KEZAR LIFE SCIENCES

H.C. Wainwright 26th Annual Global Investment Conference

September 2024

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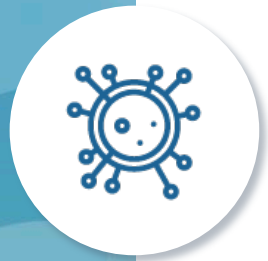
Developing Novel, First-In-Class Medicines to Transform Immunology

KEZAR LIFE SCIENCES

First-In-Class Small Molecule Therapeutic with Differentiated Approach to Treating Immune-Mediated Diseases

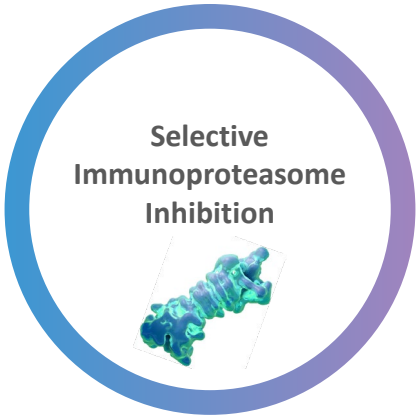


Zetomipzomib: Selective Immunoproteasome Inhibition Leads to Broad and Potent Immunomodulation without Immunosuppression

Pipeline-in-a-Product Profile with Multiple Avenues to Value Creation

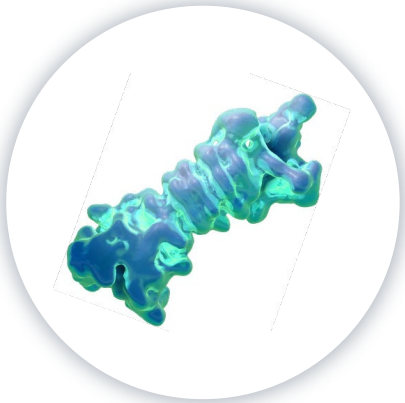
Strong Team of Research Scientists and Drug Developers

Building a First-In-Class Therapeutic Portfolio: Zetomipzomib is a “Pipeline in a Drug”



Zetomipzomib

	Preclinical	Phase 1	Phase 2	Phase 3	Key Milestone	Partner
Lupus Nephritis (LN)	PALIZADE				Top-line results expected in mid-2026	EVEREST MEDICINES *Greater China, South Korea & Southeast Asia*
Autoimmune Hepatitis (AIH)	PORTOLA – Enrollment Complete ✓				Top-line results expected in 1H 2025	

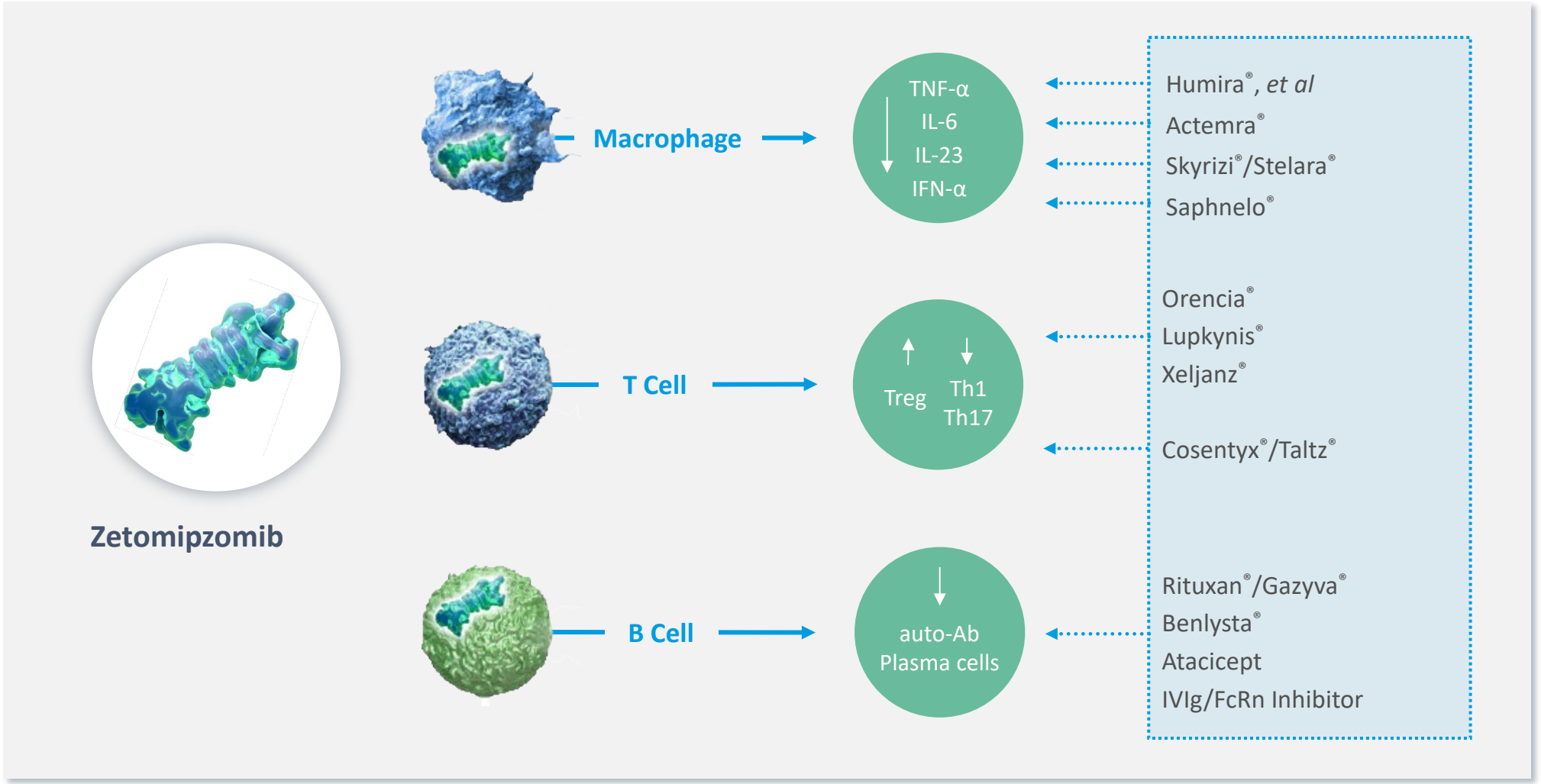


SELECTIVE IMMUNOPROTEASOME INHIBITION:

Zetomipzomib

Targeting a Range of Autoimmune Diseases Through Immunomodulation Versus Direct Immunosuppression

Zetomipzomib's Competitive Advantage: Immunomodulation Across the Entire Immune System



*Some preclinical studies were conducted with ONX 0914, a first-generation selective immunoproteasome inhibitor.

