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Research & Development Day

March 15, 2023

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OPENING REMARKS

John Fowler, MBA
Chief Executive Officer

Agenda

SPEAKERS

John Fowler, MBA
Chief Executive Officer

Noreen R. Henig, MD
Chief Medical Officer

Neel K. Anand, PhD
Senior Vice President,
Research & Discovery

Craig S. Lammert, MD
Assistant Professor of Medicine
Indiana University School of Medicine
Executive Director,
Autoimmune Hepatitis Association

4:30 PM – 4:35 PM
Opening Remarks — *John Fowler, MBA*

4:35 PM – 4:55 PM
PALIZADE: Zetomipzomib Lupus Nephritis Update — *Noreen R. Henig, MD*

4:55 PM – 5:15 PM
AIH: Overview of Current Treatment Options and Clinical Trial Considerations — *Craig S. Lammert, MD*

5:15 PM – 5:20 PM
PORTOLA: Zetomipzomib Autoimmune Hepatitis Update — *Noreen R. Henig, MD*

5:20 PM – 5:40 PM
Protein Secretion Platform Research Update — *Neel K. Anand, PhD*

5:40 PM – 5:50 PM
KZR-261 Clinical Update — *Noreen R. Henig, MD*

5:50 PM – 6:00 PM
Closing Remarks — *John Fowler, MBA*

6:00 PM – 6:15 PM
Question & Answer Session

Pursuing Paradigm Shifts in Immunology and Oncology

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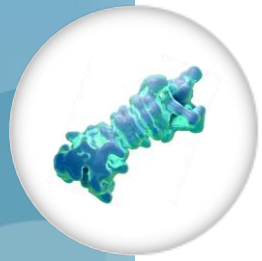
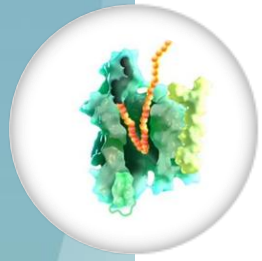
First-In-Class Therapeutic Portfolio With Two Clinical Assets Across Immunology and Oncology



Selective Immunoproteasome Inhibition With Zetomipzomib (KZR-616) Leads to Potent Immunomodulation Without Evidence of Immunosuppression Observed to Date



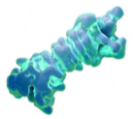
Protein Secretion Inhibition: KZR-261 Shows Broad Anti-tumor Potential by Controlling Proliferation, Metastasis and Immune Evasion in Preclinical Cancer Models

Multiple Avenues to Value Creation

- Zetomipzomib is poised to show potential as a pipeline-in-a-drug across several autoimmune indications
- KZR-261 has mechanistic rationale for both hematologic and solid tumors
- Protein Secretion Discovery Platform offers additional upside

Building a First-In-Class Therapeutic Portfolio: “Pipeline in a Drug” Candidates with Multiple Shots on Goal, Supported by Novel Discovery Platform

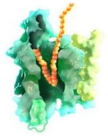
Selective Immunoproteasome Inhibition



Zetomipzomib

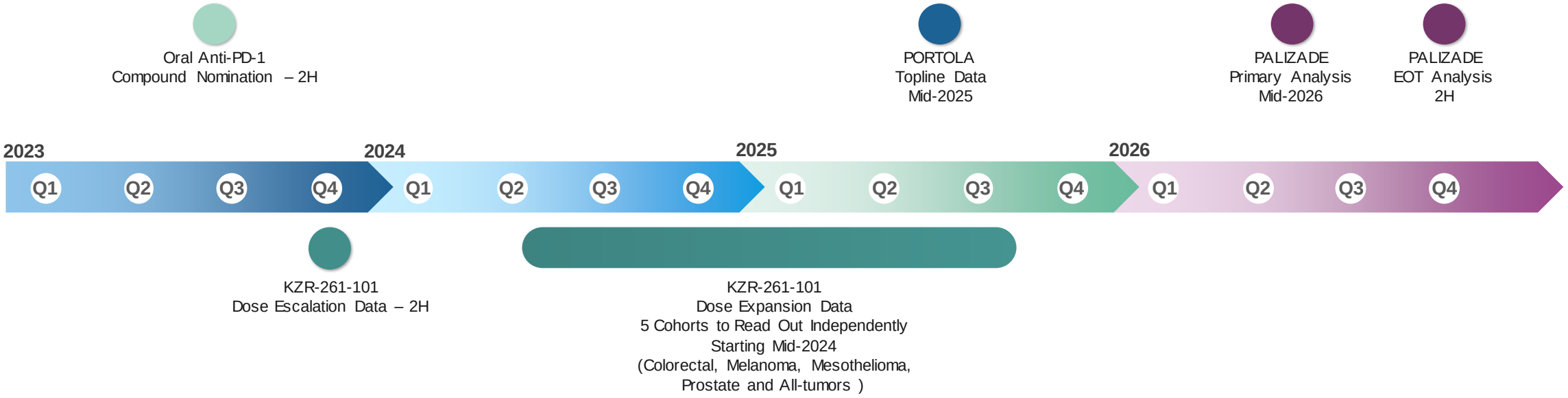
	DISCOVERY	PHASE 1	PHASE 2	PHASE 3
Lupus Nephritis (LN)			PALIZADE	
Autoimmune Hepatitis (AIH)			PORTOLA	
Dermatomyositis (DM) Polymyositis (PM)			PRESIDIO OLE	

