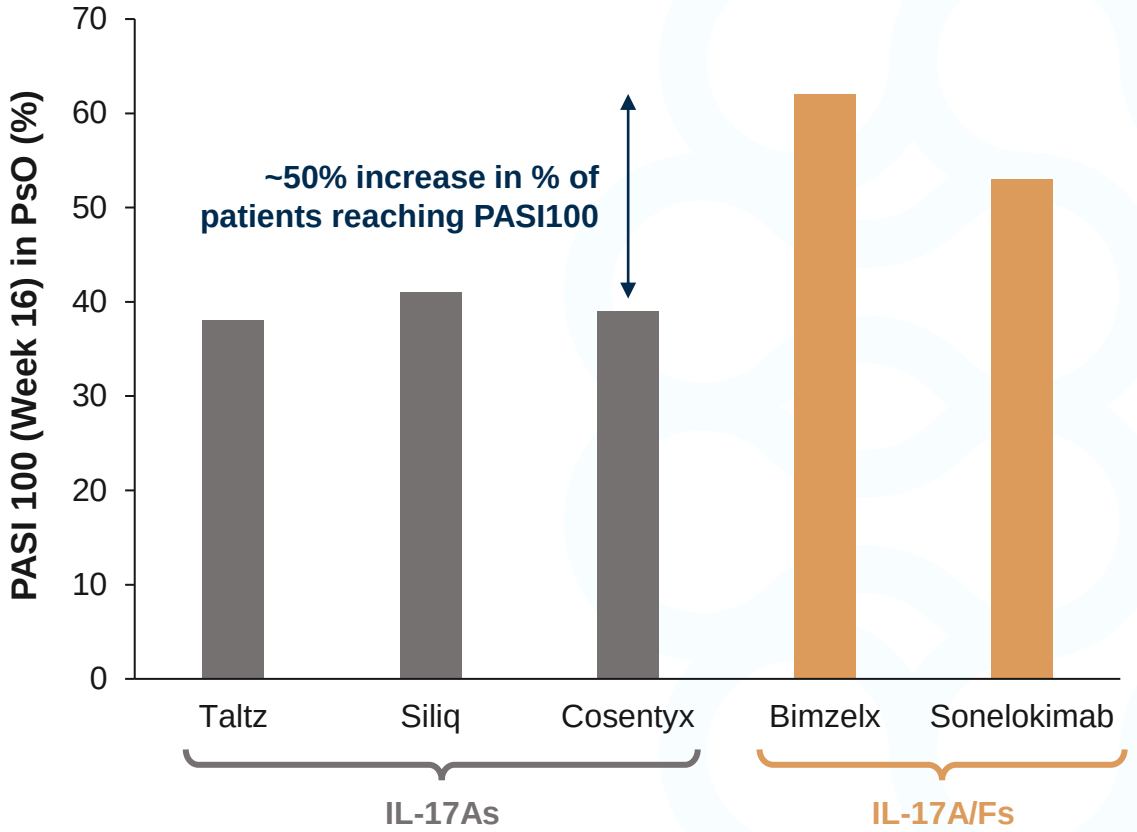
Notes: Average time from FIH to BLA/NDA reflects average of Skyrizi, Tremfya, Bimzelx, and Sotyktu
Abbreviations: FPI, first patient in; OLE, open-label extension

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

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



Superiority of IL-17A/F in PsO – the largest target market



Superior efficacy in other indications as well (e.g., PsA, HS, axSpA)

