



R&D Event

October 27, 2026



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Today's agenda and speakers



Lonnie Moulder
Founder & CEO



Lisa von Moltke, MD
Head of R&D & CMO



Haley Laken, PhD
CSO



Joseph Merola, MD, MMSc
Dermatologist, Rheumatologist,
President of the Rheumatologic
Dermatology Society, Medical
and Scientific Board of the
Lupus Foundation of America

1. Opening Remarks and Pipeline Overview

2. Obexelimab SLE: SunStone Study & Biomarker

3. IL-17 Overview and ZB021

4. Closing Remarks

5. Q&A



Opening Remarks

Lonnie Moulder
Founder & CEO



A rheumatology and neuroimmunology portfolio with recognized regulatory paths and significant commercial potential

Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Territory
Obexelimab (anti-CD19 and FcγRIIb bifunctional mAb)	IgG4-RD	May 27 th PDUFA date; positive Phase 3 INDIGO trial ¹				Global excluding BMS territories ²
	RMS	Phase 2 MoonStone trial met primary endpoint				
	SLE	Phase 2 SunStone trial data expected in 4Q 2026				
Orelabrutinib (BTK inhibitor)	PPMS	Phase 3 Primrose trial ongoing				Global
	naSPMS	Phase 3 Monarch trial ongoing				
ZB021 (Oral IL-17AA/AF inhibitor)	I&I	Clinical data expected in 4Q 2026				Global excluding China & SE Asia ³
ZB022 (Brain-penetrant TYK2 inhibitor)	I&I	Clinical data expected 2027				Global
ZB014 (half-life extended CD19 and FcγRIIb mAb)	I&I	Clinical data expected 2027				Global

Multiple clinical and regulatory milestones throughout remainder of 2026 and in 2027

Obexelimab (anti-CD19 and Fc γ RIIb)

Near-term milestones and events

Recent Events:

IgG4-RD Investor Event (Sep. 29): Zenas with Dr. Guy Katz, MD – Mass General

6th International Symposium on IgG4-RD (Oct. 8-10):

- **Open Label Extension (OLE) flare protection** data
 - 12-month probability of remaining flare-free:
 - Investigator and adjudication committee-confirmed flares: 0.93
 - Investigator-determined flares¹: 0.87
- **Glucocorticoid-associated toxicity** data
 - GTI Cumulative Worsening Score difference at week 52: -11.4; p=0.021
- **Vaccine sub-study** data
 - Vaccination during the treatment-free window:
 - 6 of 7 (86%) participants achieved serologic immunity to influenza
 - 4 of 4 (100%) participants achieved serologic immunity to COVID-19

Upcoming Events:

- **ACR Conference** (Nov. 6-11)
- **SunStone SLE Phase 2b topline biomarker and overall population results** (4Q26)
- **IgG4-RD BLA review ongoing** (May 27, 2027 PDUFA action date)

Orelabrutinib: a potentially best-in-class BTKi

Orelabrutinib (brain penetrant BTK Inhibitor):

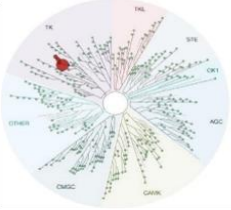
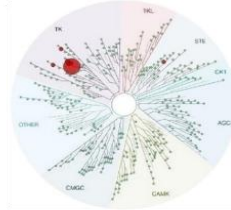
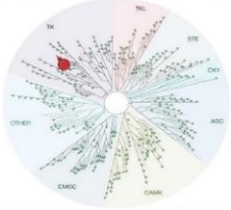
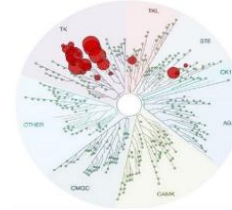
- PriMroSe (PPMS) and Monarch (naSPMS) **Phase 3 studies ongoing**

Orelabrutinib Differentiation:

- No other BTKi programs advancing in **both naSPMS and PPMS**
- Orelabrutinib is the only BTK inhibitor being developed specifically for naSPMS

Late-stage Progressive MS Landscape:

- Tolebrutinib approved in Europe for nrSPMS (FDA issued a CRL)
- Fenebrutinib successful Phase 3 in PPMS with NDA under review
- Remibrutinib positive Phase 3 in RRMS, with Phase 3 in SPMS initiated Q4 2025

	Orelabrutinib	Fenebrutinib	Remibrutinib	Tolebrutinib
Binding / dosing ¹	Covalent / 80mg QD	Non-covalent / 200mg BID	Covalent / 100mg BID (Approved dose of 25mg BID for CSU)	Covalent / 60mg QD (Highly Variable PK; CV ~60%)
Selectivity ² (scanMAX (Eurofins) kinome scan at 1µM)				
CNS concentration ³	16.7	43.1	0.783	~ 0.3 to1
Potency ⁴ (IC ₉₀)	3.5	41.3	5.9	3.1
CNS concentration to IC ₉₀ ratio	~5	~1	~0.2	~0.3