Protein Secretion Inhibition



	DISCOVERY	PHASE 1	PHASE 2	PHASE 3
KZR-261 Advanced/Metastatic Solid Tumor				
Oral Anti-PD-1 Single Target Oncology				
KZR-TBD Multi Target Oncology				

Anticipated Catalysts Across All Programs: Potential Value Creation 2023 – 2027



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ZETOMIPZOMIB
LUPUS NEPHRITIS UPDATE

Noreen R. Henig, MD
Chief Medical Officer

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

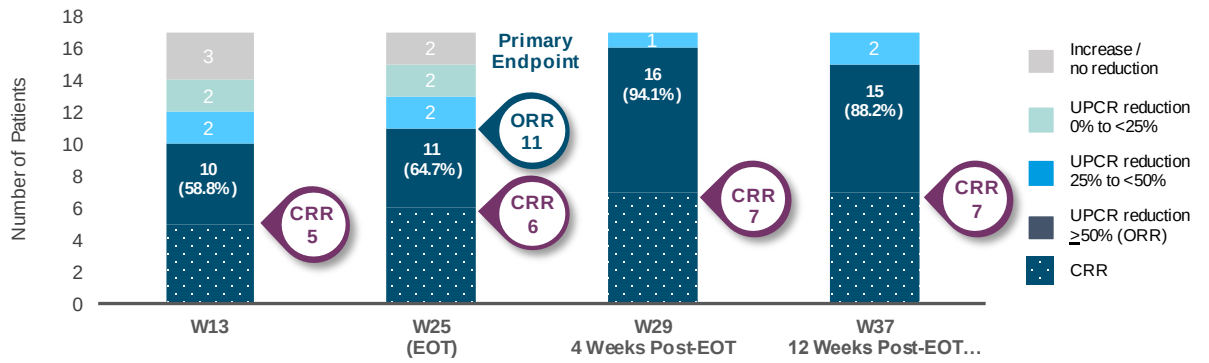
Zetomipzomib Modulates Innate and Acquired Immune Responses Without Evidence of Immunosuppression to Date

- ✓ Selective inhibition of the immunoproteasome down regulates inflammation without immunosuppression
  - Once-weekly SC administration
  - No accumulation observed with repeat dosing
  - Consistent exposure and clearance ($T_{1/2}$ <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

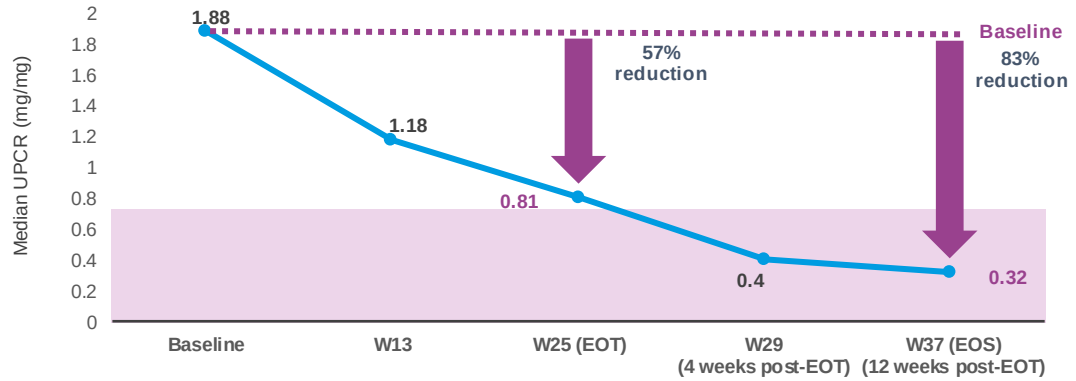
Furie R *et al.*, EULAR 2021 and Data on File.

