KEZAR LIFE SCIENCES

Corporate Presentation

September 2025

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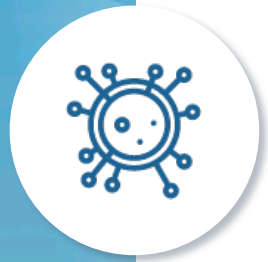
Developing Novel, First-In-Class Medicines to Transform Immunology



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

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

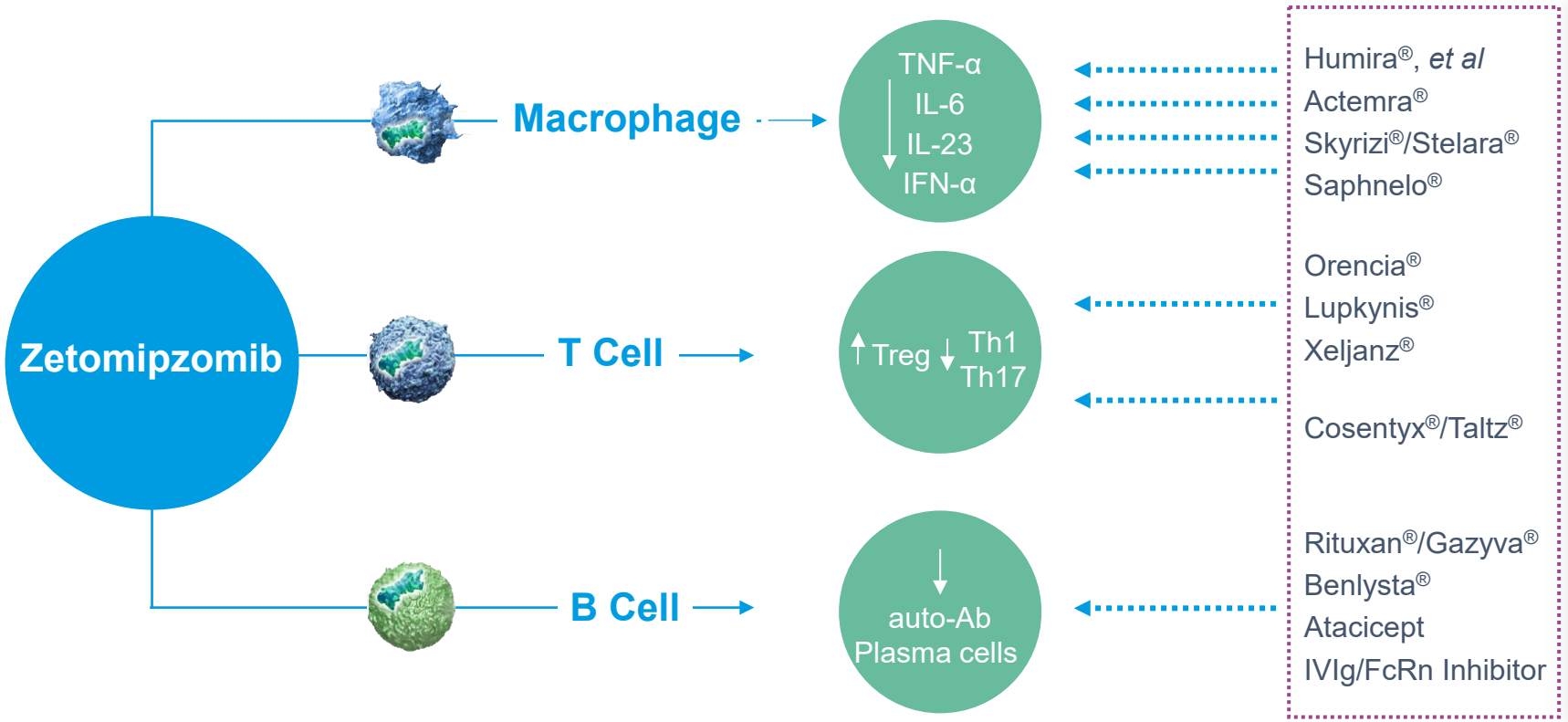
Sole Agent in Development in Autoimmune Hepatitis (AIH) with Positive Phase 2 Results Reported from PORTOLA Study

Strong, Experienced Team of Research Scientists and Drug Developers

Zetomipzomib, a First-in-Class Inhibitor of the Immunoproteasome: Broad Immunomodulation with Low Risk for Immunosuppression

Immunoproteasome Inhibition with Zetomipzomib*

Decreases pro-inflammatory cytokine production, plasma cell activity and autoantibody production, while increasing regulatory T cells activity



Zetomipzomib Advantage

Broad spectrum impact of key regulators of autoimmune diseases

- 20 years of research pioneered by Kezar scientists
- >100 publications highlighting the therapeutic potential
- Biomarker and clinical data in >200 patients demonstrates immunomodulatory activity
- Low risk of immunosuppression seen in patients

Zetomipzomib Acts Across the Innate and Acquired Immune System

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

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Selective Inhibition of the Immunoproteasome Impacts Multiple Drivers of Autoimmune Hepatitis

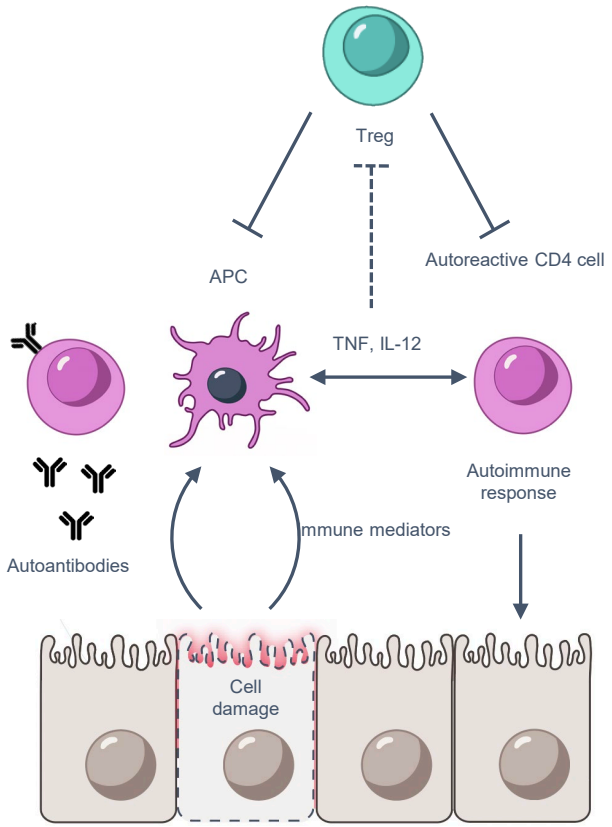
Broad Immunomodulatory Activity

- Reduction of multiple inflammatory cytokines from antigen presenting cells (APC)
- Reduced inflammatory T-cell activity (Th1 and Th17)
- Increased Treg function
- Decreased plasma cell activity and autoantibody production

