

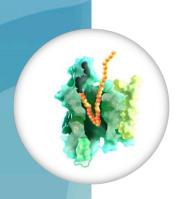
Corporate Presentation

March 2024

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Pursuing Paradigm Shifts in Immunology and Oncology



* KEZAR



Zetomipzomib (KZR-616): First-in-Class Immunoproteasome Inhibitor

- Harmonizing the immune system via immunomodulation
- Potential "pipeline in a drug"
- Successfully completed MISSION Phase 2 study in lupus nephritis

KZR-261: First Candidate from Our Protein Secretion Platform

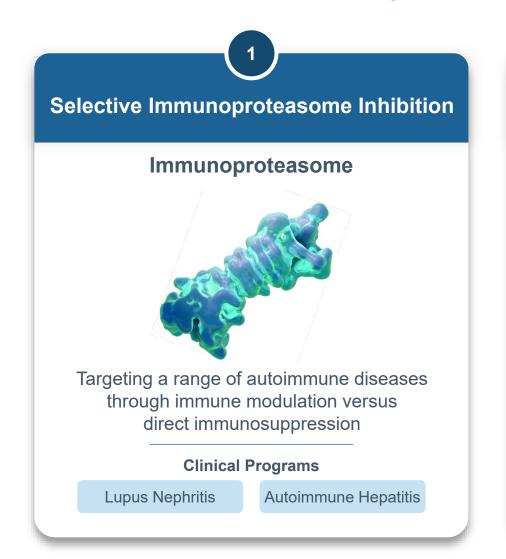
- First-in-class inhibitor of Sec61 translocon
- Impacts tumor proliferation, metastasis and immune invasion
- Currently in a Phase 1 study in solid tumors

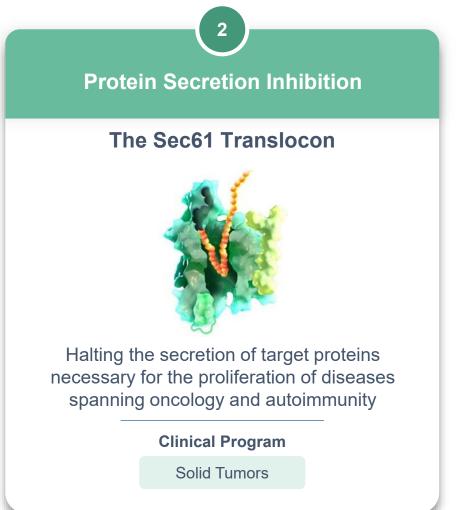
Strong Financial Position

• \$201.4M cash, cash equivalents and marketable securities as of December 31, 2023; 72.8M common shares outstanding

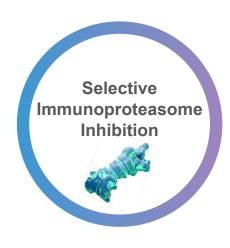
Targeting Master Regulators of Cellular Function to Treat a Range of Chronic Conditions

Kezar's Two Unique, Protein-Targeting Approaches





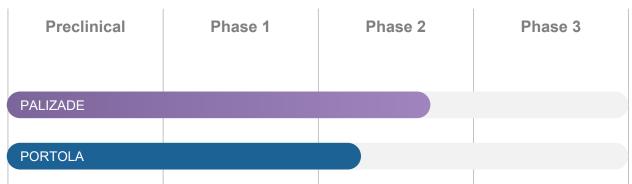
Building a First-In-Class Therapeutic Portfolio: "Pipeline in a Drug" Candidates with Multiple Shots on Goal



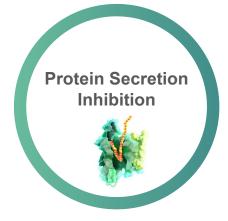
Zetomipzomib

Lupus Nephritis (LN)

Autoimmune Hepatitis (AIH)



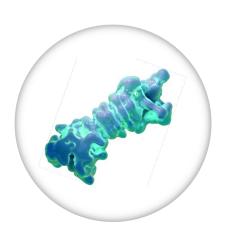




KZR-261

Advanced/Metastatic Solid Tumor

Preclinical	Phase 1	Phase 2	Phase 3	



SELECTIVE IMMUNOPROTEASOME INHIBITION:

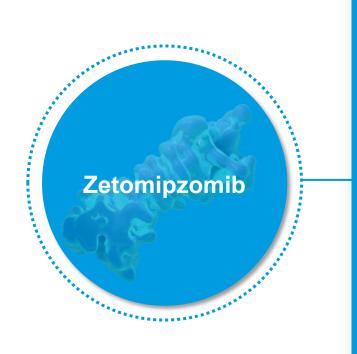
Zetomipzomib

Targeting a Range of Autoimmune Diseases Through Immune Modulation Versus Direct Immunosuppression



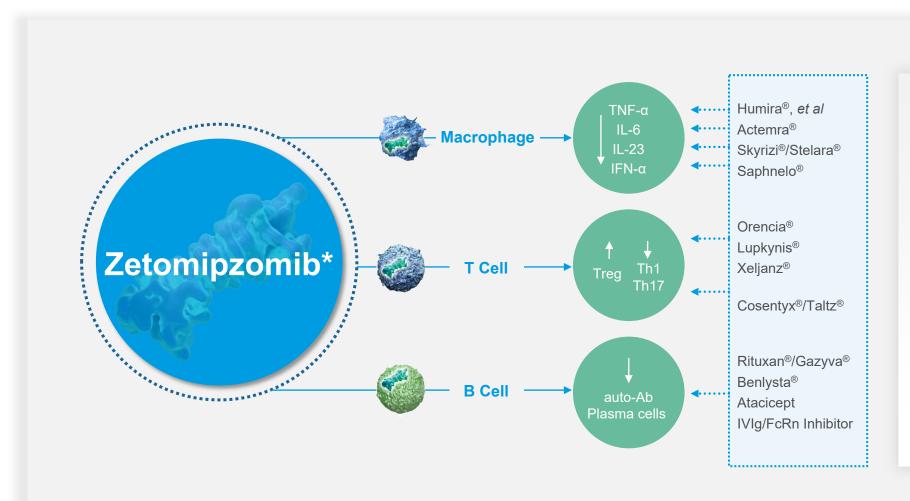
Key Attributes of Zetomipzomib, a First-in-Class Inhibitor of the Immunoproteasome