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

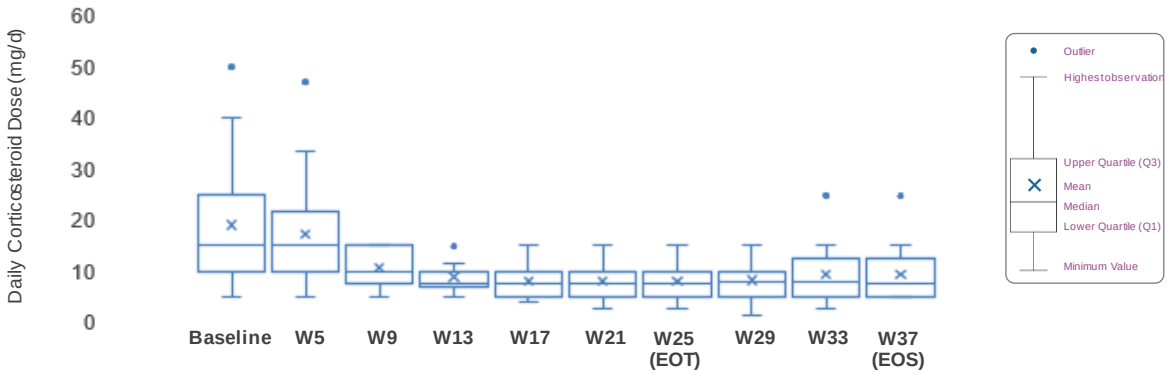
Early Renal Response with Clinically Meaningful ORR (65%) and CRR (35%) at W25…



… And Continued Improvement in UPCR Reduction Post Treatment



82% of Patients Achieving Daily Corticosteroid Dose ≤10mg by W13



Other background immunosuppressive doses remained stable throughout the study.

Promising Results in Showing Improvement in Key Extrarenal SLE Disease Activity Scores With Biomarker Support

Evaluable population reduction in systematic signs and symptoms of SLE with zetomipzomib treatment

- Improvements across SLEDAI-2K, Physician Global Assessment Score, Patient Global Assessment Score, HAQ-pain, etc.

Evaluable population improvement in key serologic biomarkers observed at Week 25 (EOT) in patients with abnormal levels at baseline

- Biomarkers included Anti-dsDNA, C3, and C4
- Cell counts remained stable in patients on study

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

Totality of Evidence for Zetomipzomib: Signs, Symptoms and Biomarkers All Move Toward Therapeutic Benefit

Promising Efficacy

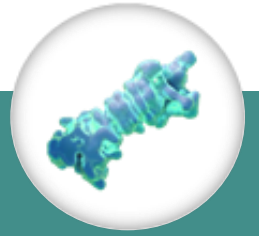
- Clinically meaningful reductions in proteinuria at W25 (65% ORR and 35% CRR)
- Early renal response at W13 (59% ORR and 29% CRR)
- Improvements in anti-dsDNA (10/12), C3 (4/5), C4 (3/4) and decrease in urinary CD163, correlated with UPCR reduction

Favorable Safety and Tolerability Profile

- Adverse events were generally mild to moderate (most common AE: injection site reaction)
- **No clinically significant opportunistic infections** reported and **without evidence** of **immunosuppression**

Steroid Sparing Potential

- 58% reduction in mean values of steroid dose, **despite no mandated taper**
- 82% of patients reduced to a daily steroid dose of ≤10 mg by W13



Opportunities Beyond LN

- Improvements observed in key SLE disease activity scores (mean score change from baseline to W25)

SLEDAI: 11.3 → 6.5

PhGA: 52.7 → 23.9

CLASI(1): 5.7 → 2.6

1. Eleven patients had active cutaneous SLE at baseline (CLASI-A >0).

Abbreviations: *AE, adverse event; C3, complement 3, C4, complement 4; CLASI, Cutaneous Lupus Erythematosus Severity Index -Activity; dsDNA, double-stranded deoxyribonucleic acid; LN, lupus nephritis; PhGA, Physician Global Assessment; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urine protein to creatinine ratio; W, week.*

Zetomipzomib Current Results Relative to Later Stage and Approved Lupus Nephritis Landscape[1]

	KEZAR	Aurinia	GSK	Roche	AstraZeneca
Product	Zetomipzomib (KZR-616)	Lupkynis[4] (voclosporin)	Benlysta[5] (belimumab)	Gazyva[6] (obinutuzumab)	Saphnelo[7] (anifrolumab)
Mechanism	Immunoproteasome inhibitor	Calcineurin inhibitor	Human anti-BAFF mAb	Humanized anti-CD20 mAb	Human anti-IFNAR mAb
Target	Immunoproteasome (Macrophages, T-cells, B-cells)	T-cells	B-cells	B-cells	Type I interferon
Last Phase of Data Reported	Open-label Phase 2	Phase 3	Phase 3	Phase 2	Phase 2
Administration	SC (QW)	Oral (BID)	IV (Q2W x 3, then Q4W) or SC (QW)	IV (Day 1, W2, 24, 26, 50, 52, Q6M starting at Week 80)	IV (Q4W)
Rapidity of Response (CRR[2] at Week 12/13)	29% (24%)[3] at Week 13	N/A	13% at Week 12	16% at Week 12	18% at Week 12
CRR[2]	35% (29%)[3] at Week 25 (EOT) 41% (33%)[3] at Week 37 (EOS)	32% at Week 24 41% at Week 52	27% at Week 36 30% at Week 104	35% at Week 36 41% at Week 104	37% at Week 36 41% at Week 52
Induction Therapy	No	Yes	Yes	Yes	Yes
Immunosuppression	None observed	Yes	Yes	Yes	Yes
Safety	No clinically significant serious or opportunistic infections observed to date	Black box warning regarding malignancies and serious infection; warnings regarding nephrotoxicity, hypertension, neurotoxicity, hyperkalemia, QT prolongation, and use with live vaccines	Label includes warnings regarding serious infections, PML, hypersensitivity reactions, depression/suicidality, and use with live vaccines	Infusion-related reactions 16% vs PBO 10% Bronchitis 19% vs PBO 8% Herpes Zoster 15% vs PBO 10%	SLE label includes warnings regarding serious/fatal infections, hypersensitivity reactions, malignancy, and use with live vaccines or biologics