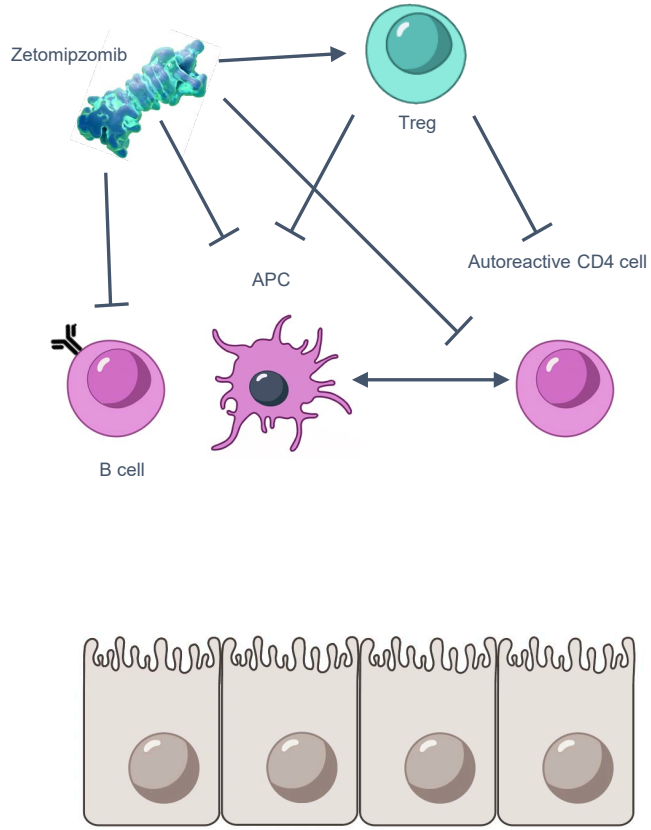
Broad Therapeutic Potential

- Rapid onset of activity
- Minimal risk for immunosuppression
- Potential as steroid sparing agent
- No lab monitoring expected
- Active in patients with severe and treatment refractory disease

Cellular Dysfunction Observed in AIH



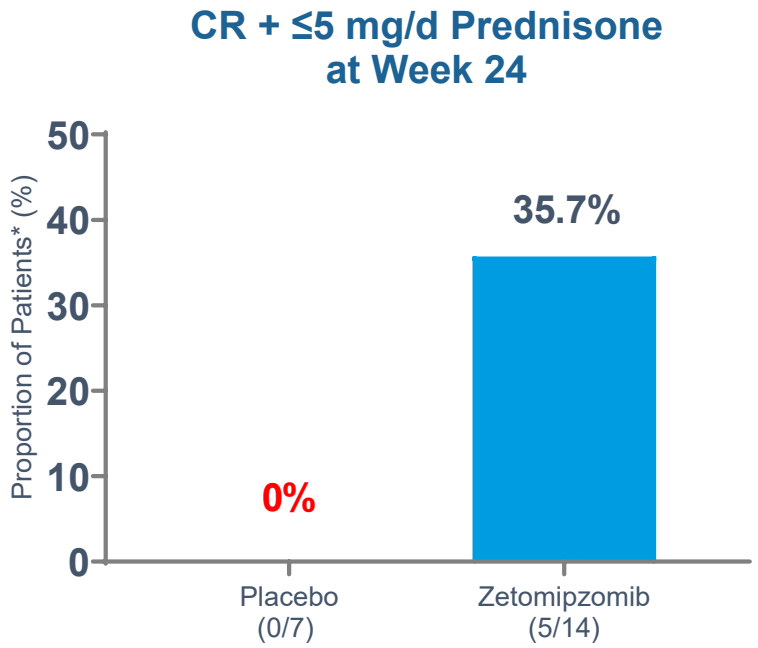
Zetomipzomib Targets Multiple Immune Effector Cells Involved in Autoimmunity



Zetomipzomib: PORTOLA

Phase 2 Placebo-Controlled Trial Evaluating Zetomipzomib in Autoimmune Hepatitis (AIH)

Zetomipzomib Treatment Results in High Rates of Steroid Sparing Biochemical Remissions (CR) in a Difficult-to-Treat AIH Patient Population



*ITT population, prespecified subset analysis of patients entering study on steroid-based therapy (N=21).

Abbreviations: mHAI, modified Histologic Activity Index.

