

Zenas BioPharma

Enabling patients with autoimmune diseases to reimagine life

Corporate Presentation

December 2024

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Disclaimer continued

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Zenas: Creating a global, immunology-based development and commercial company

Immunology Focus

Pipeline addressing significant unmet needs for patients with autoimmune disease, the 2nd largest pharmaceutical category

Global Capabilities

Establishing global development and regulatory capabilities

Experienced Team

Record of strong operational results: multiple clinical, regulatory and commercial successes Zenas BioPharma

Enabling patients with autoimmune diseases to reimagine life

Franchise Molecule

Obexelimab is a potentially differentiated B cell therapeutic in development for IgG4-RD, RMS, SLE, which combined represents a potential multi-billion-dollar commercial opportunity*

Well-funded through Meaningful Data Catalysts

Capitalized for clinical data readouts into Q4:26

Business Development Engine

Pipeline expansion planned through in-licensing and partnerships, and non-dilutive capital via regional out-licensing



* Company estimate based on disease prevalence and pricing of advanced therapies within indication

Accomplished Executive Team

Extensive experience developing and commercializing biopharmaceuticals



Lonnie Moulder CEO & Chairman



Joe Farmer President & COO



Gan Wei

SVP, Global Technical Operations

Orlando Oliveira



Jeff Held



Allen Poma, MD SVP, Clinical Development



Caroline Chevalier CHRO

COLLECTIVELY, ZENAS MANAGEMENT HAS:

- 70+ IND filings \bullet
- 30+ BLA/NDA filings
- 30+ Commercial product launches ullet
- Deep experience across numerous biotech and ٠ pharmaceutical companies



Zenas 2024 achievements towards creating a leading global, I&I development and commercial company

- Completed upsized \$200M Series C and \$259M IPO, financing Zenas through value-driving Phase 2 and Phase 3 data readouts
- Completed targeted enrollment in obexelimab Phase 3 INDIGO trial for IgG4-RD¹
- Initiated two Phase 2, multicenter, randomized, double-blind placebo-controlled trials for obexelimab:
 - Enrolling MoonStone for patients with Relapsing Multiple Sclerosis (RMS)
 - Enrolling SunStone for patients with Systemic Lupus Erythematosus (SLE)
- > Provided preliminary, interim data from Cohort 1 of the Phase 2 SApHiAre trial in wAIHA²
- > **Expanded** executive leadership with Chief Commercial Officer and Chief Legal Officer

Zenas Clinical Development Execution			
3 completed and 5 ongoing clinical trials, including fully enrolled INDIGO Study of Obexelimab for IgG4-RD	Managing over 220 clinical trial sites located in 31 countries	Over 350 patients enrolled to date	



Obexelimab: Rapidly building a global franchise

Multiple clinical catalysts during the next 12-18 months

PROGRAM	INDICATION	TRIAL/STATUS	NEXT MILESTONE
	IgG4-RD (Immunoglobulin G4-Related Disease)	Phase 3 INDIGO trial enrolled ^{2,3}	Phase 3 topline results end of 2025
Obexelimab ¹ CD19xFcyRllb Bifunctional mAb	RMS (Relapsing Multiple Sclerosis)	Phase 2 MoonStone trial enrolling ³	Primary endpoint (12-week) data Q3:25
	SLE (Systemic Lupus Erythematosus)	Phase 2 SunStone trial enrolling ³	Primary endpoint (24-week) data 1H:26

¹Zenas acquired exclusive worldwide rights to obexelimab from Xencor, Inc.