1. **This data is not based on head-to-head clinical trials, and such data is not directly comparable due to differences in study protocols, conditions and patient populations.**
2. CRR using UPCR ≤0.5 mg/kg as cutoff; percentages are based on completers only.
3. Percentages in parentheses are based on intent-to-treat population.
4. Approved for lupus nephritis. Rovin B *et al. Lancet* 2021; Lupkynis. Package Insert. Aurinia Pharmaceuticals Inc. 2021; Aurinia Clinical Program Update January 2022.
5. Approved for lupus nephritis. Furie RA et al. *NEJM* 2020; Benlysta. Package Insert. GSK plc. 2022.
6. Furie RA *et al*. *Ann Rheum Dis*. 2022.
7. Jayne D *et al. Ann Rheum Dis.* 2022.

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

Randomization[2] 1:1:1

- Zetomipzomib 30 mg SC QW + SOC[1]
- 1st dose 30 mg; Zetomipzomib 60 mg SC QW + SOC[1]
- Placebo[2] SC QW + SOC[1]

4-week SFU

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

Steroid taper to ≤5 mg/d — 52 weeks of treatment

1	5	9	13	17	21	25	29	33	37	41	45	49	53	56
									Primary endpoint				EOT / Secondary endpoint	EOS

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)

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.*

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

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ZETOMIPZOMIB
AUTOIMMUNE HEPATITIS UPDATE

Noreen R. Henig, MD
Chief Medical Officer

Autoimmune Hepatitis: An Overview of Current Treatment Options and Clinical Trial Considerations

Craig S. Lammert, MD
Assistant Professor of Medicine, Indiana University School of Medicine
Executive Director of the Autoimmune Hepatitis Association

What is Autoimmune Hepatitis?

- Autoimmune Hepatitis (AIH) is a long-term autoimmune disorder that results in inflammation of the liver
- This inflammation can cause harm to the liver and lead to scarring, eventually resulting in cirrhosis and liver failure
- The specific cause of autoimmune hepatitis is not well understood, but is believed to be the result of a combination of genetic and environmental factors
- AIH affects people of all ages and races, although it is most commonly diagnosed in young adult women
- Early detection and treatment is essential to slow the progression of the disease and prevent end-stage liver failure