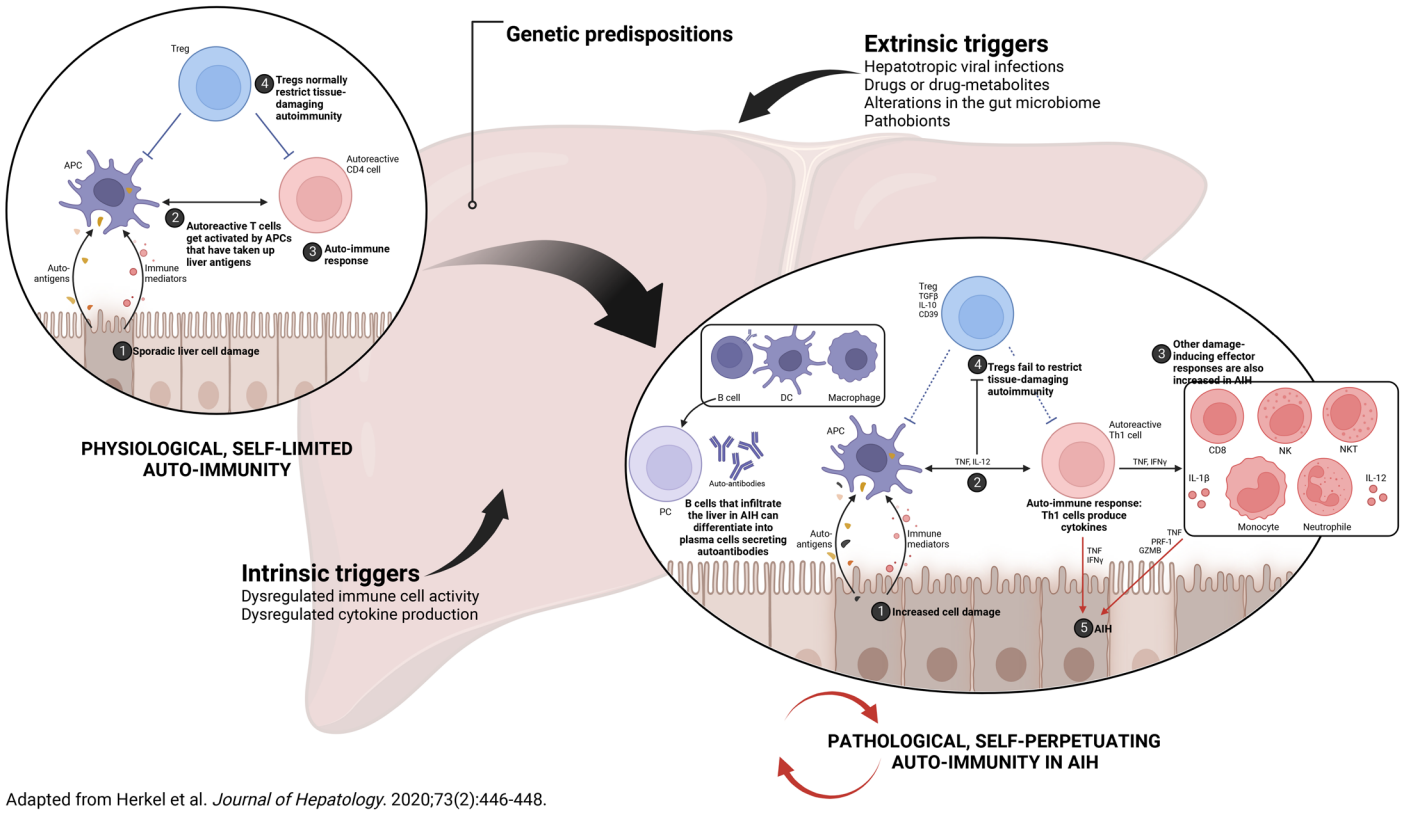
Key Efficacy Findings from PORTOLA

- Median duration of response was ~7 months (Feb 2025 data cut)
- No flares in zetomipzomib patients achieving response
- Histologic changes (reduced mHAI) corresponded to biochemical remissions

Key Safety Findings from PORTOLA

- Most common treatment emergent adverse events (TEAEs) were injection site reactions (ISRs) and systemic injection reactions (SIRs), all Grade 1 or Grade 2
- All serious adverse events (SAEs) were considered unrelated and balanced between arms

Autoimmune Hepatitis is a Complex Disease with Poor Treatment Options



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

~100,000 cases in US (similar prevalence in EU)

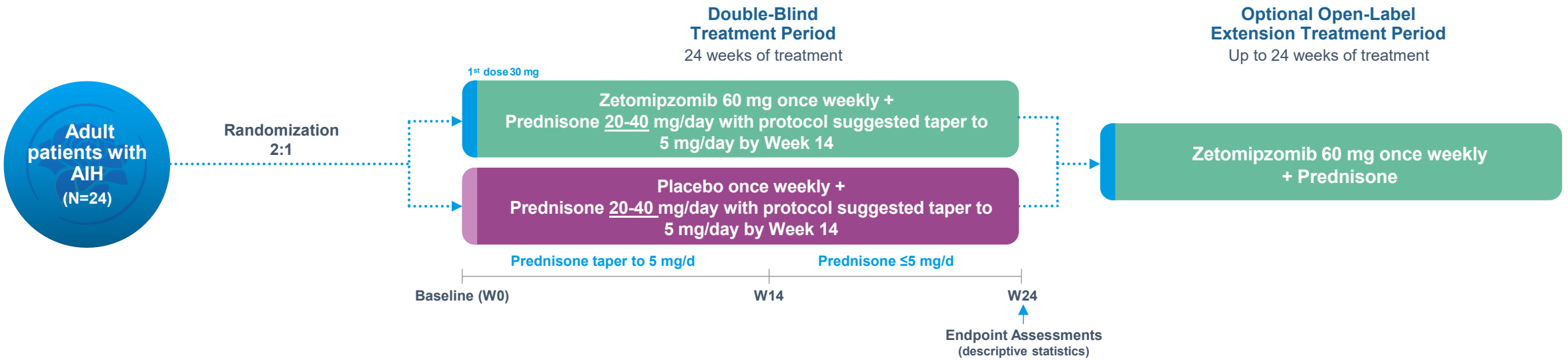
4:1 female to male

- Diagnosis involves presence of elevated liver enzymes (ALT/AST) and immunoglobulin G (IgG), inflammatory cell infiltration in the liver, elevated autoantibodies (ANA, SMA)
- Current standard of care involves long term use of corticosteroids and immunosuppressants to achieve and maintain biochemical remission

Significant Unmet Needs in AIH

- **30 – 50% fail to achieve remission, flare, or are intolerant to standard of care treatment**
- **Chronic corticosteroid use increases health risks and decreases quality of life for patients**
- **>5-fold risk of liver failure or liver related death in patients who do not achieve a complete remission by 6 months**

PORTOLA: Phase 2a Placebo-Controlled Trial Evaluating Safety and Efficacy of Zetomipzomib in Relapsed/Refractory AIH



Key Inclusion Criteria

- Active AIH despite therapy for ≥3 months or disease flare after experiencing complete response
- Liver biopsy results with Ishak score[1] (modified HAI) ≥5 (18 max) indicating active AIH (within 6 months)
- Screening ALT values that are 1.25 to 10 times ULN
- Normal hepatic function or mild hepatic impairment (Child-Pugh A)

Key Stratification

- Patients entering clinical trial (screening period) on steroid-based therapy
- 21 of 24 patients entered screening on daily steroid therapy

https://clinicaltrials.gov/ct2/show/NCT05569759 [1]Ishak K et al. J Hepatol. 1995 June;22(6):696-9.