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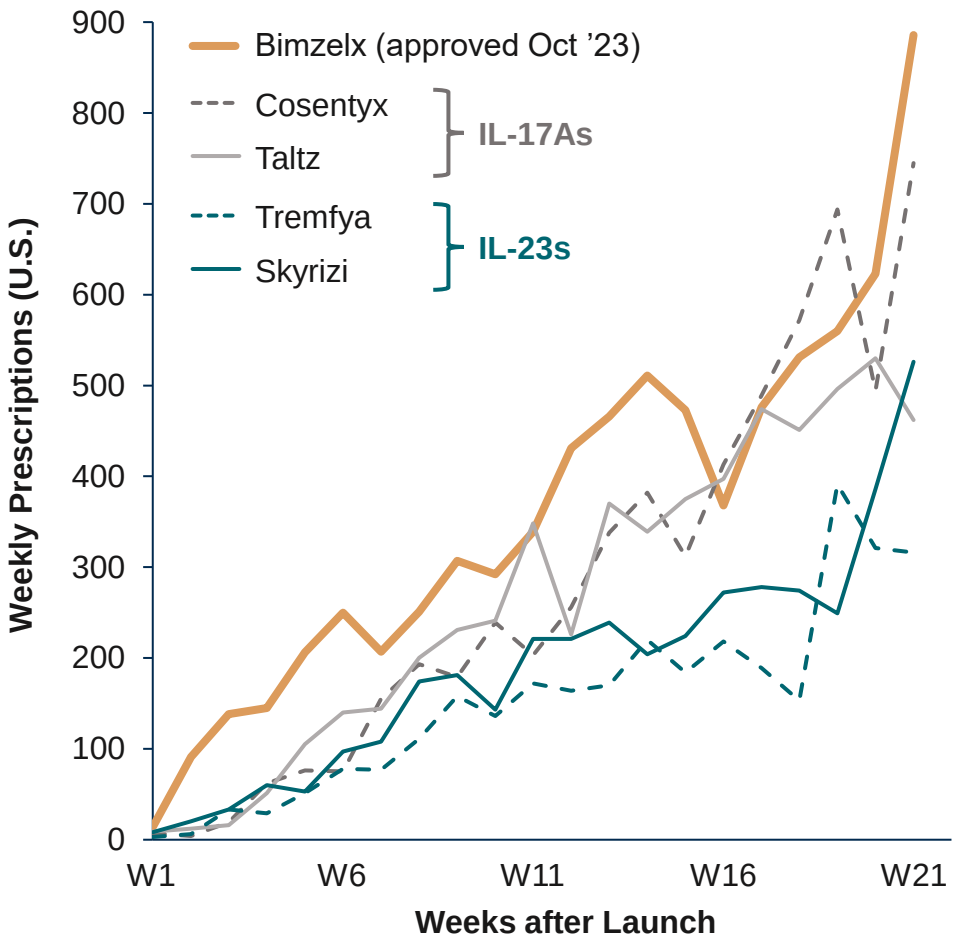
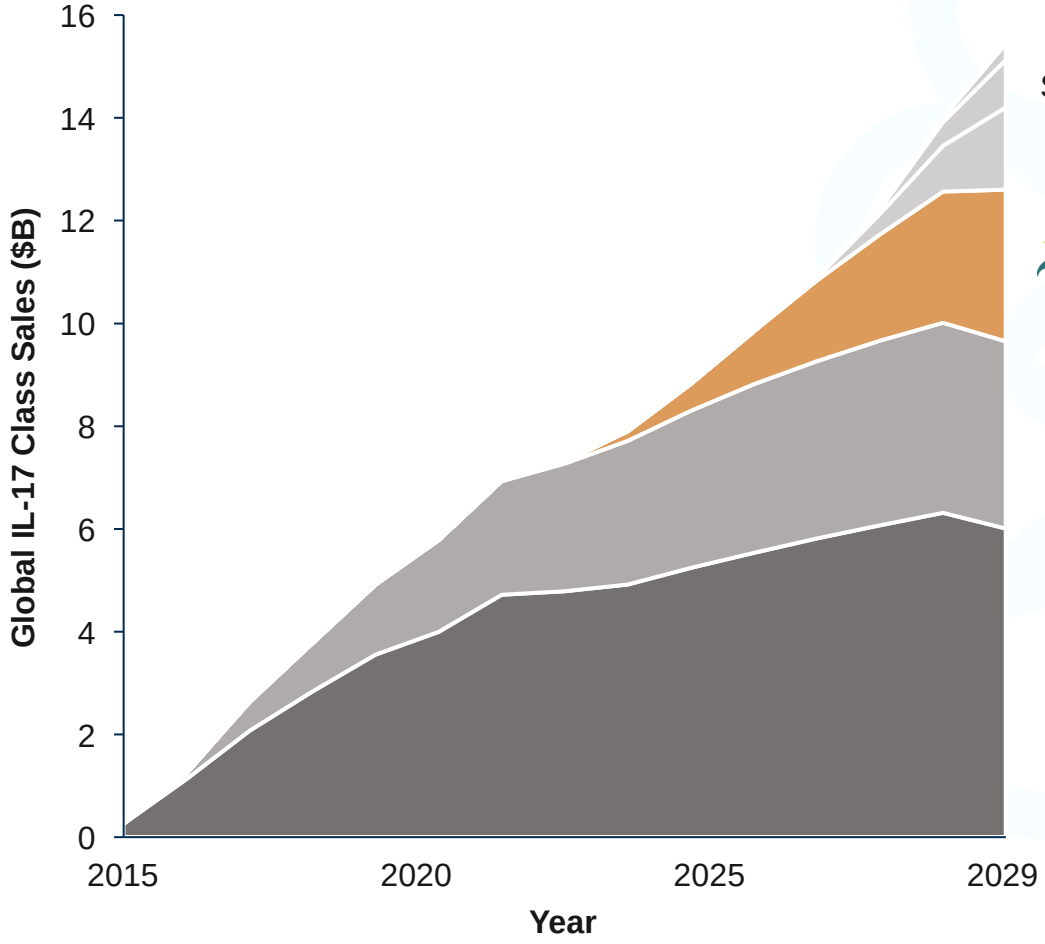
Notes & Sources: Figure adapted from 2020 Brevi (Front Immunol.); PASI 100 reflects average of Ph3 trials (best-performing group in Ph2b trial for sonelokimab), not placebo adjusted; FDA and EMA Approval Labels; UCB Press Releases; 2023 Venhoff (Lancet Rheum)