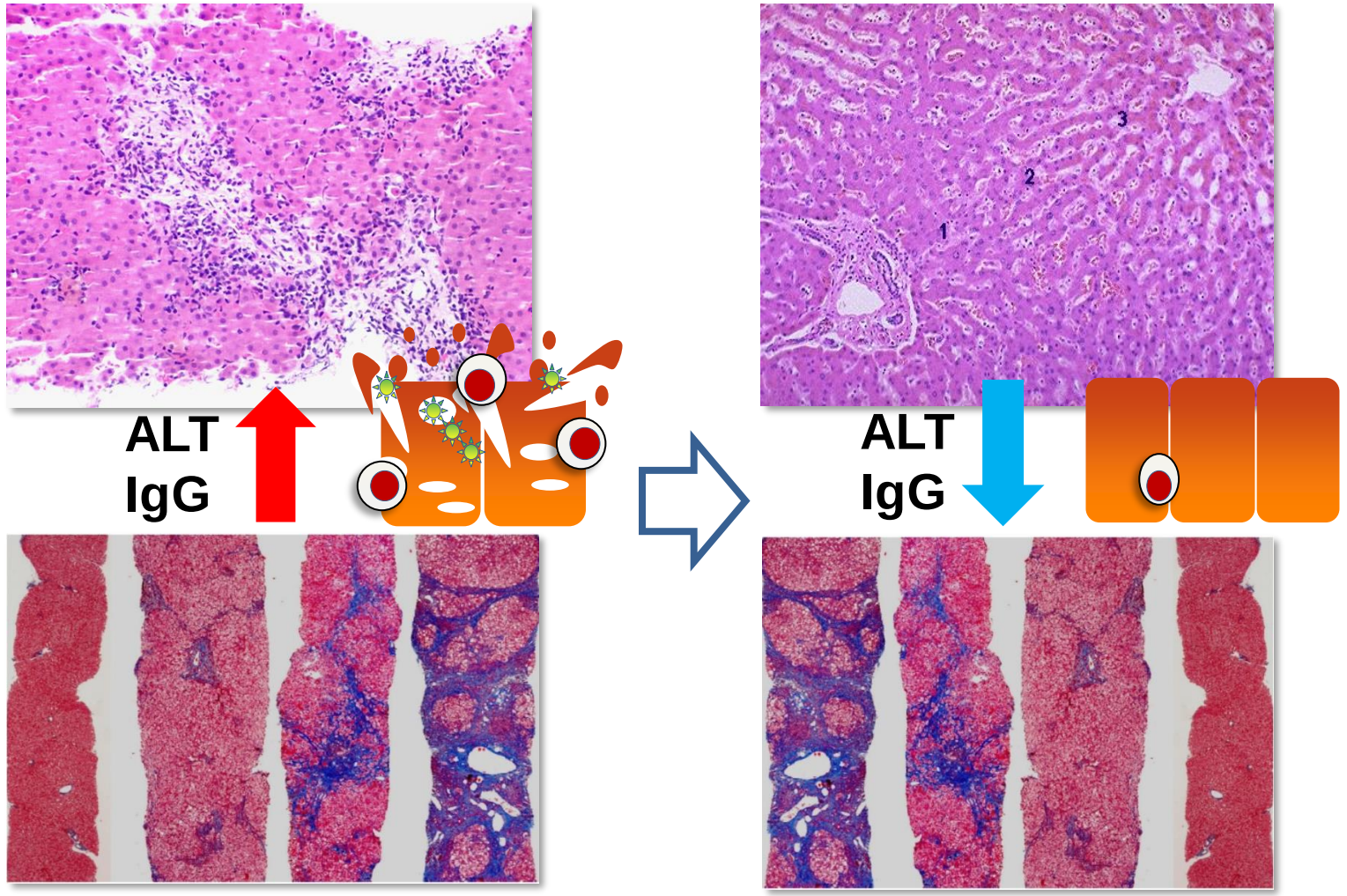
Volk and Reau. *Clinical Liver Disease.* 2021;17(2):85-89. Lowe and John. *WJH.* 2018;10(12):911-923; Czaja AJ, et al. *Gastroenterology & Hepatology*. 2013 Sep; 9(9): 561–566.

AIH Treatment Goals

- Control inflammation and prevent liver damage
- Achieve biochemical remission (normalization of serum AST, ALT and IgG levels)
- Prevent progression to cirrhosis and end-stage liver disease
- Maintain remission and improve quality of life
- Minimize long-terms effects of corticosteroids and immunosuppressive agents

Mack et al. *Hepatology*. 2020;72(2):671-722. European Association for the Study of the Liver. *J Hepatol*. 2015;63(4):971-1004.
Abbreviatons: ALT, alanine aminotransferase; AST, aspartate aminotransferase; IgG, immunoglobulin G.

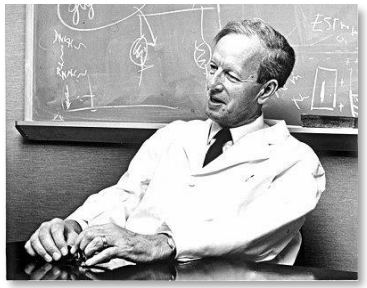
AIH Treatment Goals: Inflammation and Fibrosis