Key Attributes of Zetomipzomib, a First-in-Class Inhibitor of the Immunoproteasome

Zetomipzomib Modulates Innate and Acquired Immune Responses Without Evidence of Immunosuppression to Date

- Selective inhibition of the immunoproteasome results in broad downregulation of inflammation
- Rapid reduction of UPCR seen in the MISSION Phase 2 study with 35% of LN patients achieving CRR following only 25 weeks of treatment without induction therapy
- Promising early results in SLE demonstrating improvement in multiple measures of disease activity across organ systems
- Favorable long-term safety profile without observed signs of immunosuppression following up to two years of treatment

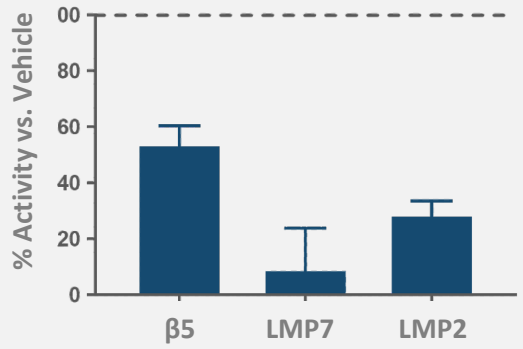
Furie R *et al.*, EULAR 2021 and Data on File.

Zetomipzomib Has Demonstrated Consistent Translation of Target Inhibition with Anti-Inflammatory Activity

Proteasome Inhibition

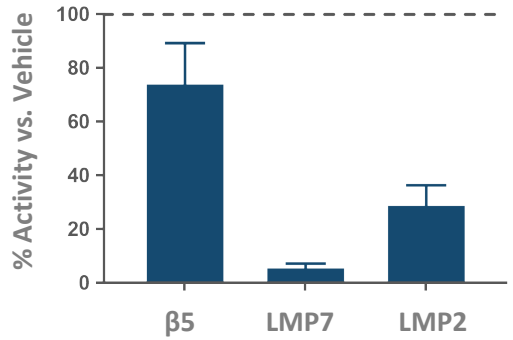
Mouse Data

Pharmacodynamics in Mice[1,2]



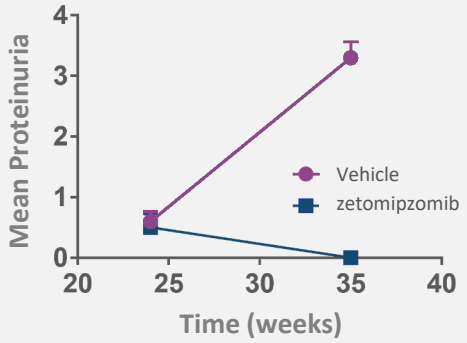
Human Data

Pharmacodynamics in Healthy Volunteers (45 mg)[1,2]

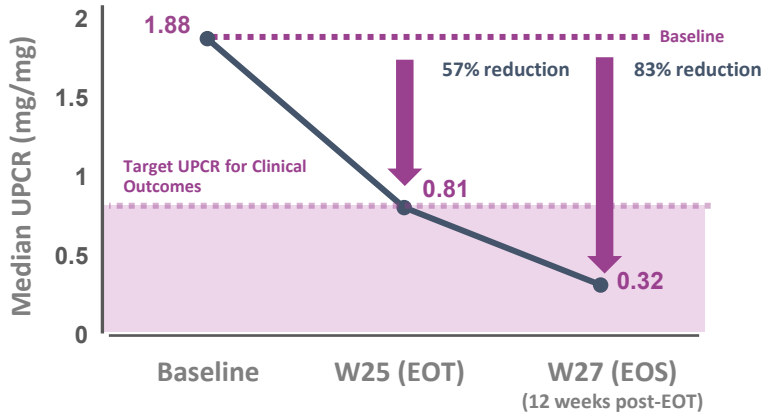


Proteinuria

Proteinuria Changes in NZB/W F1 Mice[1,2]

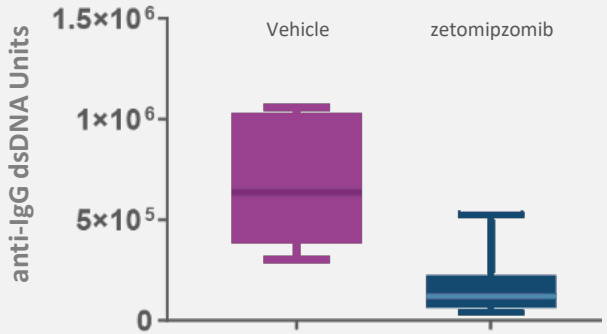


Change in UPCR in LN Patients[3]

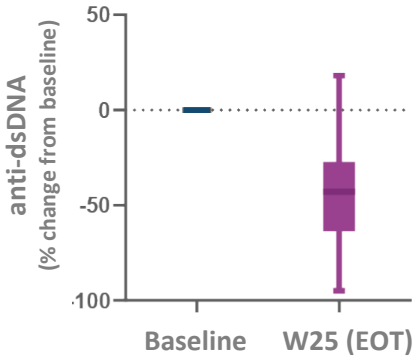


Biomarkers

Anti-dsDNA Antibody Levels in NZB/W F1 Mice[3]



Anti-dsDNA Antibody Levels in LN Patients



Source: [1]Kirk *Et al. Cells.* 2021, *11* (1), 9. [2]Muchamuel *Et al. Frontiers in immunology* 2023, *14.* [3]Saxena *Et al. Annals of the Rheumatic Diseases* 2023, *82* (Suppl 1), 891–892.