Bimzelx is showing signs of massive peak sales potential

Very strong launch in PsO shows potential, and ability to differentiate in this market



Capturable market of $15B+ across all indications by 2030



Therapy	Target
DC-806	IL-17A
Sonelokimab	IL-17A/F
Izokibep	IL-17A/A
Bimzelx® (bimekizumab-bkzx)	IL-17A/F
taltz® (ixekizumab)	IL-17A
Cosentyx® (secukinumab)	IL-17A

Notes: x-axis marks end of week
Sources: Jefferies (based on IQVIA data); Cowen; GlobalData

The two leading IL-17A/Fs leave room for improvement

		Bimzelx® (bimekizumab-bkzx)	Sonelokimab	ORKA-002 (TPP)
	Format	Full-length, dual targeting mAb	Trivalent structure with nanobodies targeting IL-17A/F, IL-17F, and albumin	Full-length, dual targeting, half-life extended mAb
PsO regimen	**Doses per year (maintenance)**			
	Single SC injection	✗	✓	✓
Safety and efficacy	**Clear dose response**	✓	✗	Expected **similar to Bimzelx**
	Minimal risk of neutralizing ADAs	~15-25% of patients had ADAs; **no clinical impact**	~30% of patients had ADAs in Phase 1; TBD in late-stage trials	Expected **similar to Bimzelx**

Sources: 2020 Adams (Front Immunol.); 2017 Glatt (BJCP); 2019 Svecova (JAAD); FDA / EMA Approval Labels; Company websites; Press releases