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



- Selective inhibition of the immunoproteasome down regulates inflammation without immunosuppression
 - Once-weekly SC administration
 - No accumulation observed with repeat dosing
 - Consistent exposure and clearance (T1/2 <5 hours)
- No immediate rebound of signs/symptoms of disease activity observed upon discontinuation
- No clinically significant opportunistic or serious infections observed
- No clinically significant immune cell depletion observed
- Not predicted to result in clinically significant drug-drug interactions (DDI)
- No off-target effects observed to date
- No teratogenicity observed in nonclinical studies
- No serum monitoring required

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



Zetomipzomib Advantage

- Targeted inhibition of immunoproteasome in immune cells and site of inflammation
- Inhibits multiple drivers of inflammation
- Normal immune response mechanisms remain intact



ZETOMIPZOMIB: MISSION

Phase 2 Study Evaluating Zetomipzomib in Lupus Nephritis



MISSION: Zetomipzomib Achieves Clinically Meaningful Overall Renal Response (ORR) in Refractory or Hard-to-Treat LN Patients Without Standard Induction Therapy

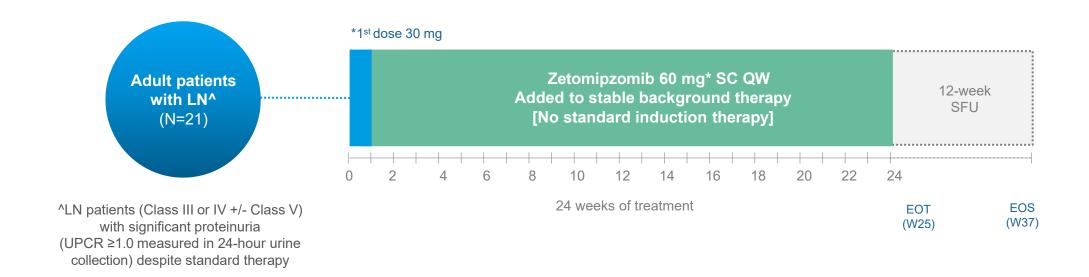




- Clinically meaningful ORR in 65% and CRR in 35% of patients at W25 (EOT)
- Renal response as early as W13 (ORR in 59% and CRR in 29%)
- Sustained renal response with additional ORRs/CRRs observed through W37
- Achievement of UPCR ≤0.5 in 65% of patients at W37 (EOS)
- Reduction of daily steroid dose to ≤10 mg/d in 82% of patients by W25 (EOT)
- Improvements in key SLE clinical disease activity scores and biomarkers
- Stable mean eGFR during the study
- Generally mild to moderate TEAEs (Grade 1/2)
- No evidence of immunosuppression (no serious/opportunistic infections or immune cell depletion)

MISSION Phase 2: Study Design Open-Label Clinical Study to Evaluate the Efficacy and Safety of Zetomipzomib in Patients With Active Proliferative Lupus Nephritis



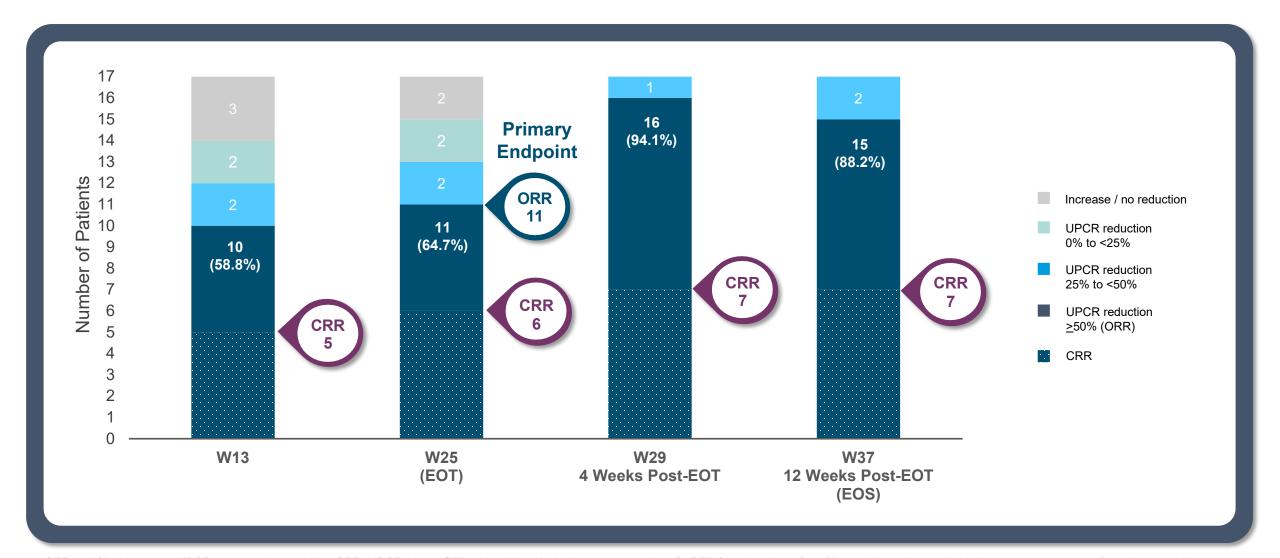


Patients in MISSION Phase 2 did not receive standard induction therapy or protocol-mandated steroid taper

Lack of induction therapy is a significant difference compared to recently published trials in LN

MISSION: Zetomipzomib Demonstrated Clinically Meaningful Renal Responses (Evaluable Population, n=17)