ZETOMIPZOMIB:

PORTOLA

Phase 2a Placebo-Controlled Study
Evaluating Zetomipzomib in AIH

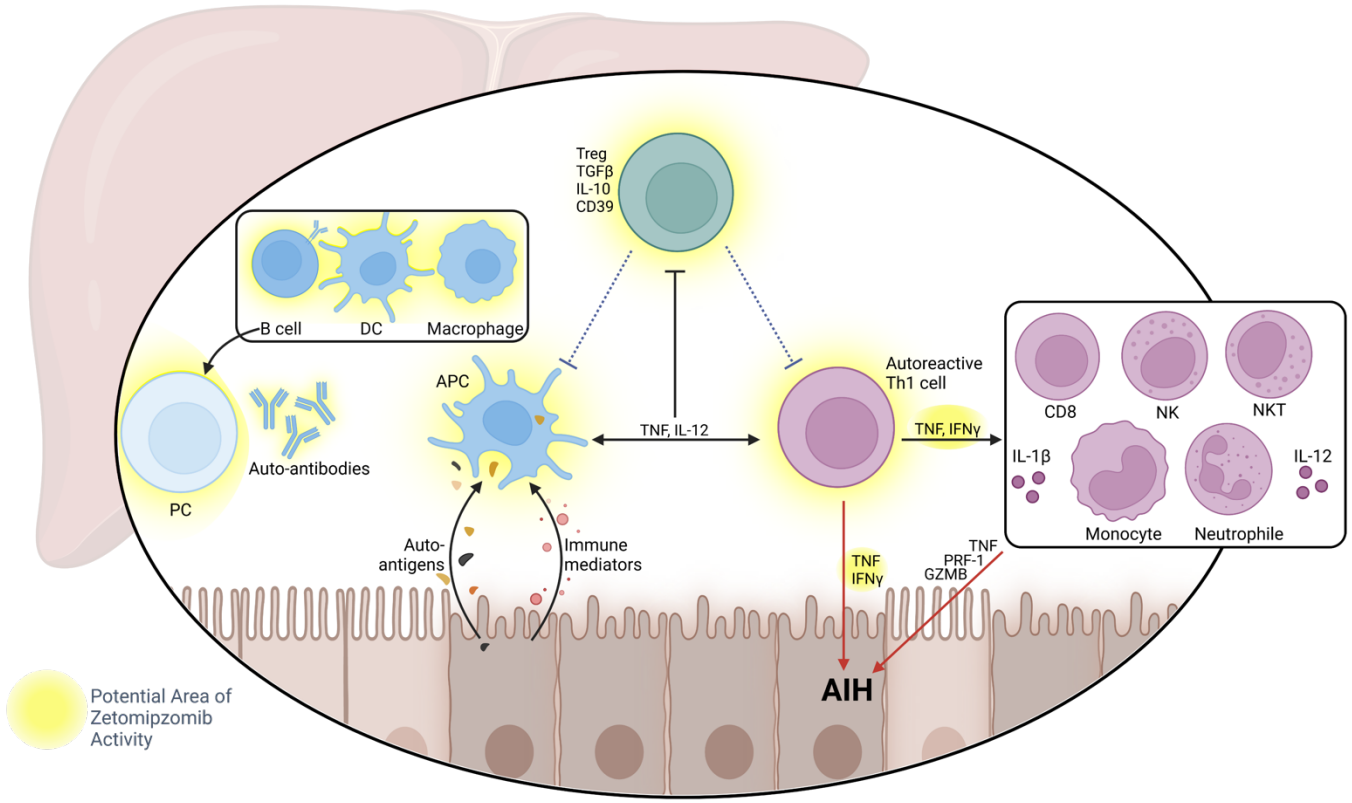
Zetomipzomib: Autoimmune Hepatitis (AIH)
Significant Need For Treatments that Reduce Use of Chronic Immunosuppression

AIH: Complex Autoimmune Liver Disease with Increasing Prevalence

Significant Unmet Need Remains:

- Chronic, immunosuppressive steroids are the mainstay treatment[1]
- 35% of patients on SOC do not go into remission[2]
- **Significant need for treatments that reduce the use of corticosteroids**

Zetomipzomib Targets Multiple Immune Effector Cells Involved in AIH



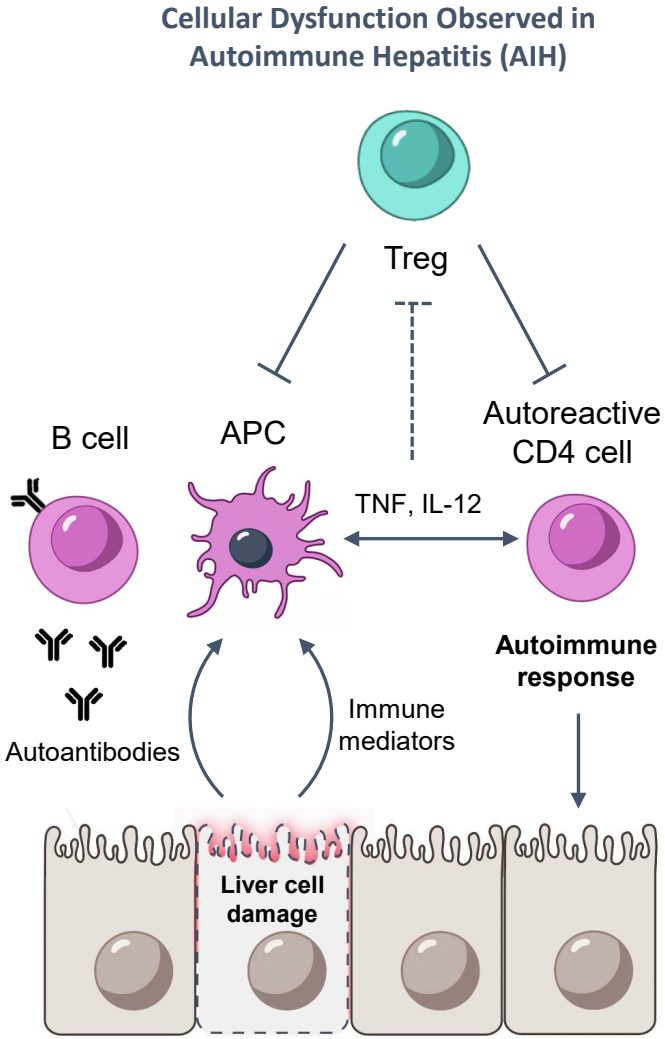
Adapted from Herkel et al., *Journal of Hepatology*. 2020,73(2):446-448.