Seventy Years of "Progress" in AIH Treatment

DISCOVERY — *INNOVATION* — *STATE OF THE ART*

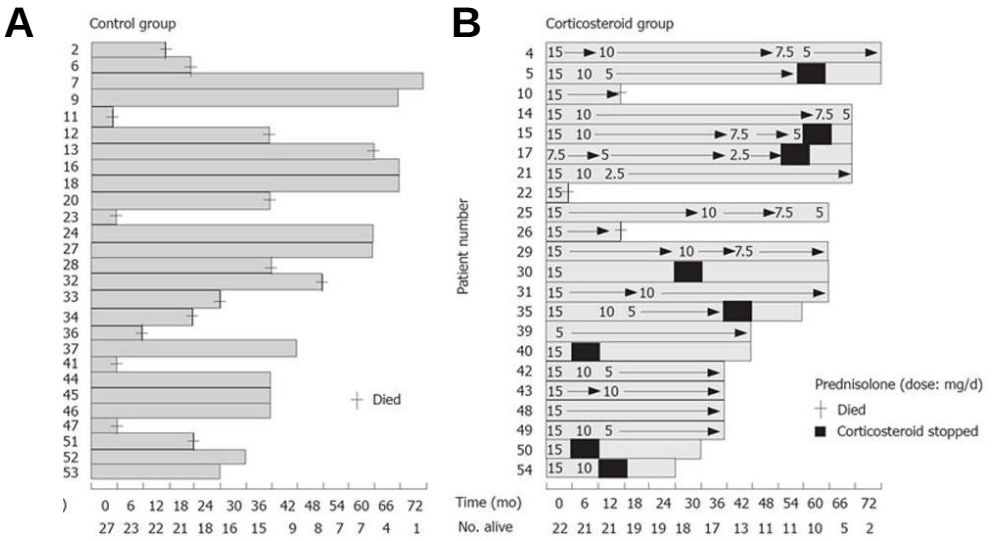
1950s — 1960-70s — 2015 — 2022



Jan Waldenstrom (1950):

Corticosteroids 1953
Azathioprine 1964

1971



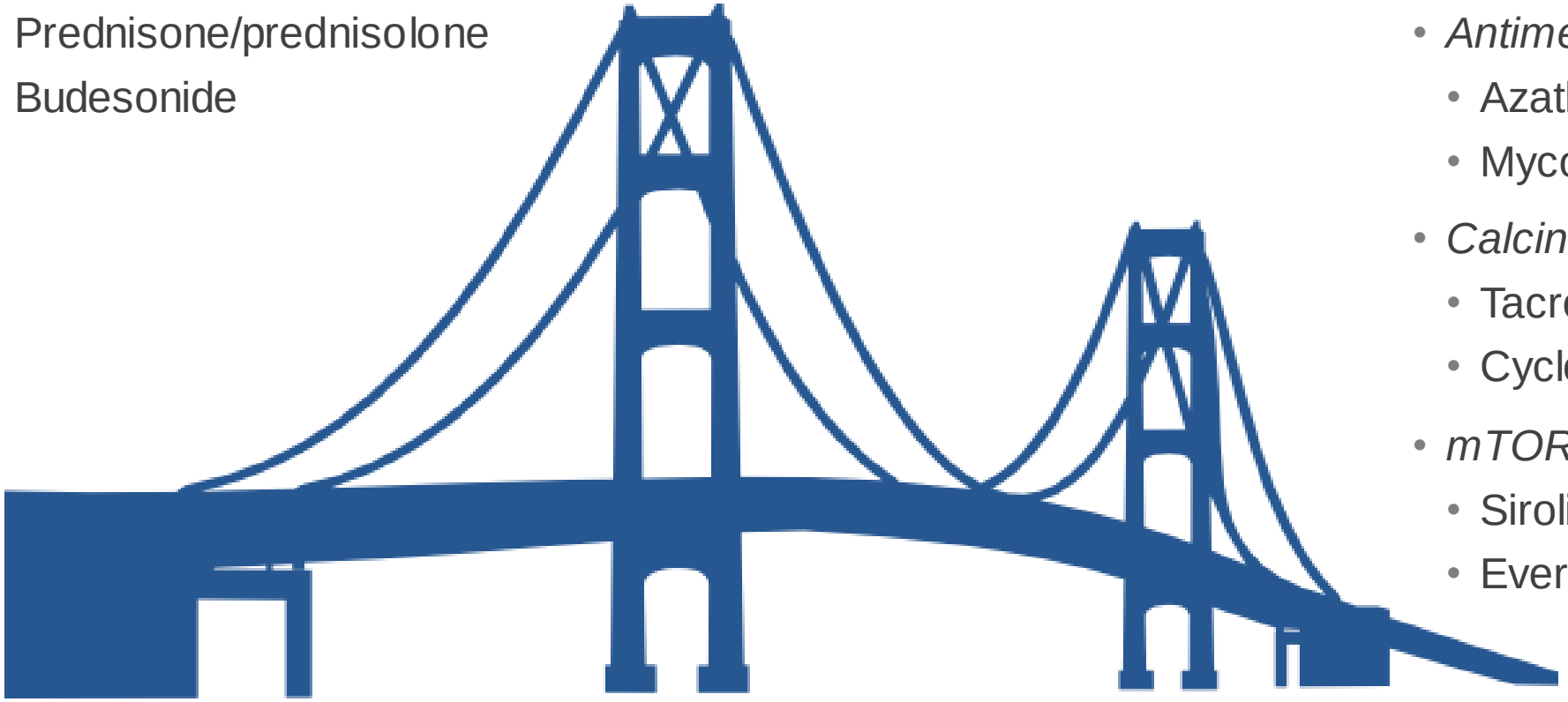
12/27 — 19/22

Cook GC, et al. Q J Med. 1971;40:159–185.