¹ InnoCare Pharma, Sanofi, and Roche published reports; ² Darragh et al. 2025; ³ Orelabrutinib: Data on file; Tolebrutinib: calculated from Cabanis et al. 2024; Fenebrutinib: American Academy of Neurology Annual Meeting 2024. ⁴ Remibrutinib: Lefevre et al ECTRIMS 2024; Orelabrutinib: Data on file; Tolebrutinib and fenebrutinib: Turner et al. 2024. Remibrutinib: Angst et al. 2020 (IC₉₀ estimated from IC₅₀); Notes: Orelabrutinib 80 mg data inferred from 150 mg dosing; Potency based on kinase activity; Based on comparisons of published data for tolebrutinib, fenebrutinib and remibrutinib, no head-to-head comparison studies were conducted; naSPMS = non-active secondary progressive multiple sclerosis; PPMS = primary progressive multiple sclerosis



Obexelimab for Systemic Lupus Erythematosus



System Lupus Erythematosus (SLE): A debilitating chronic autoimmune disease

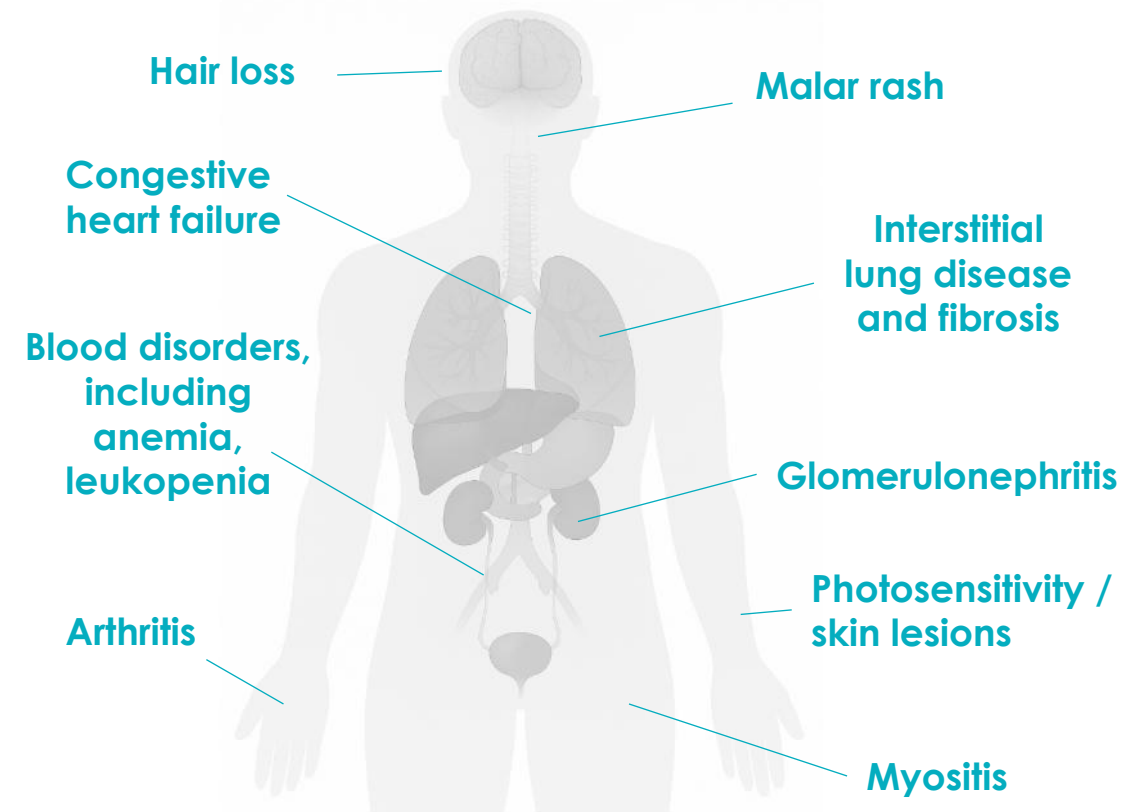
Targeting B cells is a validated approach

- **B-cell dysfunction** results in the production of autoantibodies toward cellular and nuclear components
- **B-cell directed therapies proven effective** in clinical trials
- **Clinical activity** observed in prior obexelimab Phase 2a SLE study

Important clinical study considerations

- **Confirmatory screening** for patient enrollment
- Utilizing latest guidelines for **glucocorticoid reduction**
- **Biomarker identification** to potentially select for patients who are more responsive to a B-cell targeted approach

SLE is a chronic autoimmune disease with unpredictable flares that cause progressive organ damage