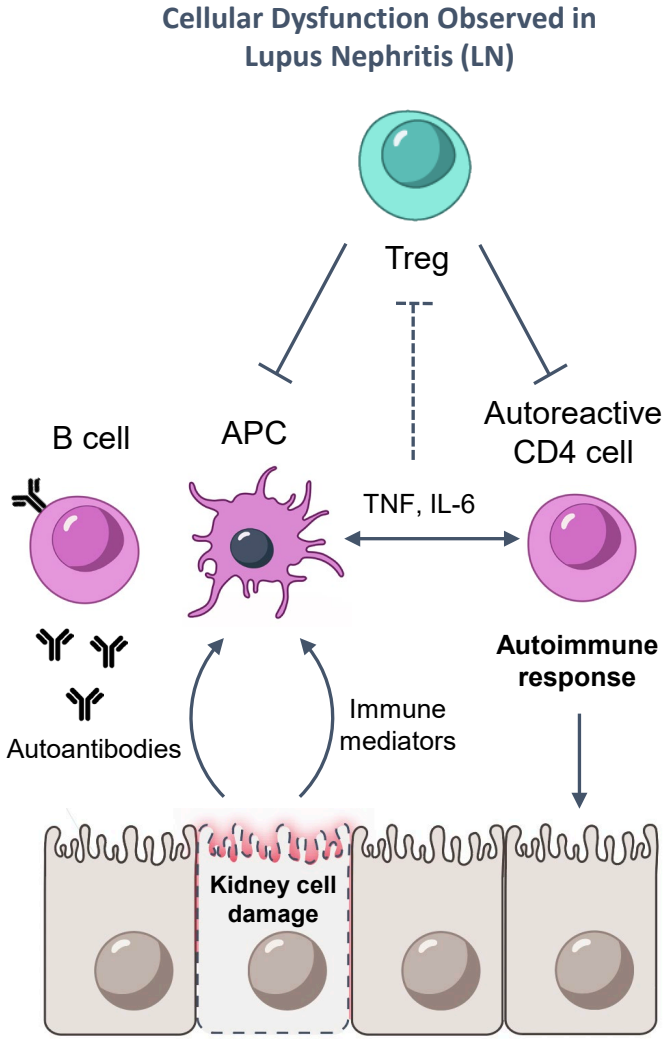
[1]Mack *et al*., *Hepatology*. 2020;72(2):671-722. [2]Volk and Reau. *Clinical Liver Disease*. 2021;17(2):85-89.
Abbreviations: AIH, autoimmune hepatitis; SOC, standard of care.

Autoimmune Disorders Such as Autoimmune Hepatitis (AIH) and Lupus Nephritis Share Common Disease Biology

Common underlying pathophysiologic cellular and molecular mechanisms in LN and AIH

- ✓ B cells and plasma cells producing autoantibodies
- ✓ Antigen Presenting Cells (APC) producing pro-inflammatory cytokines such as TNF-α, IL-6, IL-23 and Type I IFNs
- ✓ Autoreactive Th1 and Th17
- ✓ Hypoactive Treg



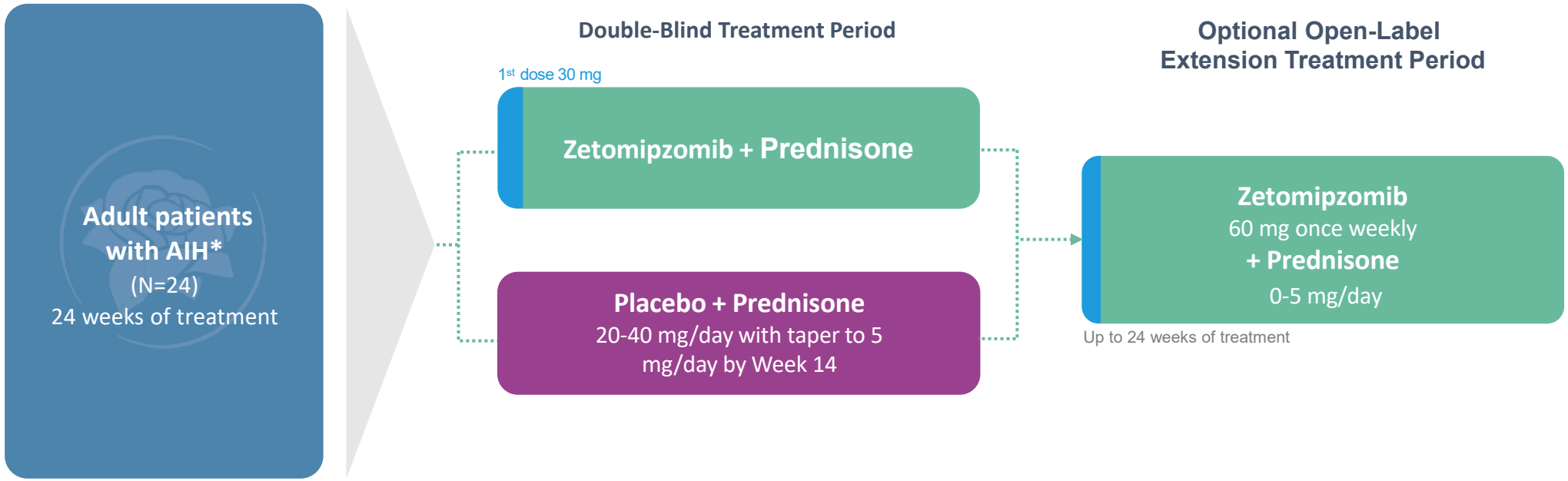


[1]Mack *et al*., *Hepatology*. 2020;72(2):671-722. [2]Volk and Reau. *Clinical Liver Disease*. 2021;17(2):85-89.
Abbreviations: AIH, autoimmune hepatitis; SOC, standard of care.

Adapted from Herkel et al., *Journal of Hepatology*. 2020,73(2):446-448.

PORTOLA: Phase 2a Placebo-Controlled Trial Evaluating the Safety and Efficacy of Zetomipzomib in Autoimmune Hepatitis

Key Eligibility: *Clinical diagnosis of AIH + active disease despite SOC therapy for ≥ 3 months



NCT05569759

Abbreviations: AIH, autoimmune hepatitis; ALT, alanine transaminase; AST, aspartate transaminase; SOC, standard of care.