Seventy Years of “Progress” in AIH Treatment

Steroids

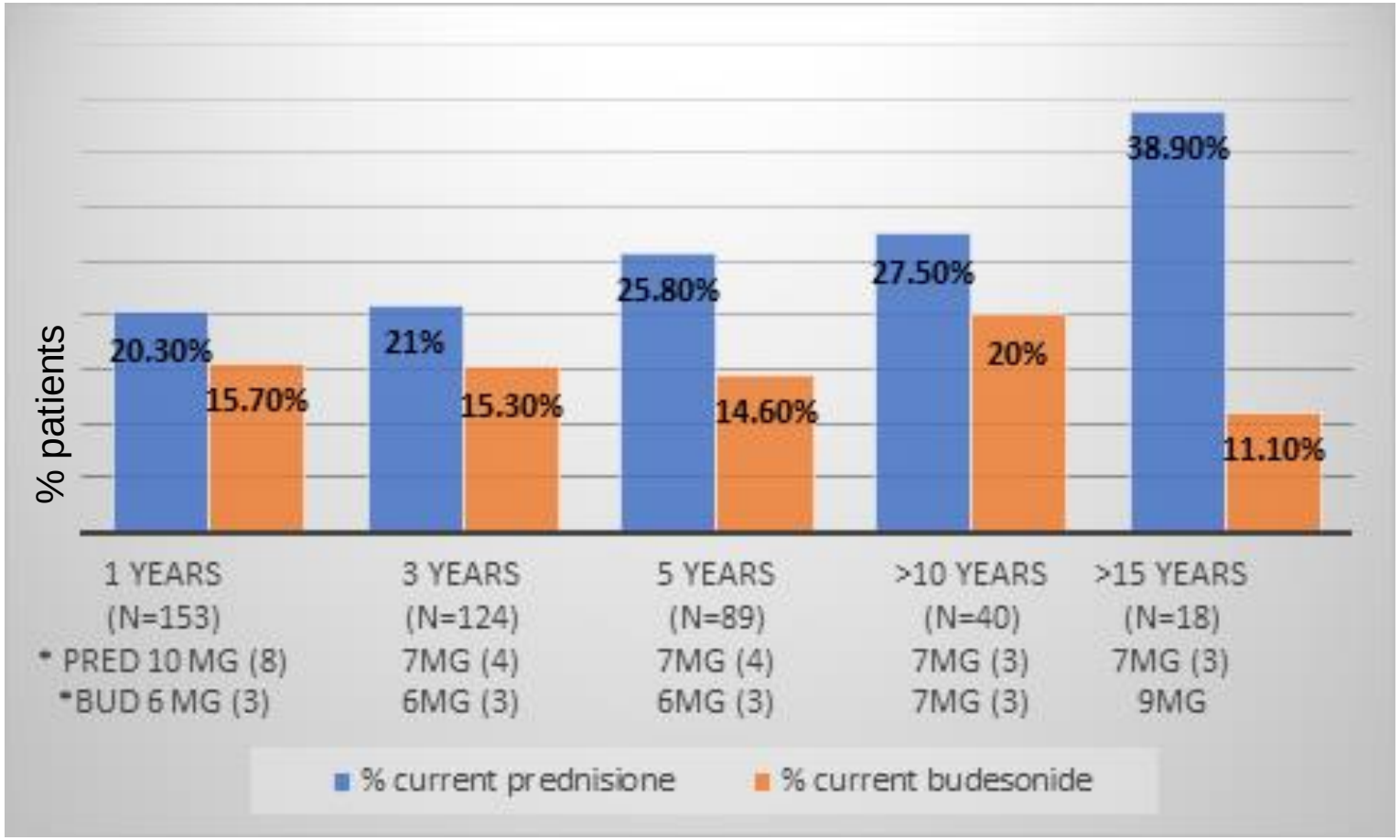
- Prednisone/prednisolone
- Budesonide



Chronic Immunosuppression

- *Antimetabolites*
  - Azathioprine/ 6MP
  - Mycophenolate mofetil
- *Calcineurin Inhibitors*
  - Tacrolimus
  - Cyclosporine
- *mTOR inhibitors*
  - Sirolimus
  - Everolimus

A Large, Consistent Proportion of AIH Patients Rely on Prednisone/Budesonide Regardless of Disease Duration