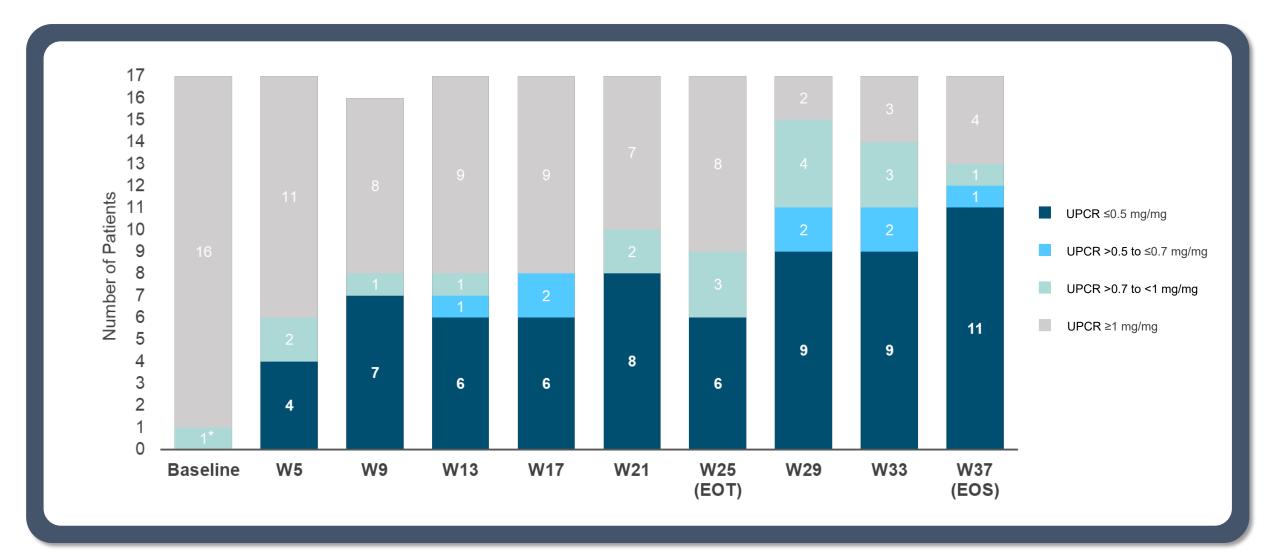


ORR: ≥50% reduction in UPCR compared to baseline; CRR: UPCR ≤0.5, eGFR ≥60 mL/min/1.73m2 or no worsening of eGFR from baseline of ≥25%, prednisone (or equivalent) ≤10 mg and no use of prohibited medication; Evaluable population (n=17) are patients that did not withdraw before Week 25; Patients received 24 weeks of zetomipzomib; End-of-treatment assessments performed at Week 25.

Abbreviations: CRR, complete renal response; eGFR, estimated Glomerular Filtration Rate; EOS, end of study, EOT, end of treatment; ORR, overall renal response; UPCR, urine protein to creatinine ratio.

MISSION: UPCR ≤0.5 Was Achieved by 64.7% (11/17) of Patients by End of Study (Evaluable Population, n=17)





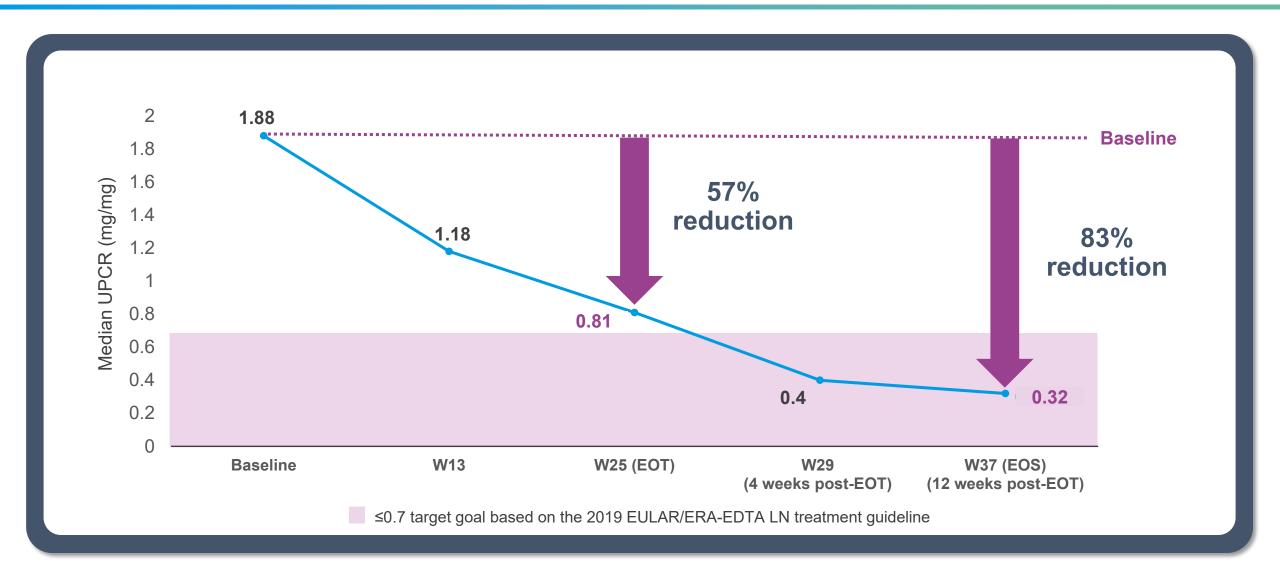
^{*}Per protocol, patients with baseline UPCR ≥1 were included in this study. One patient had screening values >1 but W1 pre-dose UPCR was <1. The baseline UPCR value is the average of screening values and W1 pre-dose UPCR values.

Evaluable population (n=17) are patients that did not withdraw before Week 25; Patients received 24 weeks of zetomipzomib; End-of-treatment assessments performed at Week 25 Abbreviations: EOS, end of study, EOT, end of treatment; UPCR, urine protein to creatinine ratio.