ZETOMIPZOMIB:

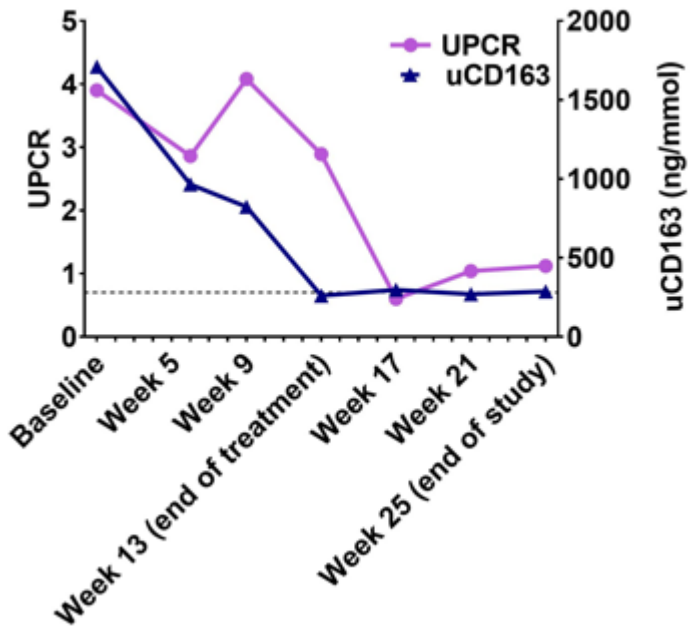
PALIZADE

(Supported by MISSION Data)

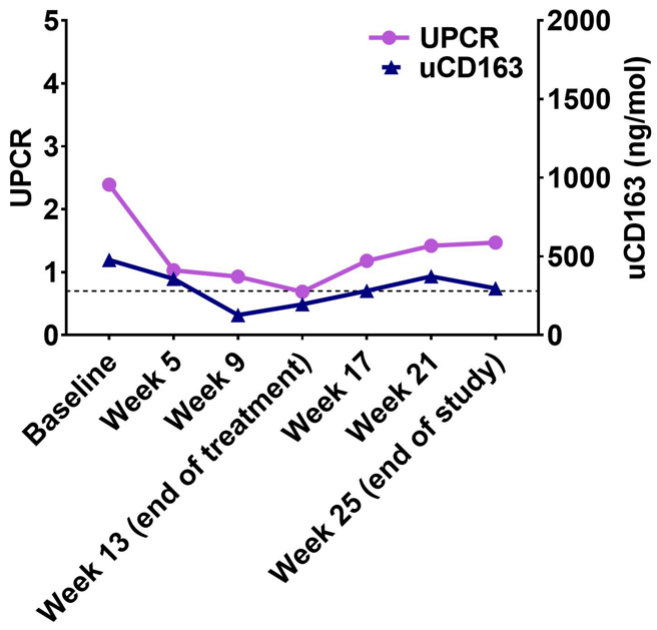
Phase 2b Global Study Evaluating
Zetomipzomib in Lupus Nephritis

MISSION Phase 1b: Zetomipzomib Reduced UPCR and uCD163 in 2 of 2 LN Patients without Induction Therapy

Patient 1
(LN class IV/V)



Patient 2
(LN class III)



uCD163 - novel noninvasive biomarker that correlates with active LN inflammation and shows moderate concordance with UPCR; normalized to urine creatinine.

- Baseline stable treatment regimen of leflunomide, hydroxychloroquine, and prednisone (10 mg/d); failed prior tacrolimus
- >50% reduction in UPCR at week 17
- Reduced anti-dsDNA at week 13

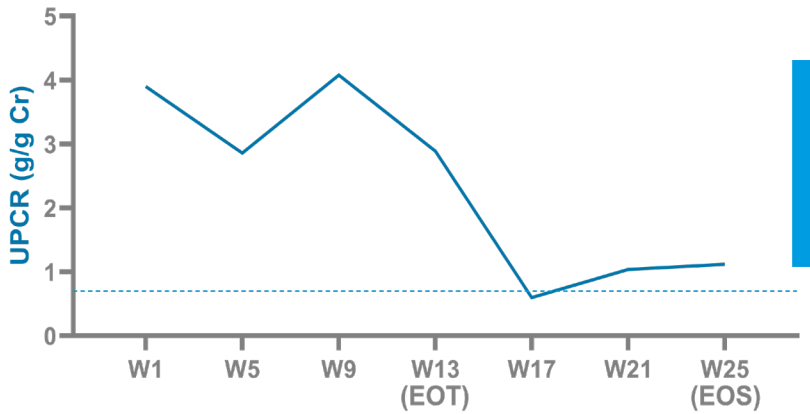
- Baseline stable treatment regimen of MMF (2 g), hydroxychloroquine, and prednisone (10 mg/d)
- >50% reduction in UPCR at week 5
- Improved symptom scores at week 5
- Reduced anti-dsDNA at week 5

Source: EULAR 2021
Abbreviations: anti-dsDNA, anti–double-stranded DNA antibody; LN, lupus nephritis; MMF, mycophenolate mofetil; UPCR, urine protein to creatine ratio; uCD163, urinary CD163.

Successful Retreatment with Zetomipzomib Following 9 Months of Stable Response

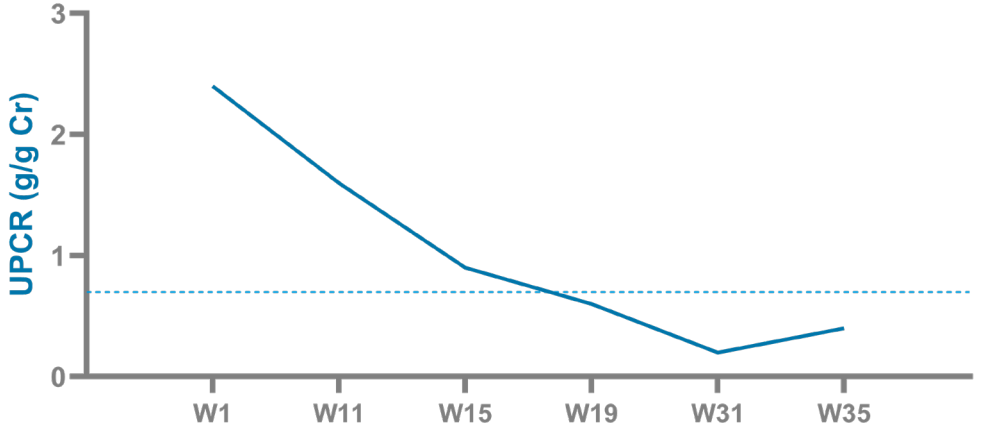
THE OHIO STATE UNIVERSITY WEXNER MEDICAL CENTER