²Bristol Myers Squibb & Co. holds exclusive development and commercialization rights in JPN, SK, TWN, HK, SGP, AUS ³Randomized versus placebo



PK, PD and clinical activity from five completed obexelimab clinical trials

	Description	Outcome
Phase 1 ¹	SAD HV, safety and PK	Demonstrated proof-of-mechanism
Phase 1b/2a ²	MAD Rheumatoid Arthritis (RA)	 Proof-of-mechanism and clinical activity established Day 85 (all dose levels): ACR20: 78%, ACR50: 33%, ACR70: 14%³
Phase 2 ⁴	Pilot Study IgG4-Related Disease	 Clinical activity established; rapid disease response (mean of 21 days), and sustained response achieved in 93% of patients
Phase 2 ⁵	Randomized Controlled Systemic Lupus Erythematosus (SLE)	 Clinical activity established Primary endpoint effect size of 17% for ITT population; 35% effect size for population with optimal exposure level (C_{trough}) Biomarkers potentially predictive of obexelimab response identified
Phase 16	Bioequivalence HV, Subcutaneous (SC) vs. Intravenous (IV) dosing	 Established subcutaneous formulation with improved tolerability, and potential for optimized drug exposure (C_{trough})

SAD = Single Ascending Dose, HV = Healthy Volunteers, PK = Pharmacokinetics, MAD = Multiple Ascending Dose

¹ Wang, X. American College of Rheumatology 2022 poster presentation

² Wang, X. American College of Rheumatology 2023 poster presentation

³ Jaraczewska-Baumann et al EULAR 2015 poster presentation (obexelimab efficacy at all dose levels)

⁴ Perugino, C. et al. Nature Reviews Rheumatology. 16, 702–714 (2020)

⁵ Merrill, J. et al. Arthritis and Rheumatology. Vol. 75, 2185-2194 (2023)

⁶ Wang, X. Japan College of Rheumatology 2023 oral presentation

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Targeting CD19 offers broad coverage of B cell lineage¹



POTENTIAL ATTRIBUTE	SUPPORTIVE EVIDENCE	
Strong clinical activity	Broad B cell lineage coverage through CD19 and potential for potent (fast and durable) activity through FcyRIIb targeting	
Less risk of infection & potential to vaccinate	Inhibitory mechanism (versus B cell depletion) may allow faster repletion of B cells	
Dosing	Self-administered, subcutaneous injection	





B cell responses are naturally downregulated by immune complexes through FcyRIIb binding

B cell responses orchestrate humoral immunity

Immune complex binding to FcyRIIb naturally downregulates B cell responses





Source: Zenas BioPharma

Obexelimab: a differentiated B cell targeted agent

Broader B cell inhibition, tissue penetrance, and non-depleting MoA provide clear differentiation

- FcγRIIb broadly expressed across B cell lineage, including pro-B cells, pre-B cells, B cells, plasmablasts and select plasma cells¹
 - Obexelimab binding affinity for human FcγRIIb increased approximately 230-fold relative to human native IgG1 due to Fc engineering²
- Obexelimab co-engagement of CD19 and FcγRIIb results in an inhibitory effect, rather than direct depletion^{3,4,5,6}
 - FcyRIIb mimics natural antigen-antibody complex for potent inhibition of B cells
 - Engineered to **avoid ADCC / CDC-mediated depletion**; nonreliance upon other immune effector cells
 - Impacts antibody production, proliferation, cytokine secretion, and antigen presentation to T cells
 - Continuous exposure results in inhibitory activity within tissue

¹Abeles *et al.* Annual Review of Immunology 2024 ² Zenas BioPharma ³ Chu *et al.* Molecular Immunology 2008 & Zenas data on file ⁴ Szili *et al.* mAbs 2014

⁵ Chu et al. Journal of Translational Autoimmunity 2021
 ⁶ Chu et al. Arthritis & Rheumatology 2014

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Rapid and broad inhibition of B cell response after obexelimab administration in clinical trials

Rapid inhibition following a single obexelimab dose



Potent inhibition across multiple B cell subtypes



Source: Perugino et al. (2023) Lancet Rheumatol 5: e442 Supplement pBTK = phosphorylated Burton's tyrosine kinase Fold-change in the induction of pBTK with anti-IgG/IgM treatment before and after treatment with obexelimab



Source: Wang, X. American College of Rheumatology 2022 poster presentation

Obexelimab inhibits B cell cytokine production, and B cell activation in tissue without depletion



Modified from Szili et al. (2014) mAbs 6 (4): 991–99

BCR = B cell receptor; aBCR = anti-BCR stimulation; CpG = unmethylated cytosine-guanine; IL = interleukin; stim = stimulation; TNF = tumor necrosis factor;



assays (average of 5 experiments shown); Adapted from Chu et al. Journal of Translational

Autoimmunity 2021.