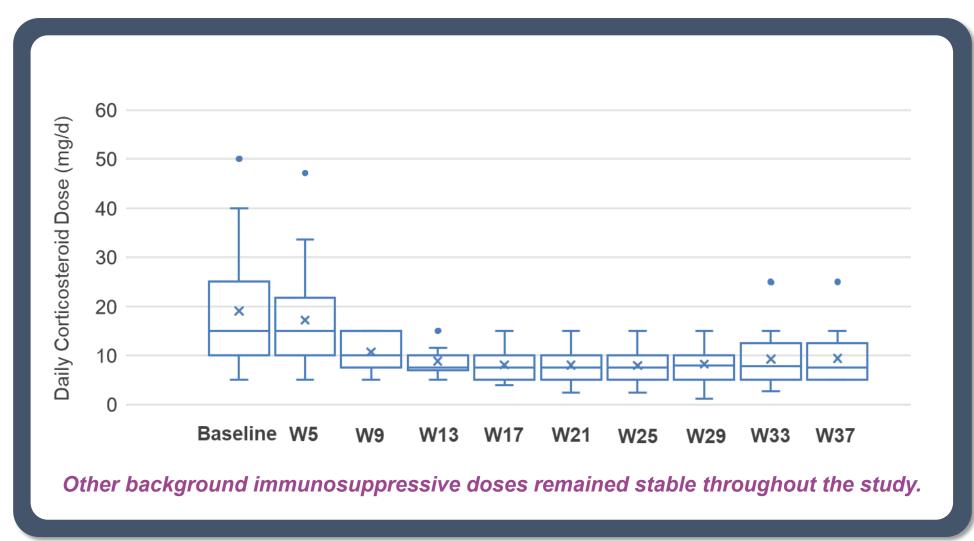
MISSION: Continued Improvement in Median UPCR Observed With Zetomipzomib Treatment (Evaluable Population, n=17)





MISSION: By Week 13, 82.4% (14/17) of Patients Achieved a Daily Corticosteroid Dose of ≤10 mg (Evaluable Population, n=17)

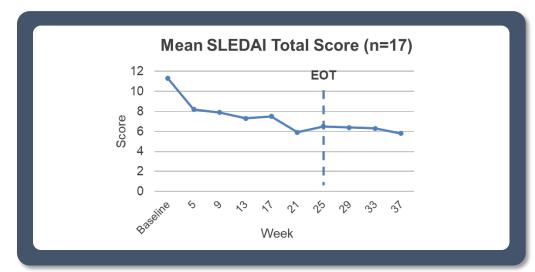


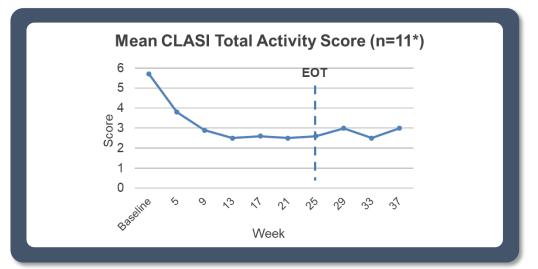


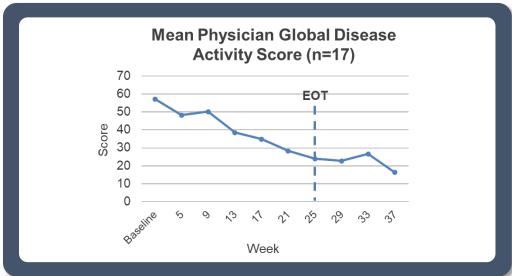
Mean Median Outlier Highest observation* Upper Quartile (Q3) X Mean Median Lower Quartile (Q1) Minimum Value

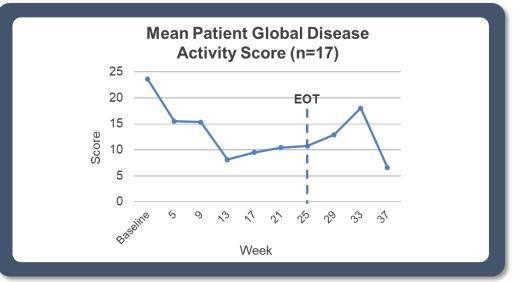
MISSION: Zetomipzomib Improved Key SLE Clinical Disease Activity Scores (Evaluable Population, n=17)











^{*11} patients had active cutaneous SLE at baseline (CLASI-A >0). There were 5 patients with tender joint count >0 at baseline and 1 patient with swelling joint count >0 at baseline.

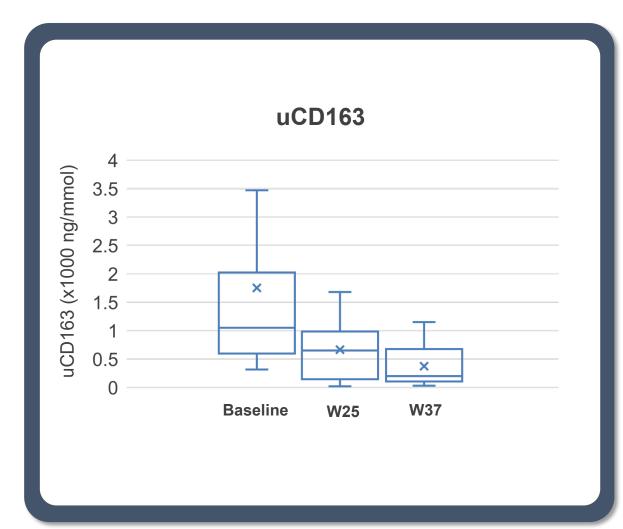
Evaluable population (n=17) are patients that did not withdraw before Week 25; Patients received 24 weeks of zetomipzomib; End-of-treatment assessments performed at Week 25

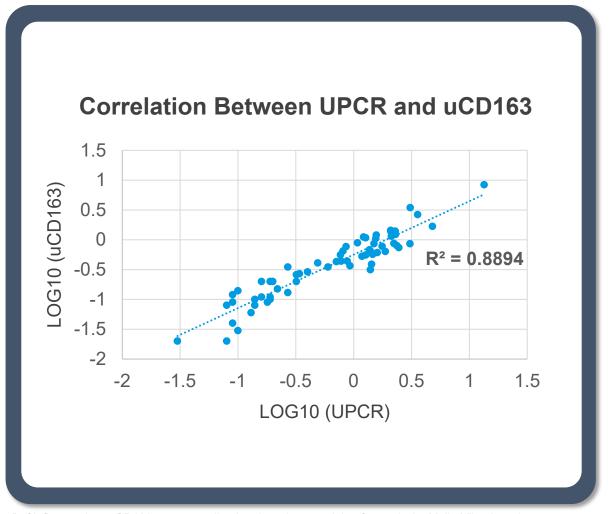
Abbreviations: CLASI, Cutaneous Lupus Erythematosus Severity Index-Activity; EOT, end of treatment; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.