Abbreviations: AIH, autoimmune hepatitis; ALT, alanine aminotransferase; HAI, Histologic Activity Index; ULN, upper limit of normal.

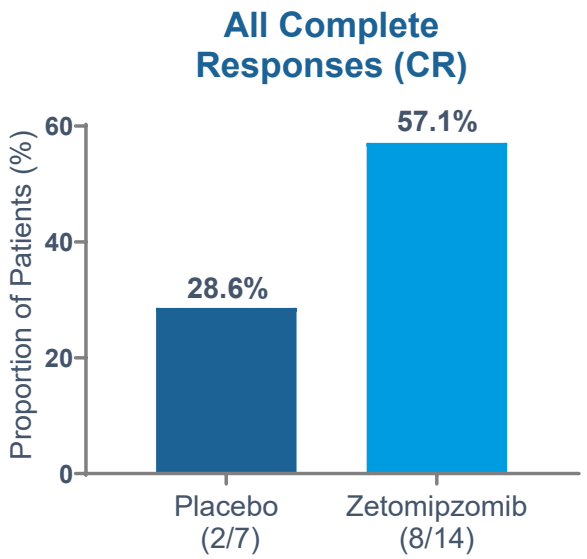
PORTOLA Endpoints Reflect Disease Characteristics and Treatment Guidelines

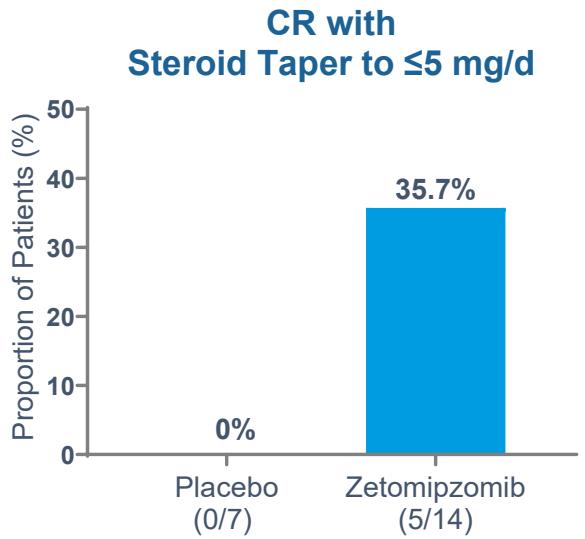
PORTOLA Endpoints	Clinical Relevance
Primary Efficacy Endpoint Proportion of patients who achieve a complete biochemical response (CR) by Week 24 without an increase in baseline steroid dose	Achieving CR defined as normalization of ALT, AST and IgG levels (if IgG levels were elevated at baseline) is required to reduce long term risk
Key Secondary Efficacy Endpoint Proportion of patients who achieve a CR and a successful glucocorticoid taper by Week 24	Treatment Guidelines (AASLD and EASL) include CR with steroid dose ≤5 mg/day by Week 24
Exploratory Efficacy Endpoint Change from baseline in liver histopathology at Week 24, based on Ishak score (modified Histological Activity Index)	Disease is Driven by Hepatic Inflammation

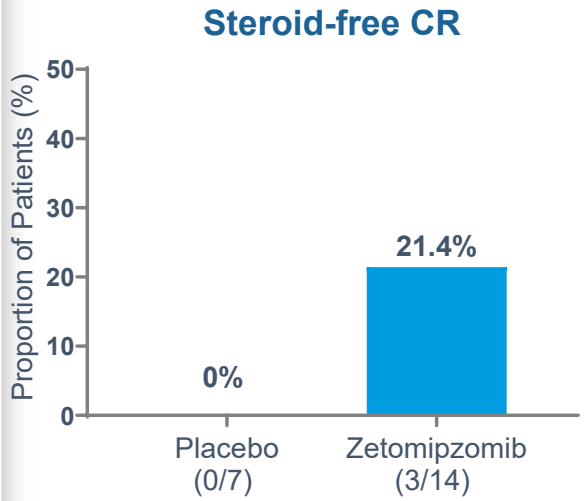
Zetomipzomib Treatment Induces Steroid-Free Biochemical Remissions

Response Rates Based on Steroid Taper in Prespecified Subset Analysis (N=21)