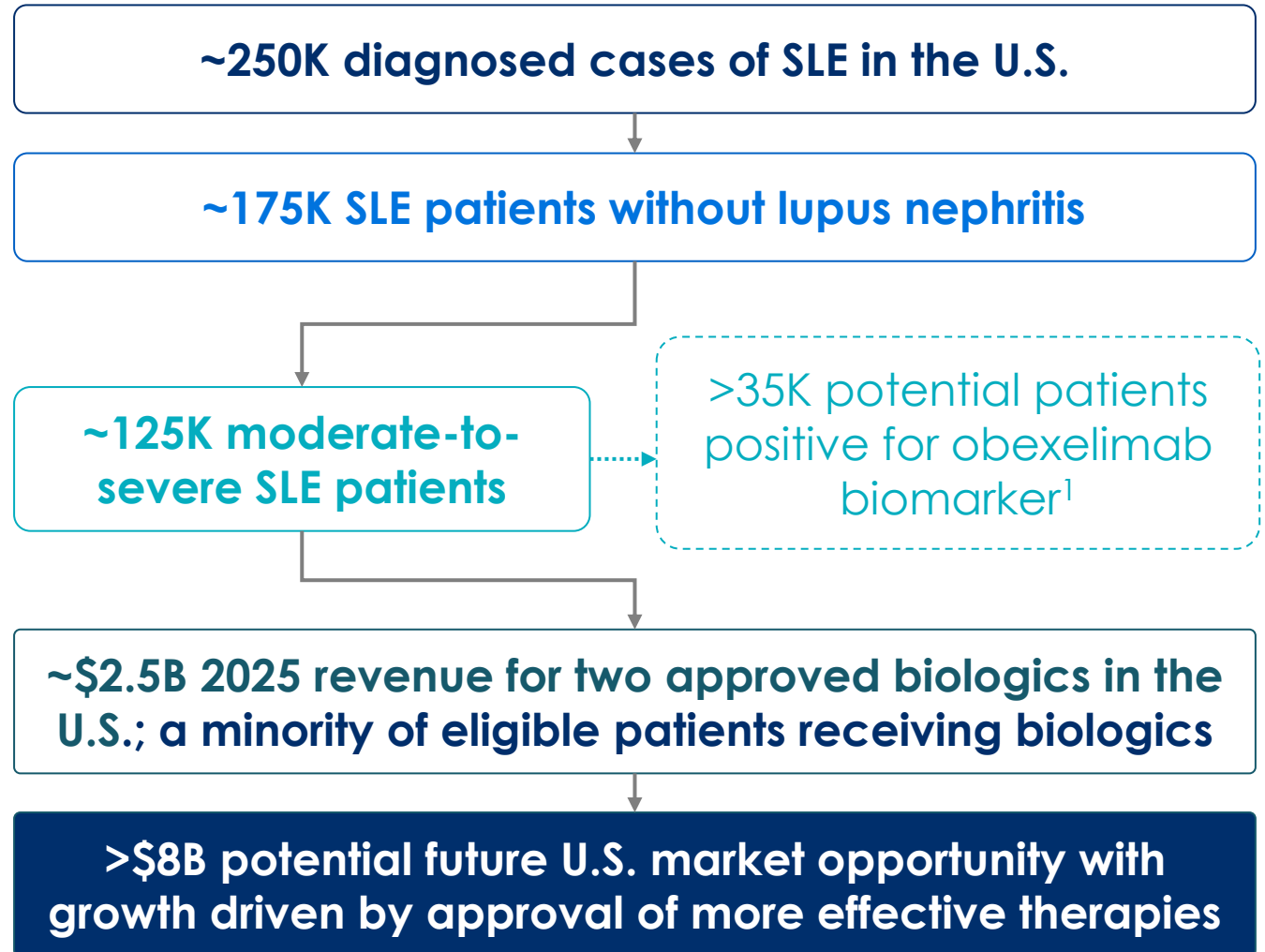


SLE represents a significant and growing commercial opportunity in the U.S. alone

**~125K
Addressable
SLE Patients**

In U.S. alone representing a
commercial market of

\$8B+





Predictive Biomarker Opportunities in SLE

Dr. Haley Laken
CSO



Fundamental analysis framework used to classify SLE patients by molecular profiles