MISSION: Zetomipzomib Decreased Urinary CD163*, an Inflammatory Marker Shown to Correlate With UPCR (n=13†)







^{*}CD163 is a transmembrane protein mainly expressed by M2c macrophages that infiltrate tissues during the "healing phase" of inflammation. uCD163 was normalized to the urine creatinine for analysis. Mejia-Vilet J et al., JASN 2020; 31(6):1335-1347.

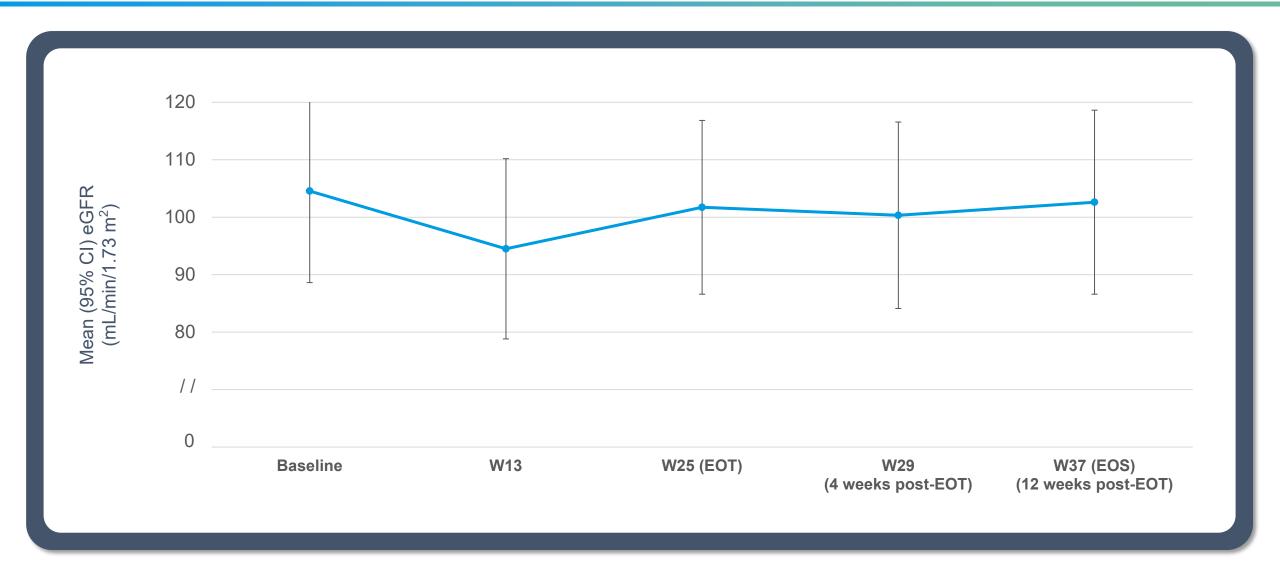
Abbreviation: UPCR, urine protein to creatinine ratio.



^{†13/17} evaluable patients consented to urine biomarker analysis.

MISSION: eGFR Remained Stable During Zetomipzomib Treatment and Post Treatment Period





MISSION: Improvements in Key Serologic Biomarkers Were Seen in Patients With **Elevated Levels at Baseline**

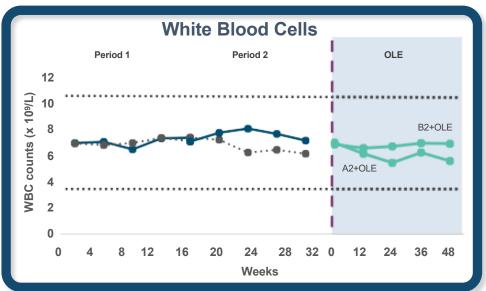


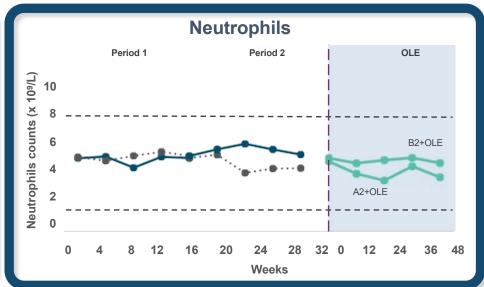
		Week 2	25 (EOT)	Week 37 (EOS)			
Biomarker	Patients with Abnormal Levels at Baseline		Patients with Normalization				
Anti-dsDNA	12	10	5	9	3		
C3	5	4	2	3	1		
C4	4	3	2	2	2		

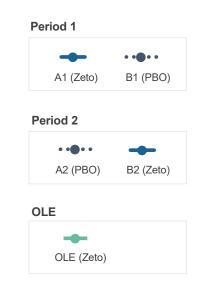
PRESIDIO Open-Label Extension (OLE): Long-Term Safety Data Demonstrates No Evidence of Immunosuppression

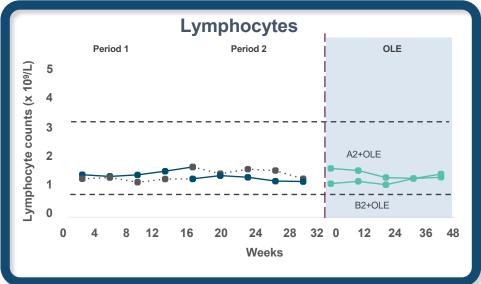


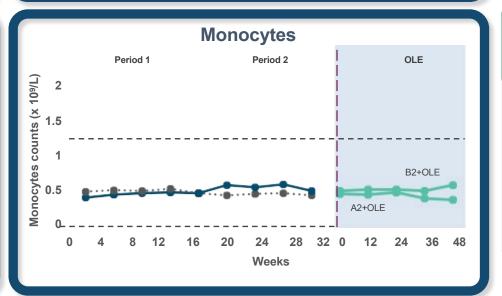
Preserved Immune Cell Counts Observed With Zetomipzomib Treatment











Patient Experiencing Adverse Events, n (%)	Zetomipzomib (A1+B2) N=25	Placebo (A2+B1) N=22	Zetomipzomib OLE N=18
nfections			
ΓEAEs	7 (28.0)	6 (27.3)	8 (44.4)
Grade 1	5 (20.0)	5 (22.7)	6 (33.3)
Grade 2	2 (8.0)	3 (13.6)	3 (16.7)
Grade 3	0 (0)	1 (4.5)*	0 (0)
Grade 4	0 (0)	0 (0)	0 (0)
Opportunistic nfections [^]	0	0	0