MISSION Ph 1b Patient 1



- 9 months post-MISSION: renal flare occurred and was not fully responsive to SOC
- Patient retreated with zetomipzomib following single patient IND

2nd Treatment with zetomipzomib



Disease activity assessment:

Instrument	Baseline	Week 13 (EOT)	Week 25 (EOS)
SLEDAI-2K	17	12	8
PGA (mm)	67	59	35

Serologic biomarkers:

- Anti-dsDNA antibody: Improvement
- C3: Improvement
- C4 values normalized after zetomipzomib treatment

Disease activity assessment:

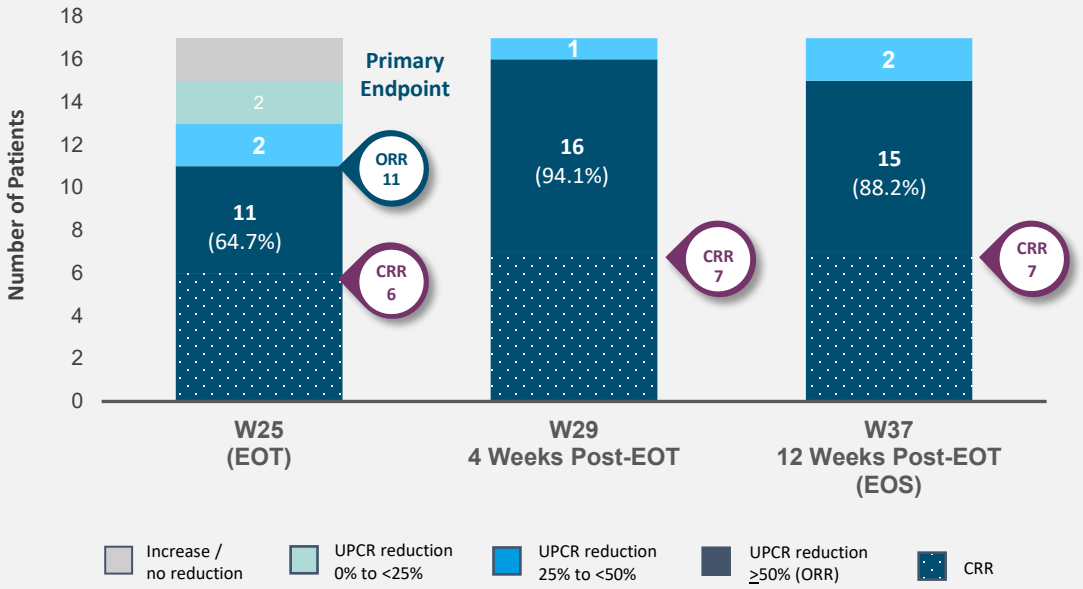
Instrument	Baseline	Week 11	Week 15	Week 27	Week 33
SLEDAI-2K	10	4	6	0	n/a
PGA (mm)	63	44	51.5	37	n/a

Serologic biomarkers:

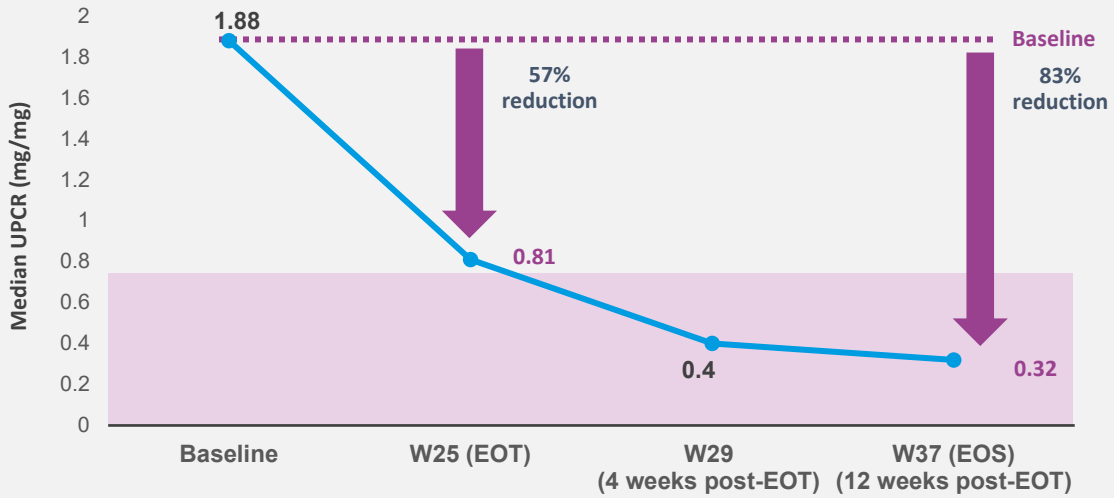
- Anti-dsDNA antibody: Improvement
- C3/C4 values normalized after zetomipzomib treatment

MISSION Ph 2a Overview: Zetomipzomib Achieves Clinically Meaningful Overall Renal Response in Refractory or Hard-to-Treat LN Patients without Standard Induction Therapy[1]

Early Renal Response with Clinically Meaningful ORR (65%) and CRR (35%) at W25…



… and Continued Improvement in UPCR Reduction Post Treatment



Mean daily prednisone background dosage was reduced from 19.2 mg at baseline to 9.1 mg at EOT and was further reduced at Week 29.

Source: ACR 2022, ASN 2022. **Abbreviation:** EOT, End of Treatment; EOS, End of Study.