AASLD and EASL Guidelines Target Treatment Goals



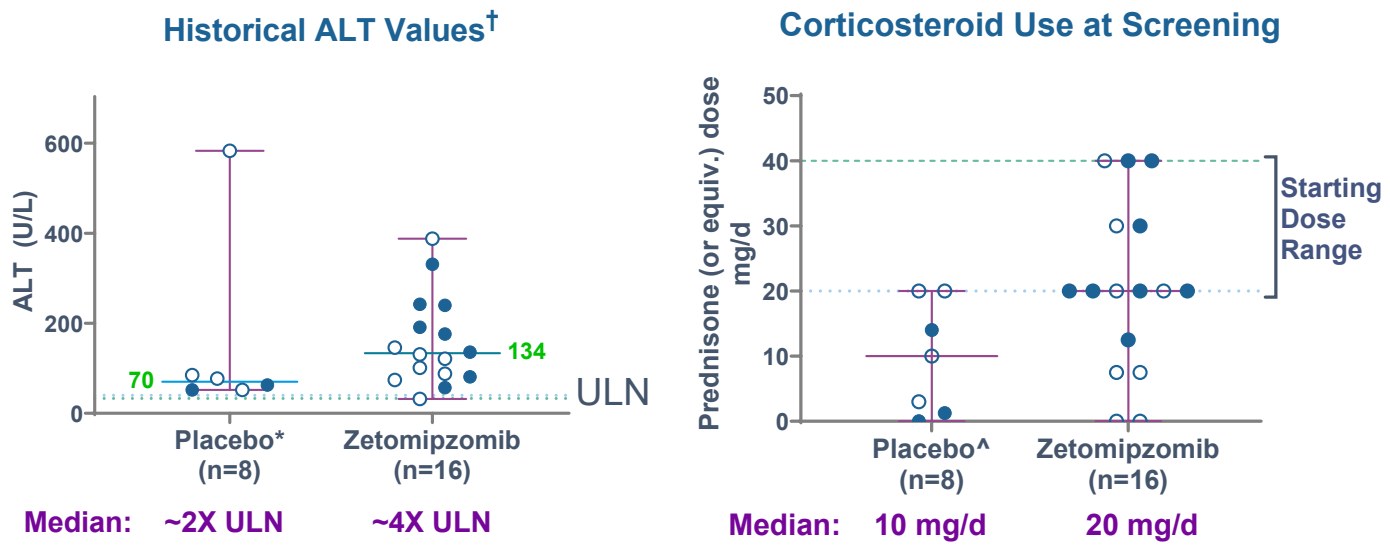




- **Median duration of response of 8 zetomipzomib CRs is 27.6 weeks (includes OLE from Feb-2025)**
- **1 Placebo patient achieved a CR with steroid taper to 5 mg/d following enrollment to OLE**
- **No disease flares in any patient achieving CR on zetomipzomib during study, including OLE**

ITT population, prespecified subset analysis of patients entering study on steroid-based therapy (N=21).
Complete Response: Normal ALT, AST, and IgG values (if IgG level is elevated at Baseline) with glucocorticoid dose not higher than starting dose (at Baseline).
ALT normal range female= 10-33 U/L; ALT normal range male= 10-40 U/L; AST normal range female= 10–36 U/L; AST normal range male= 10-43 U/L; IgG normal range= 767 – 1590 mg/dL.
Abbreviations: CR, complete response, OLE, open label extension

Patients Assigned to Zetomipzomib Arm Displayed More Severe Disease (ITT Population)



- With higher historical ALT values and median steroid dose at screening, zetomipzomib arm represented a more refractory patient population vs. placebo
- All placebo patients achieving a CR had steroid increase to 20 mg/d at study start
- 2 of 3 placebo patients achieving CR entered study on no or very low steroid dose
- 6 of 7 zetomipzomib patients achieving CR entered study at the protocol mandated starting dose of prednisone

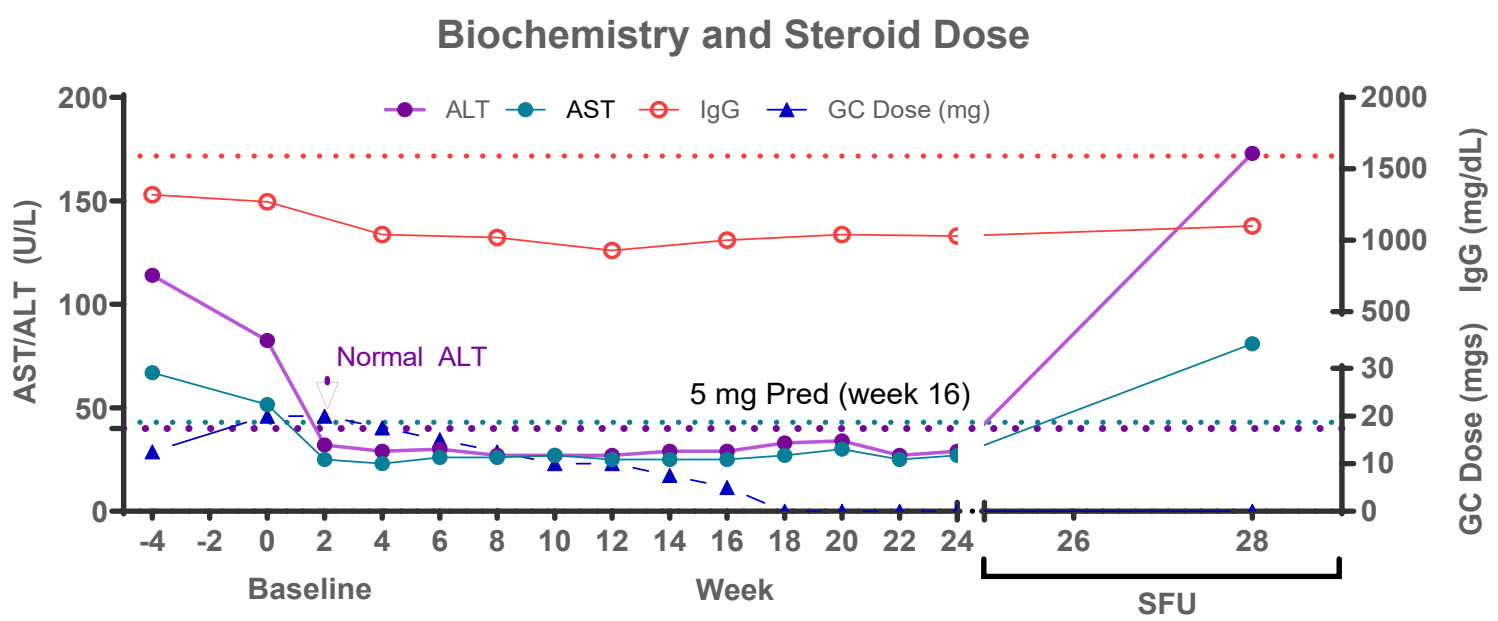
†Mean Historical ALT ≤3 months prior to Screening. | *Two patients in the placebo arm did not have available prescreening values.
^Placebo patient randomized but not dosed and did not have available prescreening values. | ALT ULN: 33 (F), 40 (M) U/L..
Abbreviations: ALT, alanine aminotransferase, CR, complete response.