BioPharma





+ CTRL = positive control (cytochalasian D); Obx = obexelimab; Unt = untreated

Source: Zenas and Kerfoot Lab collaboration, unpublished

Dose selection: Higher PK (C_{trough}) correlates with greater clinical activity as observed in Phase 2 SLE Study

Obexelimab 250 mg SC QW dose expected to maximize the potential for clinical activity by 1) providing higher C_{trough}, and 2) maintaining a comparable AUC from an efficacious dose of 5 mg/kg IV Q2W

1.00 4th Quartile C_{trough} Quartile (5 mg/kg IV) 3rd Quartile 1 st 2nd 3rd ∆th Proportion Without Loss of Improvement 0.50 0.25 2nd Quartile 1.2 2.3 3.8 Mean 6 Obexelimab 1.8 concentration Min 0.18 2.8 5.1lst Quartile $(\mu g/mL)$ 1.8 2.8 4.7 8 Max Placebo **Clinical activity** 0.00 14 28 42 70 140 154 168 182 210 224 56 Time (Days)

Portion of patients without loss of improvement (flare) by C_{trough} quartile



Obexelimab dose selection: 250 mg SC QW selected for IgG4-RD Phase 3 INDIGO Trial

Starting point: Maximum PD in Phase1 HV SAD and Phase 2 IgG4-RD with 5 mg/kg IV Q2W

	5 mg/kg IV Q2W	125 mg SC QW	250 mg SC QW ¹	250 mg SC Q2W	375 mg SC Q2W
Mean C _{max} (µg/mL)	105	13.6	24.8	14.7	22.2
Mean C _{trough} (µg/mL)	~3.0	8.8	17.1	4.0	6.6
Mean AUC µg/mL*h) (normalized to a same 14-day dose interval)	8,000	3,600	7,375	3,095	4,720

Compared with 5 mg/kg IV Q2W, 250 mg SC QW can provide:

- Optimal PK (higher C_{trough}) and comparable AUC to maintain target
 engagement to potentially enhance clinical activity
- ~4x lower Cmax to improve safety and tolerability

¹From PK simulation at the steady-state Source: Zenas BioPharma





Obexelimab: IgG4-RD

IgG4-RD: a debilitating chronic fibro-inflammatory condition that can affect multiple organ systems

Disease Overview:

 IgG4-RD may present with single or multi-organ involvement, and as disease progresses patients experience new or worsening symptoms (e.g., flare). Early inflammatory disease state moves to a fibrotic stage, which can lead to major irreversible tissue damage and organ failure

Pathophysiology:

- Expansion of CD19+ and IgG4+ B cells and plasmablasts with tissue infiltration
- These cells produce IgG4 and inflammatory cytokines, and activate T cells through antigen presentation exacerbating inflammation & fibrosis

Therapeutic Opportunity

• IgG4-RD flares do not resolve without intervention and long-term use of glucocorticoids can lead to significant toxicities and complications, including osteoporosis, high blood pressure, and diabetes

Patient Population

Approximately 40K patients in the U.S. / major countries in the EU





Phase 2 IgG4-RD trial: Obexelimab induced rapid remission of active flares and maintained durable responses

	Obexelimab (5mg/kg q14d x 12)	Rituximab (1000 mg q15d x 2)
Design	Phase 2 single-arm, open label (n=15)	Phase 2 single-arm, open label (n=30)
Baseline characteristics	RI score (12.0) Number of organs involved (4.0)	RI score (11.0) Number of organs involved (3.5)
Primary endpoint: decline of IgG4-RD RI ≥ 2 points, no flares before month six, no GCs between two to six months	12/15 (80%)	23/30 (77%)
GC use through 6 months (after tapering)	0	3/30 (10%)
Sustained disease response	13/14 (93%) responders had ongoing response at month 6	22/30 (73%): Improvement of IgG4- RD RI ≥ 2 points for 6 months
Mean time to disease response (days)	21	43
Relapses within 6 months	1/15 (6.7%)	3/30 (10%)