1. Reporting Evaluable population (n=17) - patients that did not withdraw before Week 25.

MISSION Phase 1b/2a: Zetomipzomib Treatment Improved Key SLE Disease Activity Scores in as Quickly as 13 Weeks

	MISSION 1b (n=35)		MISSION 2a (n=17)	
Tool	Baseline	EOT (Week 13)	Baseline	EOT (Week 25)
SLEDAI-2K	9.1	6.6	11.3	6.5
CLASI-A	4.3	2.3	3.7	1.9
Physician Global Assessment Score	57.0	39.7	57.2	23.9
Patient Global Assessment Score	58.3	38.2	23.6	10.7
HAQ-pain	58.5	43.1	21.3	12.2

*Evaluable population are the ITT participants that did not withdraw before Week 13/25.
Abbreviations: CLASI-A, Cutaneous Lupus Erythematosus Severity Index-Activity; EOT, end of treatment; EOS, end of study; HAQ, Health Assessment QuestionnaireSLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; TJC, tender joint count.

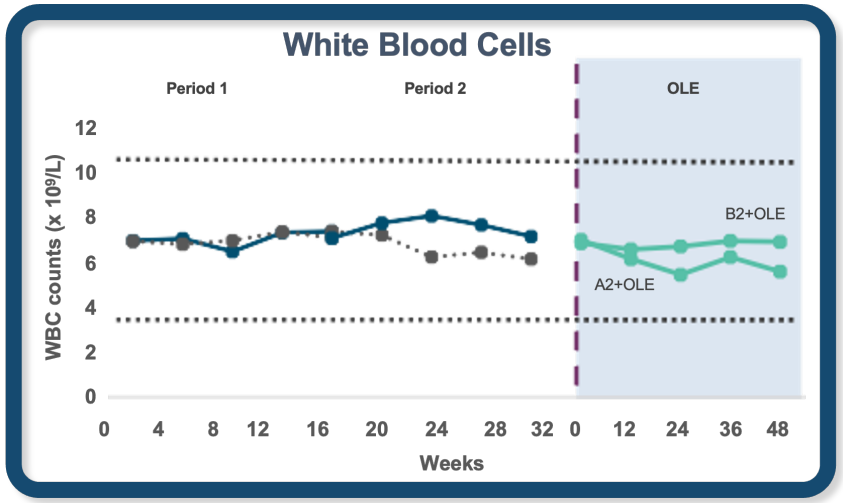
Source: EULAR 2021, ACR 2022, ASN 2022.

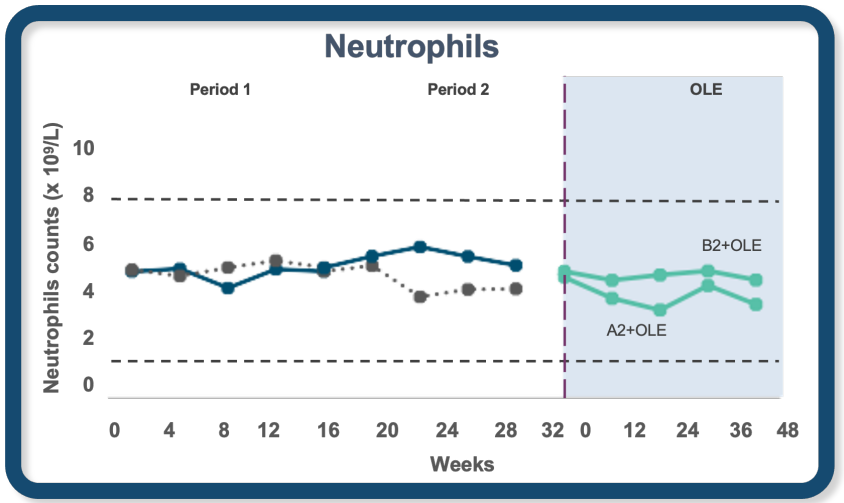
Zetomipzomib: Favorable Safety and Tolerability Profile in Patients with Autoimmune Diseases; No Opportunistic Infections Observed to Date

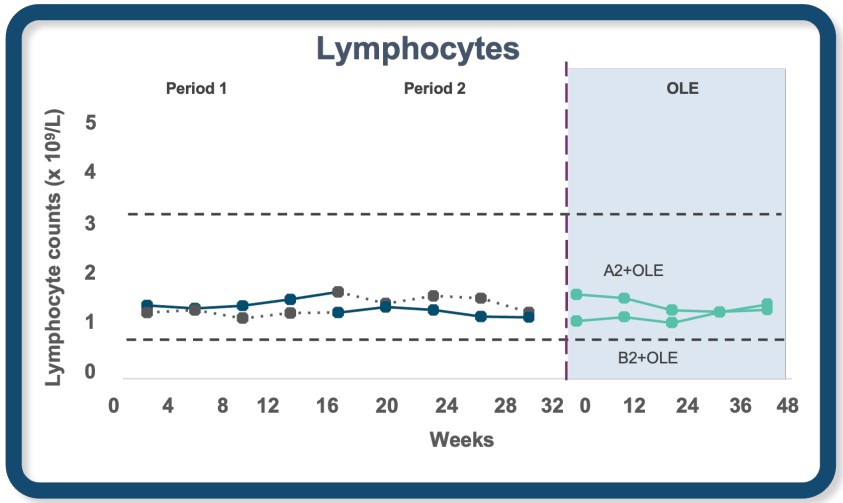
Adverse Events	MISSION Ph1b N=47 (%)	MISSION Ph2a N=21 (%)	PRESIDIO Zetomipzomib N=25 (%)	PRESIDIO OLE Zetomipzomib N=18 (%)	PRESIDIO Placebo N=22 (%)
Treatment Period (Weeks)	13	24	16	Up to 64	16
Most Common TEAE: Injection-site Reaction	20 (42.6)	15 (71.4)	18 (72.0)	14 (77.8)	3 (13.6)
TEAE Leading to Study Drug Discontinuation	10 (21.3)	4 (19.0)	1 (4.0)	3 (16.7)	0 (0)
Serious TEAE	4 (8.5)	2 (9.5)	2 (8.0)	1 (5.6)	1 (4.5)
Infectious TEAE	11 (23.4)	9 (42.9)	7 (28.0)	8 (44.4)	6 (27.3)
Grade ≥3 Infectious TEAE	1 (0.02)	0 (0)	0 (0)	0 (0)	1 (4.5)
Opportunistic Infections	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