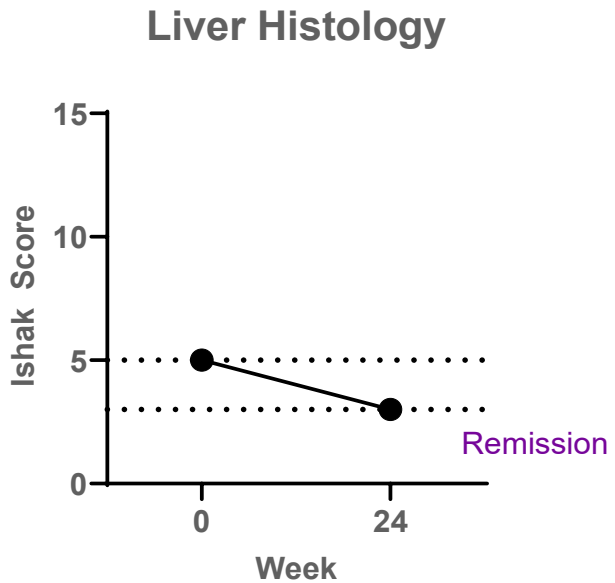
PORTOLA Patient Journey

67 y/o white male, AIH since 2021 (2.8 years), ANA+, receiving MMF + Prednisone at Baseline
Mean ALT prior to screening: 136 U/L

PORTOLA Results

- Steroid-free CR achieved by Week 18 of zetomipzomib treatment
- 6-fold increase in ALT values 4 weeks following cessation of zetomipzomib administration in safety follow up period
- Histologic Remission
- Liver Stiffness (Elastography): 25% Improvement in 6 months





ALT ULN=40 U/L; AST ULN=43 U/L; IgG ULN=1590 mg/dL
Abbreviations: DBTP, double-blind treatment period; CR, complete response; GC, glucocorticoid; MMF, mycophenolate mofetil; SFU=Safety Follow Up; ULN, upper limit of normal.

PORTOLA Safety: Favorable Safety and Tolerability Profile with Zetomipzomib Treatment (Safety Population)

Adverse Events in Double-blind Treatment Period	Placebo N=7 n (%)	Zetomipzomib N=16 n (%)
Participants with at least 1 Treatment Emergent Adverse Event (TEAE)	7 (100.0)	16 (100.0)
Most common TEAE:		
Injection Site Reaction (ISR)	4 (57.1)	15 (93.8)
Systemic Injection Reaction (SIR)	1 (14.3)	12 (75.0)
TEAE leading to study drug discontinuation	0 (0)	3* (18.8)
Grade 3 TEAE (no Grade 4 or 5 TEAEs reported)	1 (14.3)	3 (18.8)
Serious TEAE	1† (14.3)	2‡ (12.5)
Infectious TEAE	6 (85.7)	9 (56.3)
Grade ≥3 Infectious TEAE	0 (0)	1 (6.3)
Opportunistic Infections¶	0 (0)	0 (0)
Death	0 (0)	0 (0)

✓ **100% of ISR-related AEs were Grade 1 or Grade 2**

✓ **100% of SIR-related AEs were Grade 1 or Grade 2**

Specific AEs occurring within 8 to 24 hours post-dose, usually resolving within 48 hours post-dose, and consist of ≥1 of the following signs/symptoms: hypotension, tachycardia, nausea, vomiting, dizziness, headache, pyrexia, rigors, and/or chills

Safety Population (N=23) includes all patients who received ≥1 dose of study treatment.
*Grade 2 unrelated AIH flare (treatment failure per protocol), Grade 2 related hives, and Grade 1 related fatigue.
†Grade 3 unrelated variceal bleeding x2, with hematemesis and atrial fibrillation.
‡Grade 3 unrelated fever (post-liver biopsy) and unrelated Grade 3 Influenza B infection.
¶Opportunistic infections were evaluated by sponsor through clinical assessment of reported infections.

Safety Data From 300+ Patients in Multiple Autoimmune Disorders Support Benefit-Risk Profile of Zetomipzomib

Safety Across Zetomipzomib 45 mg and 60 mg Doses

Trial/Treatment arm/ Dose (N)	MISSION Ph 2 Zeto 60 mg N=21	PALIZADE Placebo N=28	PALIZADE Zeto 60 mg N=29	PRESIDIO Placebo N=22	PRESIDIO Zeto 45 mg N=25	PORTOLA Placebo N=7*	PORTOLA Zeto 60 mg N=16
Indication	**Lupus Nephritis**			**Polymyositis & Dermatomyositis**		**Autoimmune Hepatitis**	
Treatment Period (Weeks)	**24**	**52†**		**16**		**24**	
At least one TEAE, n (%)	21 (100.0)	17 (60.7)	25 (86.2)	16 (72.7)	22 (88.0)	7 (100.0)	16 (100.0)
Serious TEAEs, n (%)	2 (9.5)	3 (10.7)	8 (27.6)	1 (4.5)	2 (8.0)	1 (14.3)	2 (12.5)
Grade 3 or 4 TEAEs, n (%)	6 (28.6)	3 (10.7)	8^ (27.6)	2 (9.1)	2 (8.0)	1 (14.3)	3 (18.8)
TEAEs leading to study drug discontinuation, n (%)	4 (19.0)	1 (3.6)	4 (13.8)	0 (0)	1 (4.0)	0 (0)	3 (18.8)
Infectious TEAEs, n (%)	9 (42.9)	13 (46.4)	11 (37.9)	6 (27.3)	7 (28.0)	6 (85.7)	9 (56.3)
Grade ≥3 infectious TEAEs, n (%)	0 (0)	0 (0)	3 (10.3)	1 (4.5)	0 (0)	0 (0)	1 (6.3)
Opportunistic infections, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Death, n (%)	0 (0)	1 (3.6)	1 (3.4)¶	0 (0)	0 (0)	0 (0)	0 (0)

*One patient in the placebo arm was not dosed and is not included in these data.
†No participants completed 52 weeks.
^Four participants with serious TEAE were randomized to zetomipzomib 60 mg arm but received zetomipzomib 30 mg before SAE (2 were on the first dose).
¶Patient was randomized to the zetomipzomib 60 mg but only received an initial dose of zetomipzomib 30 mg.