SLE is a complex disease with clinical and biological heterogeneity

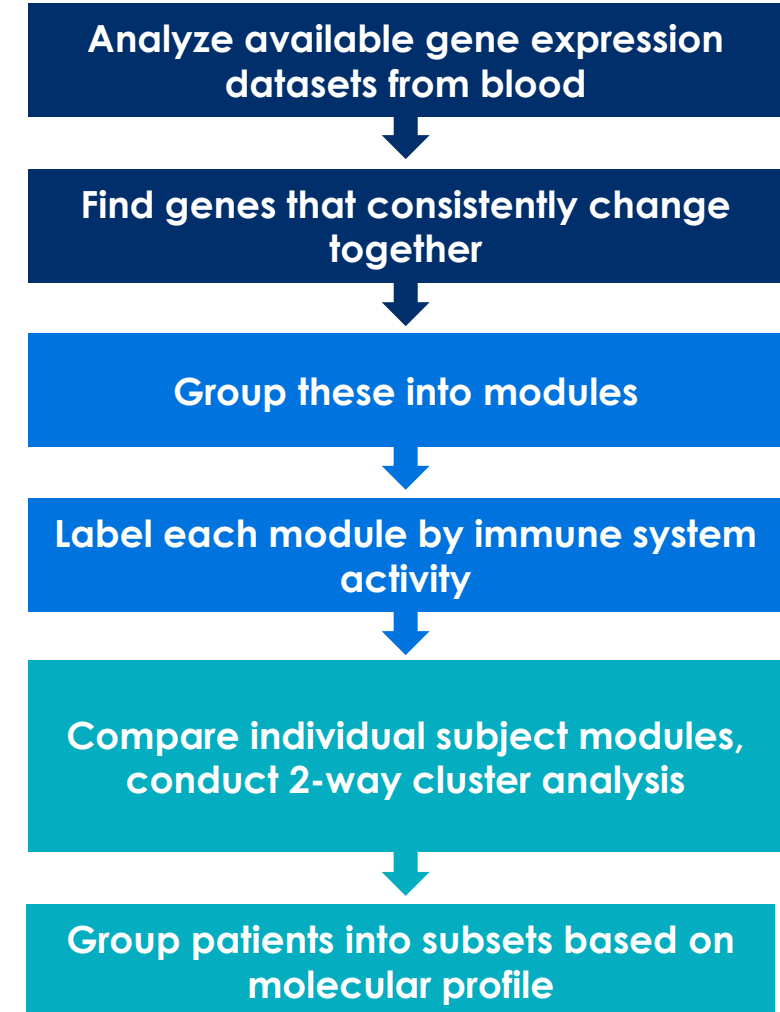
Considerations for SLE drug development

- Efficacy effect sizes and placebo response rates
- Different biologies resulting in similar clusters of clinical manifestations currently classified together

For 15+ years whole blood transcriptomics utilized to identify co-expressed gene signatures to facilitate SLE patient subgroups

- Molecular signatures cluster patients into subgroups associated with disease activity, clinical features, response to treatment¹⁻³

Opportunity to translate this data into predictive biomarkers to guide selection of patients most likely to benefit from a specific therapeutic MOA

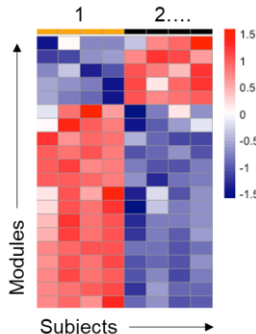



Gene expression datasets


Co-expressed genes


Module 1, 2...



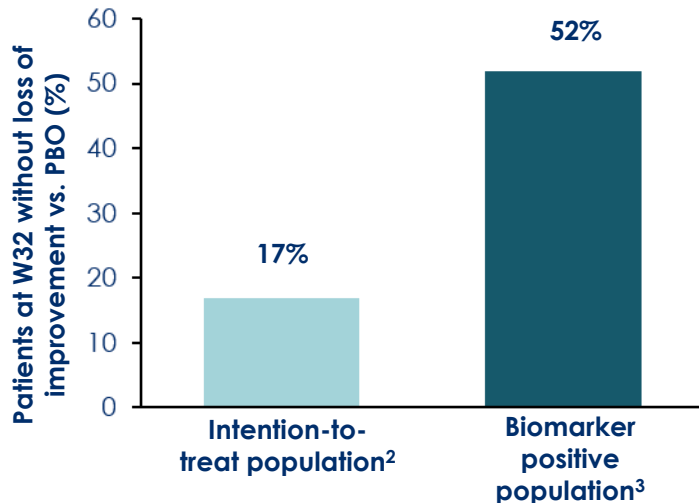



Zenas BioPharma

Incorporating predictive biomarkers into obexelimab clinical development

Phase 2 trial (Xencor) *Hypothesis generating*

Post hoc analysis identified candidate predictive biomarkers based on gene expression analysis¹



Phase 2 trial SunStone *Hypothesis testing*

Exploratory analysis of *novel* predictive biomarker⁴ identified from previous trial

Biomarker positive patients

	BICLA response	SRI-4 response
Obexelimab	TBD	TBD
Placebo	TBD	TBD

Phase 3 trial *Clinical validation*

Potential for prospective enrollment based on optimized predictive biomarker identified in SunStone