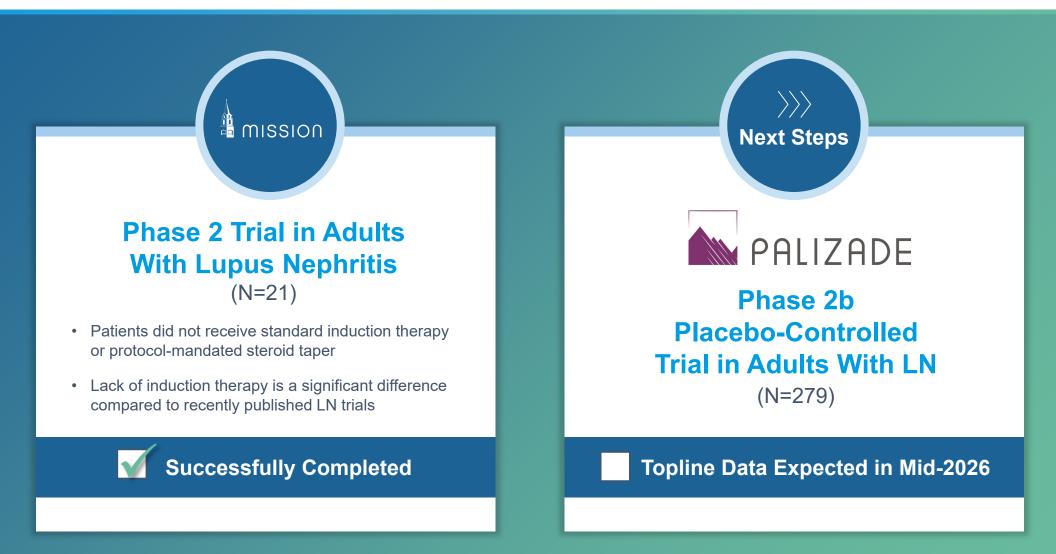
Zetomipzomib Demonstrates a Favorable Safety and Tolerability Profile No Opportunistic Infections Observed to Date



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)

MISSION: Results Suggest Zetomipzomib's Potential to Revolutionize Treatment for Lupus Nephritis as a Novel Anti-inflammatory Agent







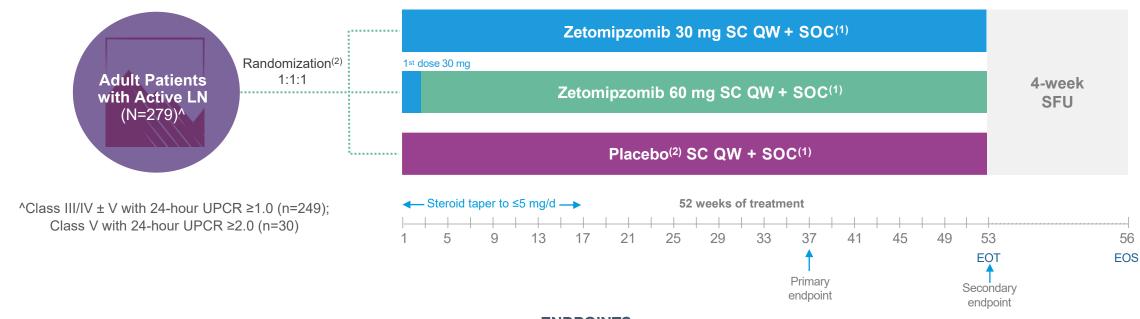
ZETOMIPZOMIB: PALIZADE

Phase 2b Study Evaluating Zetomipzomib in Lupus Nephritis



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





ENDPOINTS

Primary Efficacy Endpoint

 Proportion of patients achieving complete renal response (CRR(3)) at Week 37

Key Secondary Endpoints

- Proportion of patients achieving partial renal response (PRR(4)) at Week 37
- CRR at Weeks 25 and 53
- PRR at Weeks 25 and 53

Primary Safety Endpoint

Severity of AEs

Other Endpoints

 SLE Disease Activity Measures (e.g. SLEDAI, 28-Joint Count, SLE Flare Index, PGA)

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 m² 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.

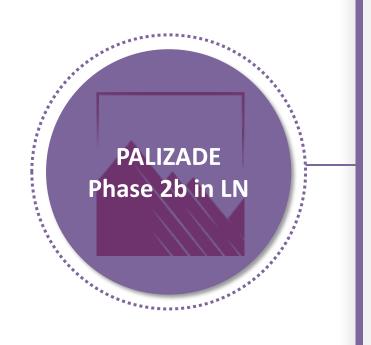
Responder requirement: Should not have received >10 mg prednisone (or equivalent) for ≥3 consecutive days or for ≥7 days in total during the 8 weeks prior to a CRR assessment and no use of rescue or prohibited medication.





PALIZADE Phase 2b in Active Lupus Nephritis: Key Differentiators





- Thoughtful trial design allowing for robust data analysis
- 37-week CRR as primary endpoint, as well as 25 and 53-week CRR and PRR endpoints, allows for better comparability with other LN trials
- Opt-out of induction therapy by MD recommendation
- Enrollment criteria allows for representation of "real-world" LN patient population
- Designed to assess extrarenal SLE disease benefits
- Potential to demonstrate efficacy without immunosuppression
- Mandated steroid taper to demonstrate steroid-sparing potential
- Built for speed and potential for efficient transition into a pivotal trial
- Full 52-week End-of-Treatment data expected in 2H 2026



ZETOMIPZOMIB: PORTOLA

Phase 2a Placebo-Controlled Study Evaluating Zetomipzomib in AIH



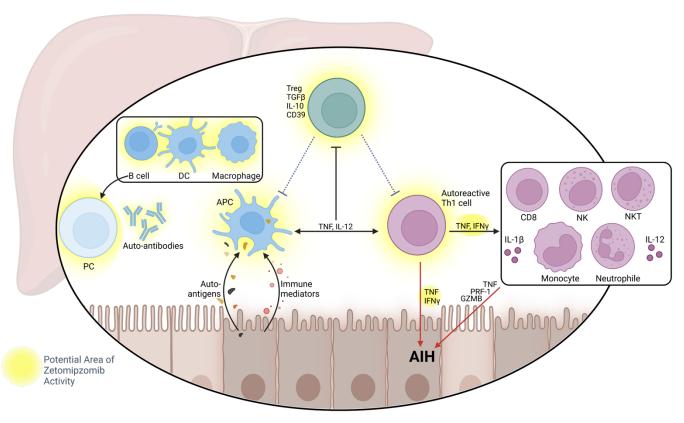
Zetomipzomib: Autoimmune Hepatitis (AIH) Significant Need For Treatments that Reduce Use of Chronic Immunosuppression

AIH: Complex Autoimmune Liver Disease with Increasing Prevalence

Significant Unmet Need Remains:

- Chronic, immunosuppressive steroids are the mainstay treatment¹
- 35% of patients on SOC do not go into remission²
- 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.