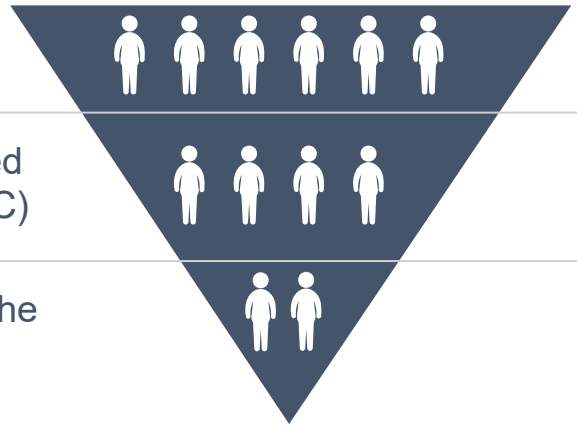
AIH is a High Unmet Need Chronic Liver Disease, Representing >$1B Market Opportunity in Relapsed/Refractory Patients in the US and EU

AIH US and EU Epidemiology Assumptions

~100,000 adult patients diagnosed in US
~130,000 adult patients diagnosed in EU

81% are eligible for treatment (no decompensated cirrhosis or concomitant diagnosis of PBC or PSC)

~46% of patients are inadequately managed by the current SOC (second line population)



Zetomipzomib is the Sole Agent in Development for AIH with Positive Results From a Randomized Clinical Trial

Zetomipzomib Has Potential To Be The First Approved Therapy in AIH

Inclusion of First-Line Patient Population Raises Peak Sales Opportunity to >$2.5B

Market research based on third party sources.
Abbreviations: AIH, autoimmune hepatitis; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis; SOC, standard of care.

Next Steps for Zetomipzomib Program in AIH

Key components of a pivotal study in AIH will likely be biochemical remission with steroid taper and histologic improvement

Align with the FDA on a potential registrational study in AIH in Q4 2025

Present full PORTOLA data at AASLD Meeting in November 2025

Zetomipzomib:
Summary of Clinical Activity in Lupus Nephritis (LN)

MISSION PALIZADE

Zetomipzomib has Shown Strong Potential in LN and Systemic Lupus Erythematosus (SLE)

Competitive Profile in SLE Based on Novel Mechanism and Broad Clinical Activity

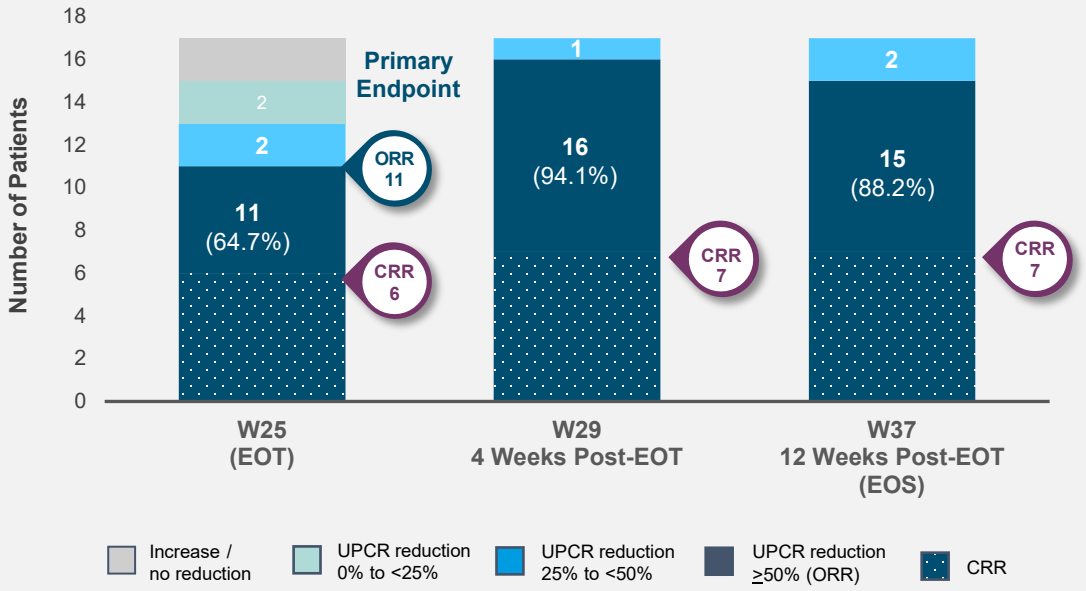
- Rapid improvements in renal function and SLE symptoms seen across 2 clinical trials and ~150 patients
- MISSION: 35% complete renal response rate after 6 months of treatment and without induction therapy
- PALIZADE: 42% of patients achieving a UPCR ≤0.5 at 6 months, a 2-fold higher rates than placebo
- Improvement in multiple measures of disease activity across organ systems in SLE patients

*In October 2024, PALIZADE Phase 2 trial terminated for strategic reasons.

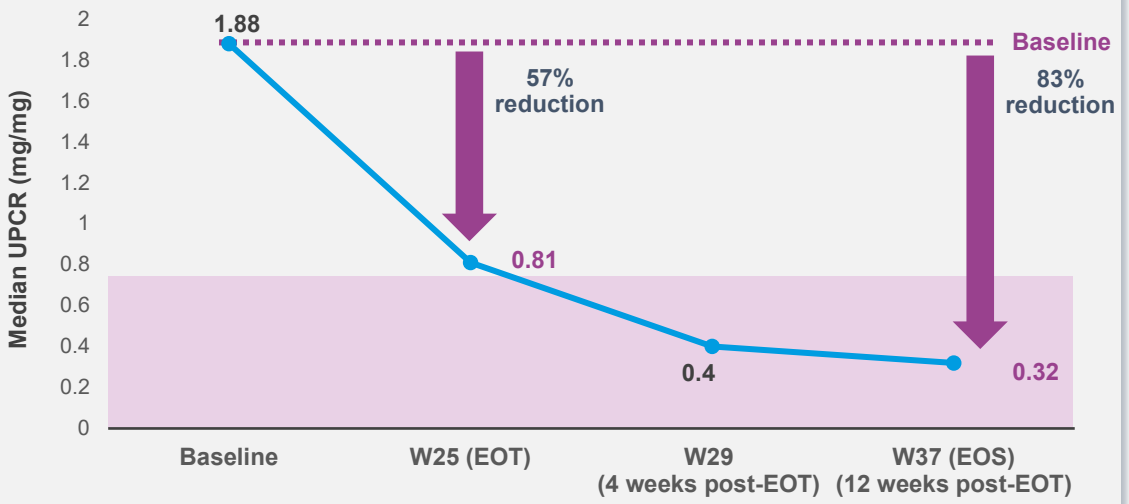
Furie R *et al.*, EULAR 2021 and Data on File.