Two opportunities for success

- Hierarchical analysis
- Biomarker only

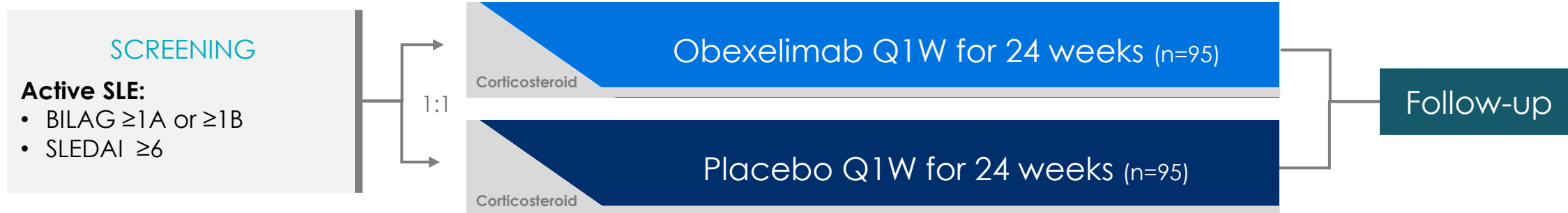


SunStone Trial

Dr. Lisa von Moltke
Head of R&D and CMO



Topline SunStone data expected 4Q 2026



Phase 2 SunStone Trial Design

- Randomized, double-blind, placebo-controlled
- Reduction of SLE disease activity at week 24 by BICLA (primary endpoint) and SRI4
- Powered to detect an approximate 20% difference between obexelimab and placebo; alpha of 0.10

Phase 2 SunStone Trial Patient Populations

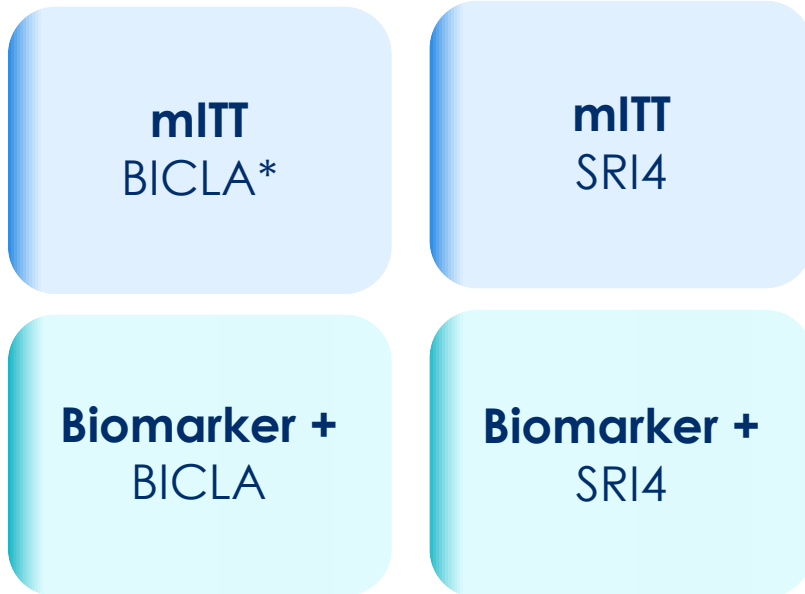
Safety Population (n=190)

mITT¹ Efficacy Population (n=160):

- Overall - BICLA (primary)
- Overall - SRI4
- Biomarker positive - BICLA
- Biomarker positive - SRI4

SunStone data: guiding the path forward

Phase 2 SunStone Trial



Phase 3 Trial Design

Patient Population

Overall (with
Hierarchical analysis)

OR

Biomarker positive only

Primary Endpoint

BICLA or SRI4

The predictive biomarker positive population expands our potential for success in the Phase 2 trial, and provides additional paths forward for Phase 3



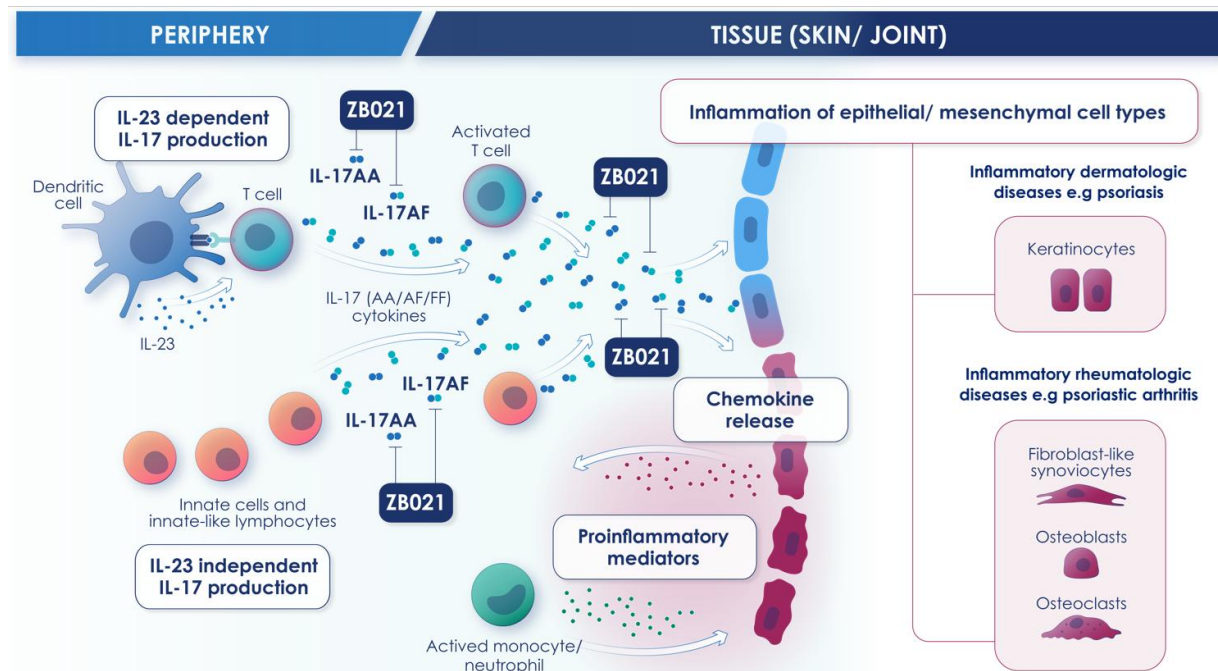
ZB021: An Oral IL-17 AA/AF Inhibitor With Best-in-Class Potential