Source: Perugino CA et al. Lancet Rheumatol. 2023; Carruthers MN et al. Ann Rheum Dis. 2015 RI=responder index Note: No comparative head -to-head trials were conducted GC=glucocorticoid



Obexelimab: Phase 2 IgG4-RD results demonstrated rapid, robust, and sustained reduction in IgG4-RD disease activity

Open-label, single-arm Phase 2 PoC trial in 15 obexelimab-treated patients with moderate to severe disease as induction and maintenance One or more organ systems involved and an IgG4-RD Responder Index (RI) of ≥3

- Primary Endpoint: Proportion of patients on Day 169 with a decrease in IgG4-RD RI ≥2 points
 - > 100% of patients who completed trial met primary endpoint
 - No flares or steroid use after Day 57
 - > 67% of patients achieved complete remission
 - 80% of patients with prior rituximab achieved complete remission
- Rapid remission and sustained response
- Obexelimab was well tolerated; most frequent AEs were IV infusion-related gastrointestinal events; three SAEs were not considered to be related to obexelimab



Rapid and sustained IgG4-RD RI response

obexelimab 5mg/kg IV Q2W x 12 doses

Reference: Perugino et al. Lancet Rheumatology 2023

Strong rationale for obexelimab in IgG4-RD

IgG4-RD is estimated to be a ~\$3 billion¹ commercial opportunity in the U.S. alone

OBEXELIMAB RATIONALE FOR IgG4-RD

Positive, POC established in prior Phase 2 trial²

De-risking of Phase 3 trial design based upon the results of the Phase 3 MITIGATE trial with Uplizna® (inebilizumab), an anti-CD19 mAb

Continuous inhibition of B cells, including in tissue

Potential for less risk of opportunistic infection and ability to vaccinate

SC at home administration

¹Company estimate based on disease prevalence and those patients estimated to require maintenance treatment and potential pricing of advanced therapies ²Perugino et al. Lancet Rheumatology 2023



Phase 3 INDIGO IgG4-RD trial enrollment complete

Trial of over 190 patients, the largest ever conducted, with topline results expected year-end 2025



INDIGO Trial Summary:

- Design: Randomized, double-blind, placebo controlled
- Treatment: weekly obexelimab 250mg subcutaneous or placebo control; GC taper to 0 mg by week 8
- Primary endpoint: Time to disease flare through week 52
- Secondary endpoints include:
 - ➢ 52-week flare rate
 - Achievement of complete remission
 - > Use and quantity of rescue medication
 - > Change in GC-associated toxicity as measured by the Glucocorticoid Toxicity Index (GTI)



Obexelimab: Multiple Sclerosis

Multiple Sclerosis: a debilitating chronic neuroinflammatory disease characterized by flares and disability progression

Disease Overview:

- Characterized by demyelinating lesions of the CNS. Symptoms include sensory and visual disturbances, coordination impairment and spasticity, fatigue, pain, weakness, and cognitive deficits
- Three major forms: relapsing MS (**RMS**), secondary progressive (**SPMS**), and primary progressive (**PPMS**). RMS is characterized by episodes of neurological dysfunction (relapses) followed by complete or incomplete recovery
 - Disability progression can occur independently of relapse activity; referred to as "smoldering" disease and can be measured clinically (PIRA)

Pathophysiology:

• B cells, including plasmablasts and plasma cells, represent the predominant cell type in meningeal inflammation

Therapeutic Opportunity:

 B cell-targeting therapeutics are considered highly effective and may affect silent progression/PIRA

Patient Population

~ 650K patients in the U.S. and ~ 670K patients in major EU countries





Strong rationale for obexelimab in MS

CD20 depleting B cell therapies Ocrevus® (ocrelizumab), Kesimpta® (ofatumumab), Briumvi® (ublituximab)dominate RMS with 50-60% market share currently and combined annual revenue of >\$9 billion¹

OBEXELIMAB RATIONALE FOR DIFFERENTIATION

Superior activity in a preclinical MS model vs. depletion comparator Potential for improved impact on "smoldering" disease (i.e., PIRA²) through broader B cell coverage with CD19 and continuous drug exposure via SC self administration