MISSION Phase 2: High Rates of 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

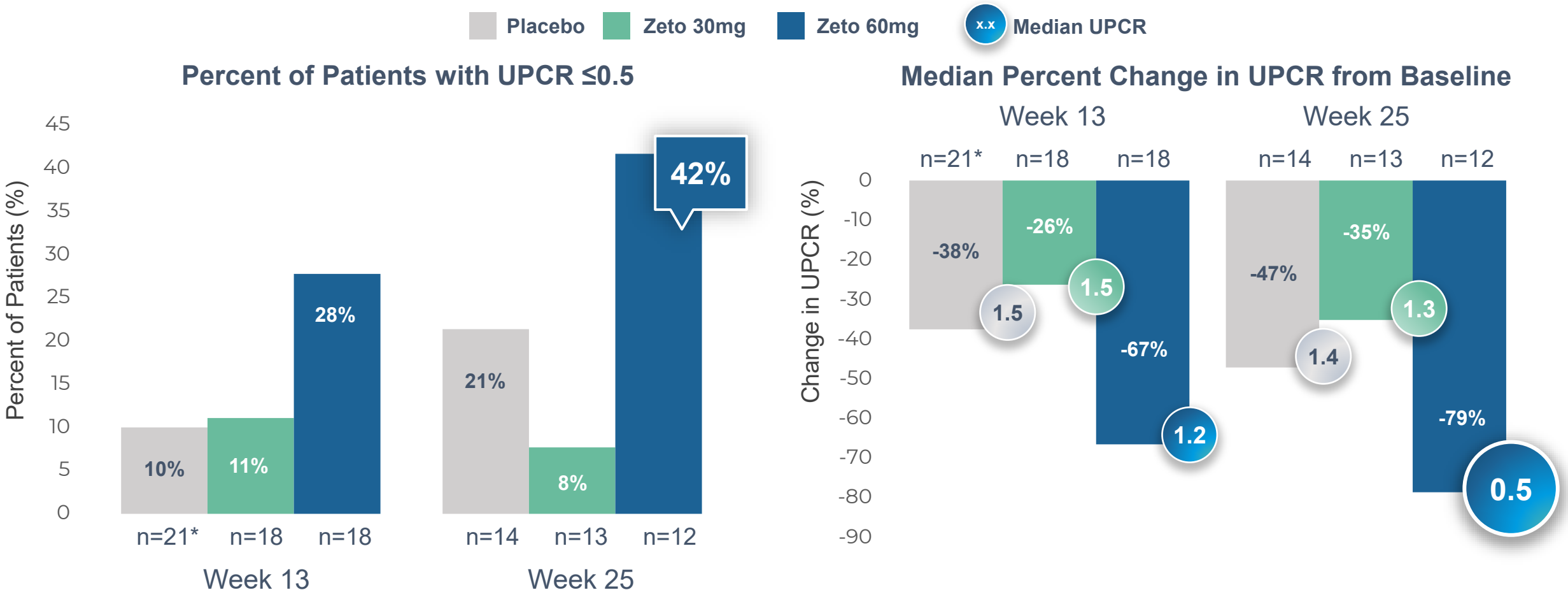


Mean daily prednisone background dosage was reduced from 19.2 mg at baseline to 9.1 mg at EOT and was further reduced at Week 29.

Source: ACR 2022, ASN 2022. **Abbreviation:** EOT, End of Treatment; EOS, End of Study, ORR, Objective Renal Response, CRR, Complete Renal Response, UPCR, Urine Protein to Creatinine Ratio.

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

PALIZADE Phase 2: Rapid Improvement in Proteinuria in Treatment Evaluable LN Patients



Topline Data from the PALIZADE clinical trial are preliminary and require further confirmation and analysis. These data may be subject to verification procedures that could result in material changes to the final data.

*Includes 1 Class IV patient in the placebo arm that was incorrectly classified as Class V.
Abbreviation: UPCR, Urine Protein to Creatinine Ratio.

Improvements in Key Serologic Markers of SLE Were Observed in Patients Across MISSION and PALIZADE

Serologic Biomarkers*	MISSION Ph2 Zeto 60 mg N=17 (Treatment Evaluable Population)	PALIZADE Placebo N=25†	PALIZADE Zeto 30 mg N=23	PALIZADE Zeto 60 mg N=26
Anti-dsDNA				
Number of patients with elevated anti-dsDNA at baseline	12	21	17	21
Mean % change from baseline at Week 25	**-40.9%**	**33.0%**	**-38.4%**	**-68.3%**
Complement 3 (C3)				
Number of patients with low C3 at baseline	5	11	13	16
Mean % change from baseline at Week 25	**33.7%**	**15.9%**	**22.7%**	**69.0%**
Complement 4 (C4)				
Number of patients with low C4 at baseline	4	4	3	9
Mean % change from baseline at Week 25	**74.0%**	**32.5%**	**86.1%**	**236.2%**

*No statistical test has been conducted yet.
†Includes 1 Class IV patient in the placebo arm that was incorrectly classified as Class V.

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

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

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

Sole Agent in Development in Autoimmune Hepatitis (AIH) with Positive Results Reported from PORTOLA Study

Strong, Experienced Team of Research Scientists and Drug Developers

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