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

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

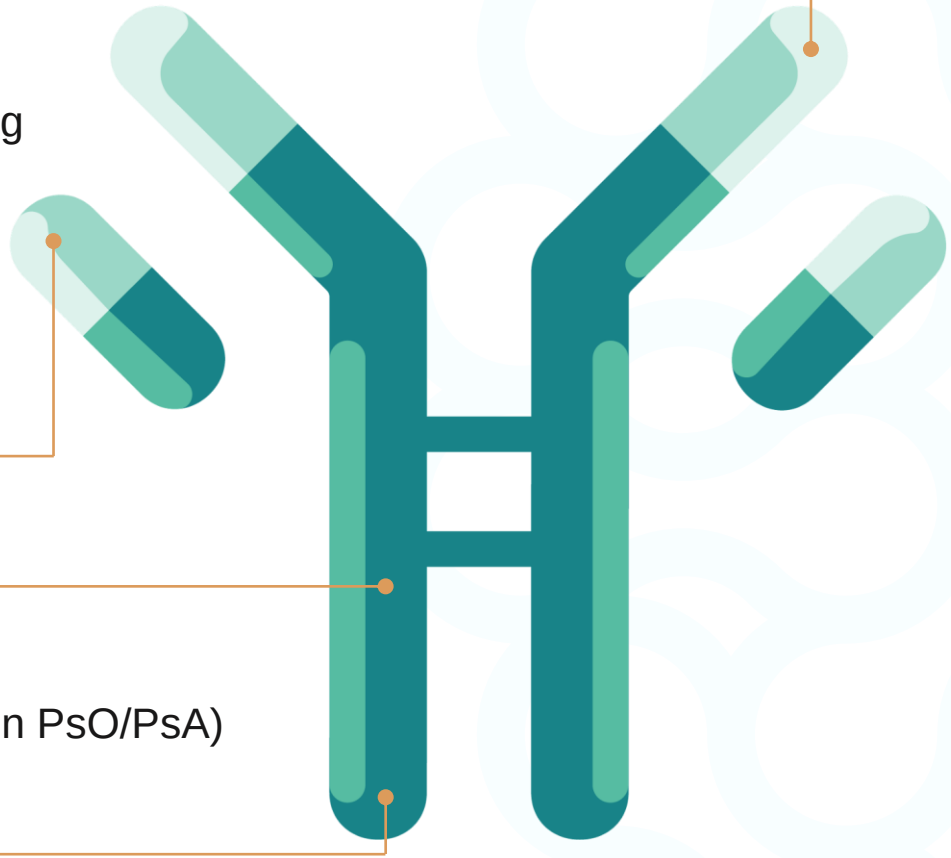
- Validated mechanism of action
- Binds **IL-17A and IL-17F** to prevent homodimer and heterodimer signaling
- **Equal or greater affinity** vs. bimekizumab
- Predicted **equivalent safety**
- Predicted to **meet or beat efficacy**

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



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 inhibition, with **$15B+ in future market potential**

Best profile

Skyrizi-like dosing intervals in a convenient single injection while minimizing biological risk by pursuing the Bimzelx MoA

Limited competition

Only two clinical stage IL-17A/F dual inhibitors, with lengthy timeline to biosimilar entry

Rapid development path

Ph1 HV study de-risks PK and dosing interval, with potential for **rapid development path** (Bimzelx took ~6 years from IND to BLA)

Corporate

Single fundraise could support multiple inflection points

$275M raise supports company through 2027, more than one year past multiple inflection points

Building rapidly with backing from Paragon

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Lawrence Klein
CEO

Joana Goncalves
CMO

Arjun Agarwal
SVP, Finance

Laura Sandler
SVP, Operations

Christopher Finch
VP, Corporate Development & Strategy

Eugenia Levi
VP, Medical Affairs

Christina Liang
Sr. EA & Operations Manager

Andrew Blauvelt
Chair of Scientific Advisory Board

Board of Directors

Peter Harwin
Managing Member, Fairmount

Sam Kulkarni
CEO & Chairman, CRISPR Therapeutics

Cameron Turtle
CEO, Spyre Therapeutics

Carl Dambkowski
CMO, Apogee Therapeutics

Lawrence Klein
CEO, Oruka Therapeutics

PARAGON THERAPEUTICS

FAIRMOUNT

CRISPR THERAPEUTICS

Celgene

NOVARTIS

Protagonist Therapeutics

LEO

bridgebio

APOGEE THERAPEUTICS

SPYRE THERAPEUTICS

ARCA and Oruka transaction summary

Overview

- **Transaction**: Transaction between ARCA Biopharma, Inc. (***ARCA***), including its wholly owned subsidiaries Atlas Merger Sub Corp. (***First Merger Sub***), Atlas Merger Sub II, LLC (***Second Merger Sub***), and Oruka Therapeutics, Inc. (***Oruka***)
- **Transaction Structure**: ARCA to acquire 100% of Oruka equity interests in reverse-triangle merger with Merger Sub, with Oruka surviving the merger as a wholly owned subsidiary of ARCA (followed by merger of Oruka with and into Second Merger Sub)
- **Rebrand**: Post-closing, ARCA will be renamed Oruka Therapeutics, Inc.
- **Interim Operating Covenants**: Customary interim covenants that limit both Oruka and ARCA to ordinary-course operations between signing and closing, subject to certain exceptions
- **Survival**: No survival of reps and warranties
- **Director / Officer Indemnification**: Oruka (post-closing) will be obligated to maintain indemnification of D&Os for at least 6 years post-closing. ARCA (pre-closing) required to procure six-year D&O insurance tail policy
- **Outside Date**: Six months from execution, with possible 60-day extension if Form S-4 is not effective
- **Timing**: Closing expected to occur during third quarter 2024
- **Post-Closing Shares Outstanding**: On an as-converted basis and after accounting for these transactions, the total number of shares of common stock of the company outstanding post-closing is expected to be approximately 596,040,033