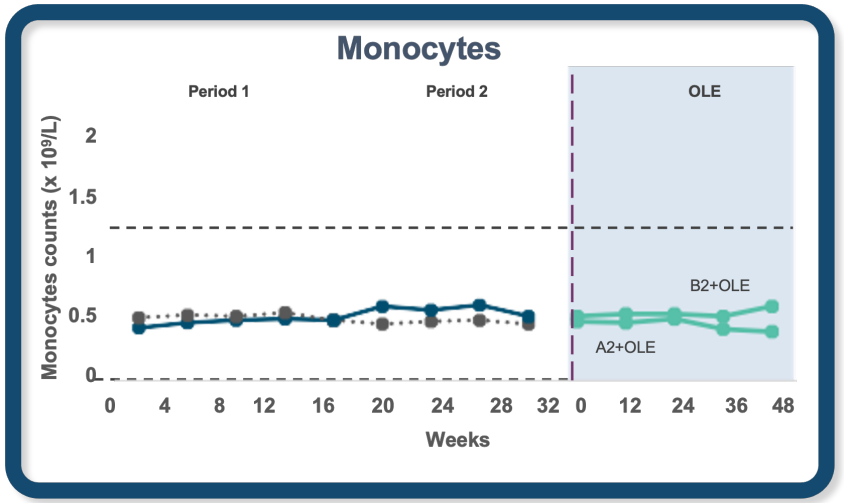
Abbreviation: TEAE, treatment emergent adverse event; additional TEAEs include nausea, vomiting, and headache
Source: EULAR 2021, ACR 2022, ASN 2022, ACR 2023

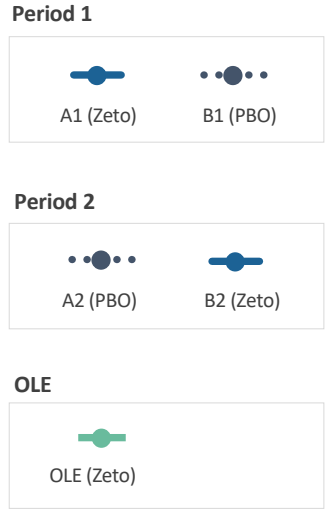
PRESIDIO: Long-Term Safety Data Demonstrates No Evidence of Immunosuppression; Preserved Immune Cell Counts Observed with Zetomipzomib Treatment











Zetomipzomib's Mechanism of Action is Differentiated from Other Agents in this Therapeutic Area

Broad mechanism of action targets multiple immune cell subtypes including macrophages, T-cells, and B-cells

Rapid reduction of UPCR with multiple CRR (5 of 17 patients) seen as soon as Week 13 without induction therapy

No evidence of immunosuppression, with no clinically significant serious or opportunistic infections observed to date

PALIZADE: Phase 2b Global, Placebo-Controlled Trial Evaluating the Efficacy and Safety of Zetomipzomib in Active Lupus Nephritis

Key Eligibility: ^Class III/IV ± V with 24-hour UPCR ≥1.0 (n=249); Class V with 24-hour UPCR ≥2.0 (n=30)

Adult Patients with Active LN (N=279)
52 weeks of treatment

Zetomipzomib
30 mg SC QW + SOC[1]

1st dose 30 mg

Zetomipzomib
60 mg SC QW + SOC[1]

Placebo[2]
SC QW + SOC[1]

ENDPOINTS

Primary Endpoints
- Complete renal response (CRR[3]) at week 37
- Safety & Tolerability

Key Secondary Endpoints
- Partial renal response (PRR[4]) at Week 37
- CRR at Weeks 25 and 53
- PRR at Weeks 25 and 53

Other Endpoints
- SLE Disease Activity Measures

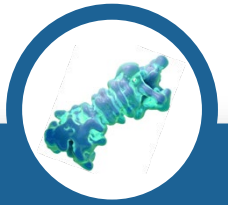
NCT05781750

1. MMF or equivalent (target dose 2 gm/d), oral corticosteroids (0.3-0.5 mg/kg/d, maximum 40 mg/d) and IV methylprednisolone (500 mg-1 gm, up to 3 gm, with opt-out for AE or lack of response).
2. Volume matched placebos with patients randomized 2:1 (zetomipzomib 30 mg: placebo) 2:1 (zetomipzomib 60 mg: placebo).
3. CRR: UPCR ≤0.5 and eGFR ≥60 mL/min/1.73 m^2 or no confirmed decrease of >20% from Baseline eGFR.
4. PRR: ≥50% reduction of UPCR from Baseline, and to <1.0 if the Baseline UPCR was <3.0 or to <3.0 if the Baseline value was ≥3.0.

Responder requirement: Should not have received >10 mg prednisone (or equivalent) for ≥3 consecutive days or for ≥7 days in total during the 8 weeks prior to a CRR assessment and no use of rescue or prohibited medication.

***Abbreviations**: AE, adverse event; CRR, complete renal response; EOT, end of treatment; EOS, end of study; LN, lupus nephritis; PGA, Physician's Global Assessment; QW, once every week; SC, subcutaneous; SLE, Systemic Lupus Erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; UPCR, urine protein to creatinine ratio; SFU, safety follow up.*

Looking Ahead: Key Upcoming Expected Milestones



Zetomipzomib: Selective Immunoproteasome Inhibition

- Report PORTOLA Phase 2a topline results in patients with AIH in 1H 2025
- Report PALIZADE Phase 2b topline results in patients with LN in mid-2026

Strong cash position to fund future catalysts

$164M cash, cash equivalents and marketable securities as of June 30, 2024

Abbreviations: AIH, autoimmune hepatitis; LN, lupus nephritis.

Developing Novel, First-In-Class Medicines to Transform Immunology

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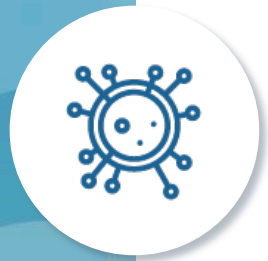
First-In-Class Small Molecule Therapeutic with Differentiated Approach to Treating Immune-Mediated Diseases



Zetomipzomib: Selective Immunoproteasome Inhibition Leads to Broad and Potent Immunomodulation without Immunosuppression

Pipeline-in-a-Product Profile with Multiple Avenues to Value Creation

Strong Team of Research Scientists and Drug Developers

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