ZB021 is an oral IL-17 AA/AF inhibitor with significant opportunity in multiple inflammatory indications

IL-17 is a well-validated target for numerous dermatologic and rheumatologic diseases

- Focal point for **acute and chronic inflammation** in skin and joint-related diseases
 - Several upstream cytokines including IL-23 promote Th17 cells and innate-like lymphocytes to secrete **IL-17 as the primary driver of the inflammatory processes**
 - Cytokines, chemokines and other proinflammatory mediators can cause **dysfunction of cells in tissues**
 - Strong **clinical confirmation of role in pathogenesis** of multiple inflammatory diseases

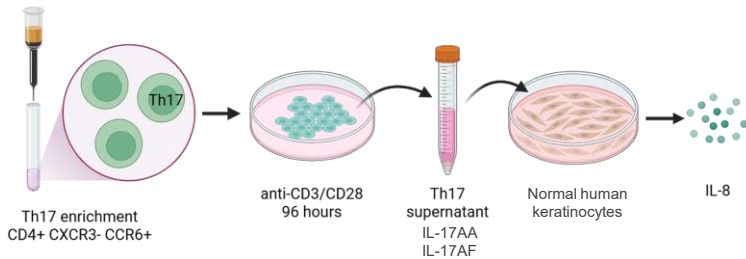


Growing interest in small molecules against targets established by biologics

- Recent FDA approval and successful launch of an oral IL-23 agent for plaque psoriasis establishes the clinical and commercial relevance of oral therapies within a market of **established biologics**

ZB021 is a potent allosteric blocker of IL-17

Functional inhibition of IL-17AA and IL-17AF observed *in vitro*



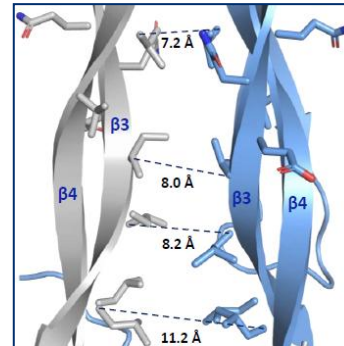
Th17-stimulated keratinocyte assay[†]

IC ₅₀ (nM)	IC ₉₀ (nM)
1.5 ± 0.49	6.8 ± 8.5

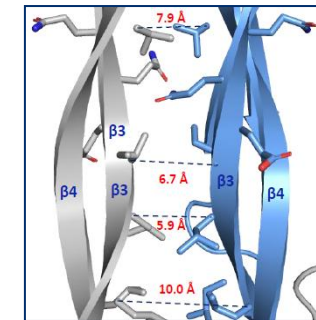
[†]**Keratinocyte assay:** Inhibition of IL-8 production after stimulation of keratinocytes with Th17 cell supernatant; Th17 pooled human donors n=3