Continuous inhibition of B cells, including in tissue

Potential for less risk of opportunistic infection and ability to vaccinate

SC at home administration

¹Source: Roche, Novartis, and TG Therapeutics company reports and SEC filings ² Progression independent of relapse activity



Obexelimab surrogate mAb suppressed disease activity in EAE model without B cell depletion vs. an anti-CD20 depleting mAb

EAE: a gold-standard nonclinical model for assessing autoimmune-mediated CNS disease



EAE = Experimental Autoimmune Encephalomyelitis

huFcyRIIb transgenic mice (human FcyRIIb knock-in). Obexelimab and anti-CD20 mAb dosed 10 mg/kg intraperitoneally 2x per week beginning day -7 continuing through day 24. Whole blood Immunophenotyping performed at day -5 by flow cytometry to measure percent B cells. Disease induction: Human MOG protein in Complete Freund's Adjuvant administered on day 0 followed by pertussis toxin at days 0 and 3. Daily clinical scores measured from day 2 through day 27; mice sacrificed at clinical score of 4



Phase 2 MoonStone RMS trial enrolling

Gold-standard design with MRI measurements; highly predictive of successful outcome in large randomized trials



MoonStone Trial Summary:

- Design: Double-blind, randomized, placebo controlled with placebo crossover at week 12
- Treatment: obexelimab 250mg SC weekly vs. placebo control (first 12 weeks)
- Primary endpoint: Number of new T1 Gd-enhancing lesions at week 12
- Secondary endpoints: Utilizing standardized assessments, imaging and biomarkers to evaluate impact on disease progression/silent progression
- 90% power to detect 90% reduction in T1-Gd lesions vs. placebo at week 12





Obexelimab: Systemic Lupus Erythematosus

System Lupus Erythematous (SLE): a debilitating chronic autoimmune disease that attacks healthy tissue

Disease Overview:

• SLE is a complex, chronic autoimmune disease characterized by unpredictable flares in joints, skin, kidneys and other vital organs that cause progressive organ damage. Comorbidities, such as infections, malignancies, hypertension, lipid disorders and diabetes increase risk of patient disability and death

Pathophysiology:

 B cell dysfunction resulting in abnormal regulation of immune responses and the production of autoantibodies toward cellular and nuclear components results in tissue inflammation and multi-organ damage

Therapeutic Opportunity

- GC and immunosuppressants are the mainstay of treatment, only two
 moderately effective therapies are approved for moderate-to-severe disease
- Long-term GC use and irreversible organ damage has been reported to be a predictor of morbidity and mortality in SLE²

Patient Population

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~170K patients in the U.S. and ~150K patients in major EU countries

¹ BENLYSTA[®] and SAPHNELO[®]





Strong rationale for obexelimab in SLE

Currently approved therapies (Benlysta® (belimumab) and Saphnelo® (anifrolumab) are considered to have modest efficacy (effect sizes of 12-17% over placebo on SRI-4/BICLA assessments)

SLE is estimated to be a \sim \$9 billion¹ commercial opportunity in the U.S. alone

OBEXELIMAB RATIONALE FOR DIFFERENTIATION

Potential for improved efficacy based on continuous inhibition of broad B cell lineage via optimal drug exposure

Refined, robust, and rigorous design of ongoing Phase 2 trial with an innovative biomarker approach Continuous inhibition of B cells, including in tissue

Potential for less risk of opportunistic infection and ability to vaccinate

SC at home administration

¹Company estimate based on disease prevalence and those patients estimated to require maintenance treatment and potential pricing of advanced therapies

Potential for improved clinical activity with an optimized obexelimab dosing regimen

Higher clinical activity observed with optimized exposure, and in biomarker positive population



Efficacy evaluable (EE)¹ primary analysis (vs. ITT analysis)