Autoimmune Hepatitis (AIH): A Strong Overlap of Disease Biology and MOA of Zetomipzomib



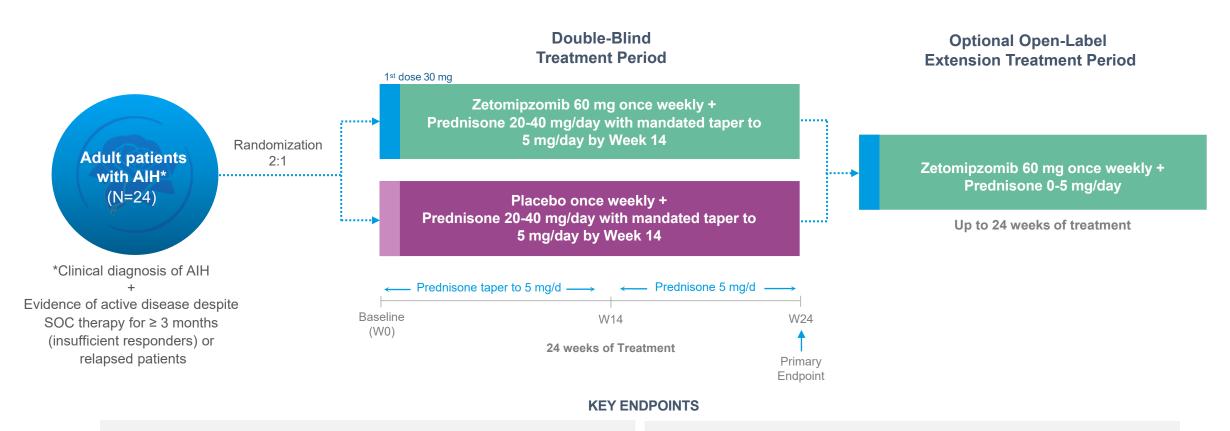


- ✓ Current treatment reliant on high-dose chronic steroids
- √ Rare disease
- ✓ Quantitative endpoints; earlier inflection points
- ✓ Strong patient advocacy community (AIHA)





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



Primary Efficacy

NCT05569759

 Proportion of patients who achieve complete remission (ALT/AST normalization) with successful corticosteroid taper by Week 24

Primary Safety

Proportion of patients who experience adverse events and severe adverse events



PROTEIN SECRETION INHIBITION:

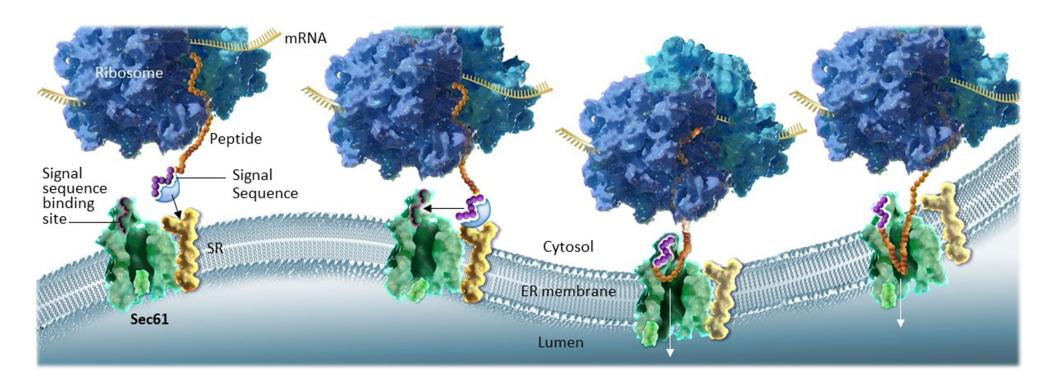
KZR-261

KZR-261: A First-in-Class Anti-Cancer Agent Targeting the Sec61 Translocon

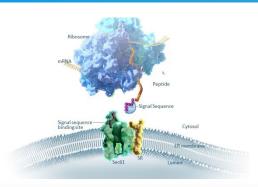


The Sec61 Translocation Channel (Translocon) is the Initiation of the Protein Secretion Pathway and a Novel Drug Target

- Highly conserved process, functional in all cells
- Approximately 6,000 secreted and transmembrane proteins utilize Sec61 to enter the endoplasmic reticulum (ER)
- Each protein has a unique signal sequence domain that guides it to the Sec61 translocon



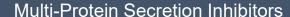
Kezar's Novel Platform for Drug Discovery Targets the Sec61 Translocon and the Protein Secretion Pathway



- Unique drug discovery engine with applications in multiple diseases
- Opportunity for orally bioavailable inhibitors of 1 or more high value targets with a single compound

Multi-Target

Target Selective



- Inhibition of <u>multiple</u> secreted/membrane proteins
- Combination therapy in a single molecule
- Multiple potential oncology indications (tumor agnostic)