Crystallization of IL-17AA and ZB021 identified MOA

Unbound IL-17AA homodimer Open pocket

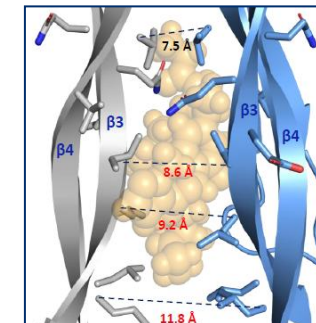


IL-17AA bound to IL-17RA[†] Closed pocket



IL-17
signaling

IL-17AA bound to ZB021, no binding to IL-17RA Open pocket

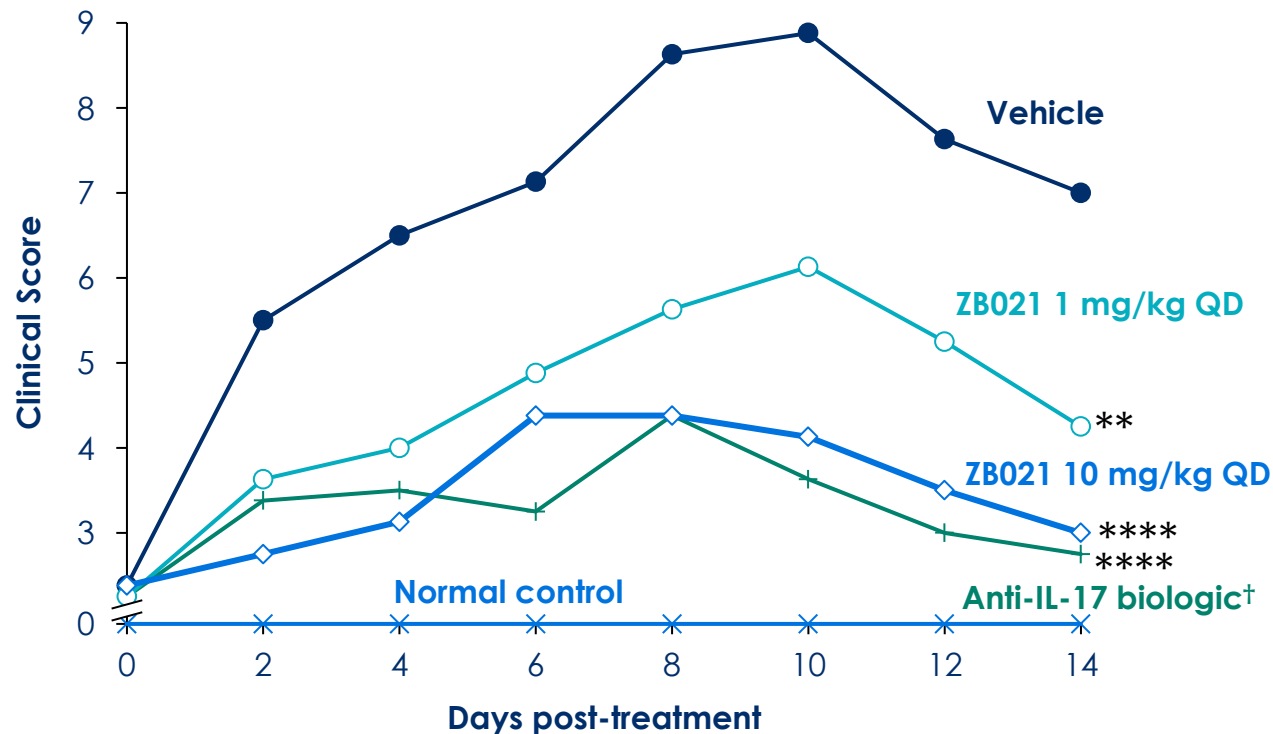


No IL-17
signaling

Simulation predicts ZB021 binds IL-17AF in central pocket at dimer interface, with same binding mode as for IL-17AA

Robust *in vivo* activity: comparable to a reference anti-IL-17 biologic in rat CIA model

In vivo activity in a rat CIA model

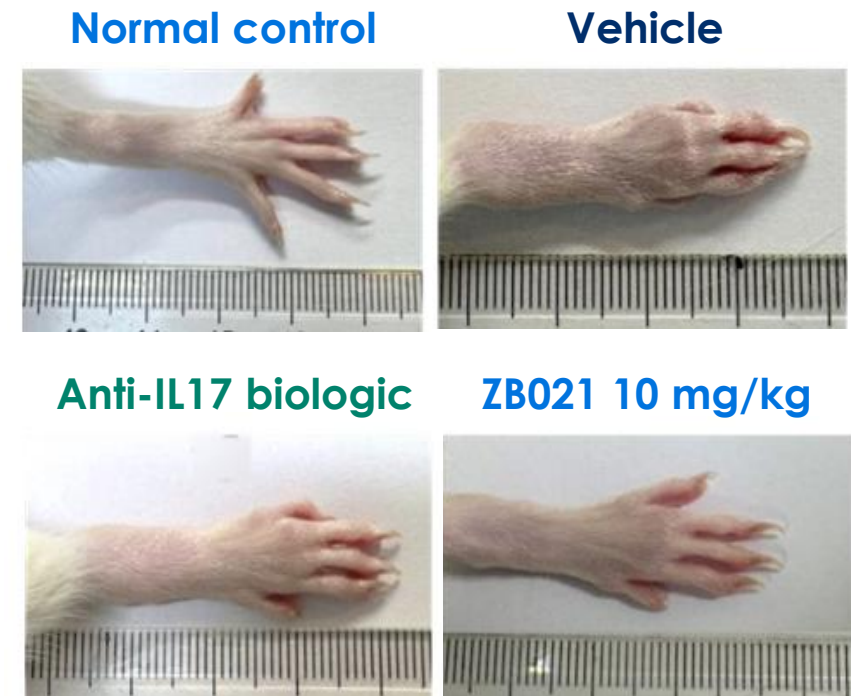


Note: Data points represent group mean and error bars represent standard error of the mean (SEM). Compared with vehicle group, **P < 0.01, ***P < 0.001, ****P < 0.0001. Normal control group did not receive collagen immunization

Rats were immunized with collagen 14 days prior to treatment initiation (Day 0) once clinical signs were observed.