- EE disproportionately affected by higher placebo dropouts
- 29% of placebo-treated patients achieved the primary endpoint impacting the primary outcome (13% effect size; obexelimab 42%, placebo 29%)²
- Undersized study assumed a placebo flare rate of only10%
- Intent to treat population effect size of 17%
 - Defined as all randomized patients receiving at least one dose of study medication
- Dose optimization increased effect size to 35%
 - C_{trough} Quartiles 3 & 4 in EE analysis
- Biomarker positive population increased effect size to 52%
 - Biomarker positive defined as patients in lupus phenotypic gene expression clusters 3 & 6 (~38% of evaluated population)

Source: Merrill et al. Arthritis Rheumatol. 2023

¹ Efficacy evaluable defined as all patients remaining in trial through week 32 or who withdrew early due to flare or treatment toxicity. Primary endpoint not achieved with statistical significance (p=0.183)
 ² Primary endpoint defined as the proportion of patients without loss of improvement in SLE disease activity
 ³ Defined as all randomized patients receiving at least one dose of study medication

31 ⁴C_{trouah} Quartiles 3 & 4 in efficacy evaluable analysis

⁵ Biomarker positive defined as patients in predefined lupus phenotypic gene expression clusters 3 & 6 (~38% of evaluated population)



Phase 2 SunStone SLE trial¹ enrolling

Designed to confirm obexelimab activity in all-comer and biomarker populations

Incorporates learnings from previous Phase 2 to increase POS

- > SC dosing to improve PK (steady state C_{trough} above Phase 2 top (4th) quartile for all patients)
- Treatment vs. maintenance design powered on appropriate placebo response and effect size assumptions
- Strict adjudication for eligibility and assessment (moderate/severe patients only); strict corticosteroid tapering rules to reduce placebo responses



• Primary Endpoint: Reduction of SLE disease activity at week 24 by BILAG-Based Composite Lupus Assessment (BICLA)





Obexelimab: warm Autoimmune Hemolytic Anemia (wAIHA)

Preliminary results from Phase 2 open label SApHiAre trial (wAIHA)

Open Label Safety and Dose Confirmation Run-In Period (SRP)



- Nine patients (8 patients with primary wAIHA, 1 patient with secondary wAIHA due to autoimmune disease) enrolled over approximately one year
 - Less than 30% of screened patients eligible for enrollment
- 5/8¹ patients achieved an increase of >1 g/dL of hemoglobin from baseline during weeks 8-24 and without influence of concomitant medication
 - A hemoglobin increase of ≥ 2 g/dL measured from Hgb nadir to peak observed in 5 of 8 patients; none received transfusions
- > Obexelimab was well tolerated, 3 related TEAEs; all Grade 1 with no discontinuations
- > Proof-of-mechanism established with increased hemoglobin and positive effect on other clinical markers
- No plan to progress to a registration program considering long and expensive Phase 3 expectations, and hematology not aligned with the Company's therapeutic strategy

Obexelimab demonstrated improvement in anemia and corresponding markers in patients with wAIHA

Phase 2 Open Label Study: Primary wAIHA or Secondary wAIHA due to Autoimmune Disease



For patients who received concomitant medication, change from baseline is after 28

- 5 of 8 patients achieved Hgb increase ≥ 1 g/dL over baseline during Week 8-24, without influence of concomitant medication
- A Hgb increase of ≥ 2 g/dL measured from Hgb nadir to peak observed in 5 of 8 patients; none received transfusions
- LDH and Total bilirubin levels decreased overall during Week 8-24



AI = Autoimmune Hepatitis



Zenas: Creating a global, immunology-based development and commercial company

Obexelimab, an I&I franchise molecule

Deeply experienced team Obexelimab is a potentially differentiated B cell therapeutic in development for IgG4-RD, RMS and SLE, representing a potential multi-billion-dollar commercial opportunity^{*}

Record of strong operational results: multiple clinical, regulatory and commercial successes

Multiple Phase 2 and Phase 3 data updates over the next 12-18 months Obexelimab Phase 3 pivotal trial results expected for INDIGO (IgG4-RD), and Phase 2 results for MoonStone(RMS) and SunStone (SLE)

Well-funded through results of ongoing obexelimab clinical trials

2024 year-end cash estimated to be \$350M; capitalized for clinical data readouts into Q4:26



* Company estimate based on disease prevalence and pricing of advanced therapies within indication