Post-Closing Ownership; Closing

- **Post-Closing Ownership:** Oruka holders to own ~97.6% (~58.3% attributable to PIPE shares) of combined enterprise (f.d.) and ARCA holders to own ~2.4%, assuming ARCA Net Cash at closing of $5M and a PIPE of $275M, subject to certain limited adjustments for customary items
- **Certain Closing Conditions:**
  - **Form S-4**: Form S-4 shall have become effective with SEC (see “SEC Filings” below)
  - **Reps Bringdown**: materiality scrape on MAE- and materiality-qualified reps, brought down to MAE standard; capitalization rep brought down flat, subject to de minimis exceptions; fundamental representations brought down in all material respects
  - **Interim Covenants**: perform or comply in all material respects; no MAE
  - **Oruka Stockholder Approval**: holders representing (i) majority of capital stock on as-converted basis and (ii) a majority of Series A preferred shares
  - **ARCA Stockholder Approval**: holders representing majority of common stock
  - **Lock-Up Agreements**: lock-up agreements delivered at signing shall remain in place
  - **PIPE**: PIPE proceeds of at least $175M shall have been received by Oruka
  - **Nasdaq Application**: Nasdaq application covering merger shares shall be submitted
  - **ARCA Dividend**: ARCA dividend of net cash in excess of $5M, if any, shall have been received by Transfer Agent

PIPE

- **Concurrent Investment:** ~$275M of PIPE proceeds, including ~$80M from existing Oruka investors and ~$195M from new investors, led by Fairmount
- **Registration Rights Agreement**: Company agrees to register any shares that would be subject to Rule 144 limitations (i.e., affiliates) on resale registration statement
- **Certain Closing Conditions (Subscription Agreement):**
  - **Reverse Merger:** Closing conditions under the merger agreement must have been met
  - **Reps:** MAE- and materiality-qualified reps brought down flat; other reps brought down in all material respects
  - **Interim covenants:** Use commercial reasonable efforts to comply
- **Closing:** Expected to occur immediately prior to closing of the reverse merger

Other Agreements

- **SEC Filings:**
  - Parties expect to file Form S-4 in May 2024 registering the ARCA shares to be issued (and “constructive” registration of Oruka offering to ARCA stockholders per Rule 145(a))
  - Directors & Executive Officers to file Forms 3, 4 & 5 following the Closing Date
  - Resale registration statement covering Oruka affiliates to be filed promptly post-closing
- **Support Agreements:** Directors / officers and certain affiliated investors to sign support agreements, agreeing to vote in favor of and otherwise support the transaction
- **Lock-Up Agreements:** Directors / officers and certain affiliated investors to sign 180-day lock-up agreements prohibiting (subject to certain exceptions) post-closing transactions in Oruka’s securities during the lock-up period

Estimated capitalization following close of transactions

		Shares on an as-converted basis	Expected ownership of the combined company	Estimated dividend per share
ARCA biopharma	• Shares of common stock outstanding	14.5M	**2.4%[1]**	**$1.38[2]**
Oruka Therapeutics	• Shares of common stock outstanding	72.6M	**97.6%**	**N/A**
	• Series A shares	153.5M		
Pre-closing financing[3]	• Shares of common stock	270.4M		
	• Pre-funded warrants	85.0M		
Estimated total shares of common stock of the combined company post-closing		**596,040,033**		

Please refer to ARCA's SEC filings for additional information

(1) The percentage of the combined company owned by ARCA's stockholders is subject to adjustment based on the amount of ARCA's net cash at the closing date; (2) ARCA is expected to contribute $5 million to the combined entity and expects to pay a dividend to pre-merger ARCA stockholders of ~$20 million immediately prior to the close of the merger; (3) Oruka has secured commitments for a $275 million private investment in Oruka common stock and pre-funded warrants from a syndicate of healthcare investors, which is expected to close immediately prior to completion of the merger.


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