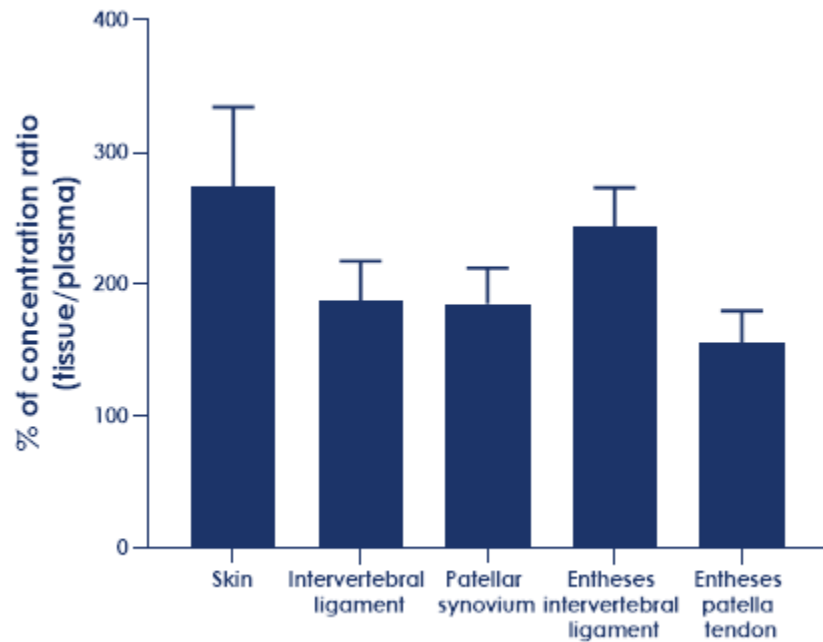
†CJM112 (20 mg/kg) was dosed twice by SC administration on Days 0 and 2. CJM112 is a rat cross-reactive fully human anti-IL-17A antibody with 10-fold higher affinity to IL-17A and greater than 200-fold higher affinity to IL-17AF than Cosentyx® (secukinumab) and with similar affinity to both human IL-17A and IL17AF
CIA = collagen-induced arthritis

Representative photos at end of study



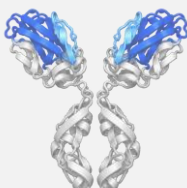
ZB021 properties support potential differentiation

ZB021 distributes into tissues at concentrations similar to or exceeding plasma concentrations in the mini pig



10 mg/kg ZB021 was administered to mini pigs orally for 5 days. On day 5, terminal plasma and tissue samples were collected at 4 or 24 hrs (N=3/time point), and ZB021 concentrations were measured by LC/MS/MS. Data shown is at 24 hours

High oral bioavailability and tissue penetration of ZB021 hypothesized to result in local inhibition of IL-17

		Molecule size	Oral bioavailability	Tissue penetrance
ZB021		~0.6 kDa Reference (1x)	High	High
Peptide inhibitor		~1.5-7 kDa ~12x Larger	Low	High
Affibody		~6-19 kDa ~10-31x Larger	N/A	Mod.
Nanobody		~15-40 kDa ~25-65x Larger	N/A	Mod.
Monoclonal antibody (IgG)		~150 kDa ~250x Larger	N/A	Low

ZB021 development program designed for rapid dose evaluation and to establish proof-of-concept in patients

**Multiple Ascending Dose (n=8 per dose*)
Daily for 7 days**

Single Ascending Dose (n=8 per dose*)

**Proof of Concept Study in Patients at 2
Dose Levels**

**Evaluate efficacy
and PD biomarkers**

Phase 1 objectives:

- Primary
 - **Safety and tolerability** of single dose or multiple dose oral ZB021 in healthy participants
- Secondary
 - **Evaluate PK** characteristics
 - Compare safety, tolerability and PK under **fed and fasted** conditions

Study population: healthy participants (*6 active, 2 placebo)

Study explores the maximum clinically safe dose

Dose selection:

Safely and consistently achieve drug concentrations (C_{average}^1) exceeding IC_{90}

Informing dose selection:

- ZB021 C_{average} **based on once daily dosing**
- IC_{90} characterized with primary human cells
- **Tissue penetration** in relevant tissues



Fireside with Dr. Merola

Dr. Joseph Merola, M.D., M.M.Sc.

Dermatologist, Rheumatologist,

President of the Rheumatologic Dermatology Society,

Medical and Scientific Board of the Lupus Foundation of America





Closing Remarks and Q&A



Multiple upcoming clinical and regulatory milestones

Upcoming Data

Obexelimab (anti-CD19 and FcγRIIb)

- **SunStone SLE Phase 2b topline biomarker and overall population data** (4Q26)

ZB021 (oral IL-17 AA/AF Inhibitor)

- **SAD and MAD data** (4Q26)

Upcoming Medical Conferences

- ACR (Nov. 6-11)

This is an exciting time for Zenas as we continue to prepare for commercialization and advance our pipeline programs



Enabling patients with
autoimmune diseases
to reimagine life