KZR-261: 1st clinical candidate

Subset Protein Secretion Inhibitors

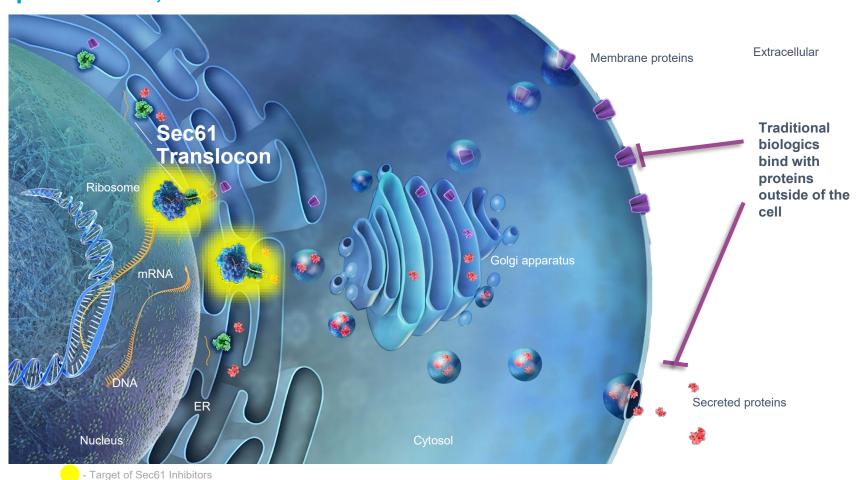
- Inhibition of relevant <u>subset</u> secreted/membrane proteins
- Non-cytotoxic agents
- Indications: oncology, immuno-oncology, immunology

Single Protein Secretion Inhibitors

- Inhibition of a <u>single</u> secreted/membrane protein
- Preclinical oral PD1 inhibitor: KZR-540
 - Data presented at SITC 2022
- Non-cytotoxic agents
- Indications: Many...

KZR-261: Novel Small Molecule Targeting the Sec61 Translocon

Tumor cells utilize the Sec61 translocon for proliferation, metastasis and immune evasion



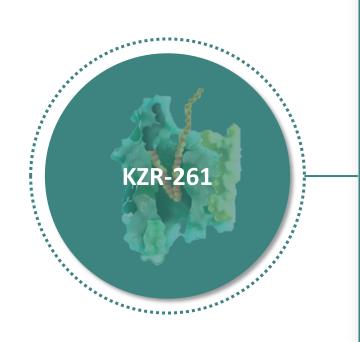
Membrane Proteins (partial list)

EGFR (ERBITUX®)
IL-6R (ACTEMRA®)
PD-1 (OPDIVO®)
PDL1 (TECENTRIQ®)
CTLA4 (YERVOY®)

Secreted Proteins (partial list)

TNF-α (HUMIRA®)
IL-17 (COSENTYX®)
PCSK9 (REPATHA®)
IL-6 (SYLVANT®)
BAFF (BENLYSTA®)

KZR-261: A Potential First-In-Class Anti-Cancer Agent Targeting the Sec61 Translocon



- Tumor cells utilize the Sec61 translocon for the transit of secreted and transmembrane proteins used for proliferation, metastasis and immune evasion
- ~10% inhibition of Sec61 with KZR-261 potently inhibits expression of multiple oncogenic factors (e.g. EGFR), immune checkpoints (e.g. PD-1) and microenvironment factors (e.g. VEGF)
- Broad anti-tumor activity in preclinical models including chemo-resistant in vivo models
- Profile supports potential for monotherapy and combination partner in multiple tumor settings; Ph 1 trial investigating monotherapy activity
- Combination therapy in one drug which can potentially treat a variety of hematologic and solid tumors

KZR-261: Combination Therapy in a Single Small Molecule

In vitro Protein Secretion Assays

	Immune Checkpoints							Oncogenic Factors									
CTLA-4	PD-1	TT-Q4	LAG3	EWI1	LIBIL	96QD	VISTA	В7Н3	CD73	CD47	PDGFRa	VGFR2	IL-7R	EGFR	VEGF	HER3	Prolactin

IC ₅₀ (nM)				
1				
100				
250				
500				
750				
900				
>1000				

Direct Effects on Tumor Cells

- Tumor cell death via proteotoxic stress
- Reduced growth factor & oncogenic RTK expression



Tumor Microenvironment Modulation

- Reduced angiogenic factor expression (e.g., VEGF)
- Reduced immune checkpoint expression

Phase 1 Trial Ongoing

KZR-261: First-in-Human Study Ongoing

KZR-261-101 Phase 1 Trial Design Dose Escalation **Dose Expansion** (N=75)Malignant/Uveal Melanoma (n=15[^]) **Colorectal Carcinoma** (n=15[^]) i3+3 Design **Prostate Cancer** (n=15[^]) **Patient Population:** All Comers; No Available Mesothelioma **Treatment Options All Comers Arm** (n=35)NCT05047536 *Maximum Tolerated Dose ^Fifteen subjects will be enrolled in each tumor specific cohort and may be increased to 35 subjects if sufficient efficacy is observed.



Key Outcome Measures

- Safety, tolerability & PK
- Recommended Phase 2 dose (RP2D)
- Anti-tumor efficacy
- Biomarker validation

Goals for KZR-261-101

- · Establish single agent activity
- Maximize opportunities for success for KZR-261
- Identify/confirm potential predictive biomarkers

KZR-261-101: Encouraging Early Safety and PK Data from Phase 1 Study



Dose Escalation is Continuing

- Cohort 1 (1.8 mg/m²) 4 (12 mg/m²) with rapid escalation without significant safety concerns
- Cohort 5 (18 mg/m²)
 - Dose approximates MED in preclinical studies
- 2 patients greater than 6 months
 - 1 melanoma
 - 1 mCRC
- Cohort 9 (80 mg/m²)
 - Enrolling



First 8 Cohorts

- Single DLT in cohort 4 (12 mg/m²)
 - Asymptomatic lipase elevation
- 1 SUSAR (infusion-related reaction) in cohort 5 (18 mg/m²) abated with use of prophylaxis at subsequent administrations



PK Demonstrates Consistent and Reproducible Pharmacology

- Dose proportional exposure
- No signs of accumulation or altered PK with repeat dosing
- T_{1/2} >25 hours and measurable levels at Day 8 indicate continuous exposure with weekly dosing



Data from Dose Escalation Expected 4Q 2024

NCT05047536

Abbreviations: DLT, dose-limiting toxicity; mCRC, metastatic colorectal cancer; MED, minimum effective dose; PK, pharmacokinetics; SUSAR, Suspected Unexpected Serious Adverse Reaction.

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- Currently in a Phase 1 study in solid tumors

Strong Financial Position

• \$201.4M cash, cash equivalents and marketable securities as of December 31, 2023; 72.8M common shares outstanding

% KEZAR LIFE SCIENCES

CONTACT US

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