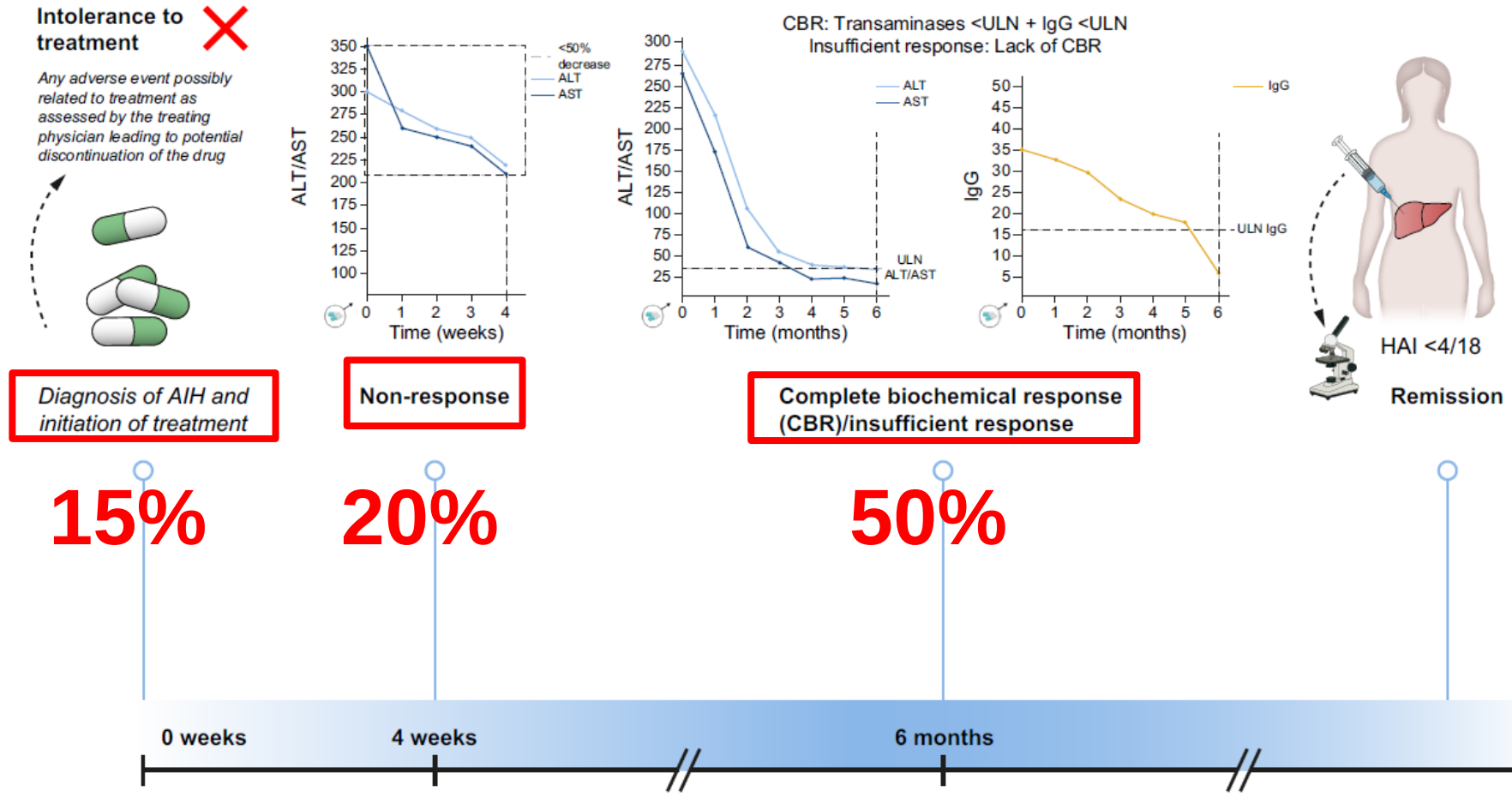
Autoimmune Hepatitis Association. Data on File.

Current AIH Treatments Have Several Limitations

- **High dependency on corticosteroids:** Up to 40% of patients with AIH remain on steroids for disease control no matter disease duration.
- **Inadequate response to standard therapies:** Approximately 30% of patients with AIH do not respond adequately or are intolerant to standard treatments such as corticosteroids and immunosuppressants
- **High risk of relapse:** A high rate of relapse (up to 87%) after treatment withdrawal among patients with AIH who were treated with corticosteroids and immunosuppressants
- **Toxicity of immunosuppressants:** Long-term use of immunosuppressants, such as azathioprine and mycophenolate mofetil, can lead to significant side effects, including increased risk of infections, bone marrow suppression, and malignancies
- **Lack of specific targeted therapies:** No current therapies focused on targeting AIH pathophysiology

Autoimmune Hepatitis Association. Data on File; Lowe and John. *WJH*. 2018;10(12):911-923; Mack et al. *Hepatology*. 2020;72(2):671-722; Volk and Reau. *Clinical Liver Disease*. 2021;17(2):85-89.

AIH Treatment Goals: Response Criteria



Pape S, et al. *J Hepatol.* 2022.

Seventy Years of "Progress" in AIH Treatment

DISCOVERY — *INNOVATION* — *STATE OF THE ART*

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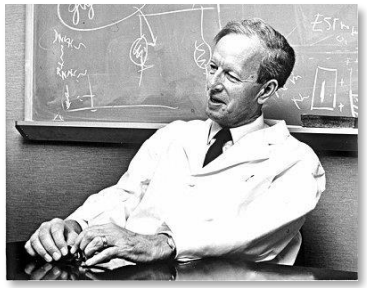
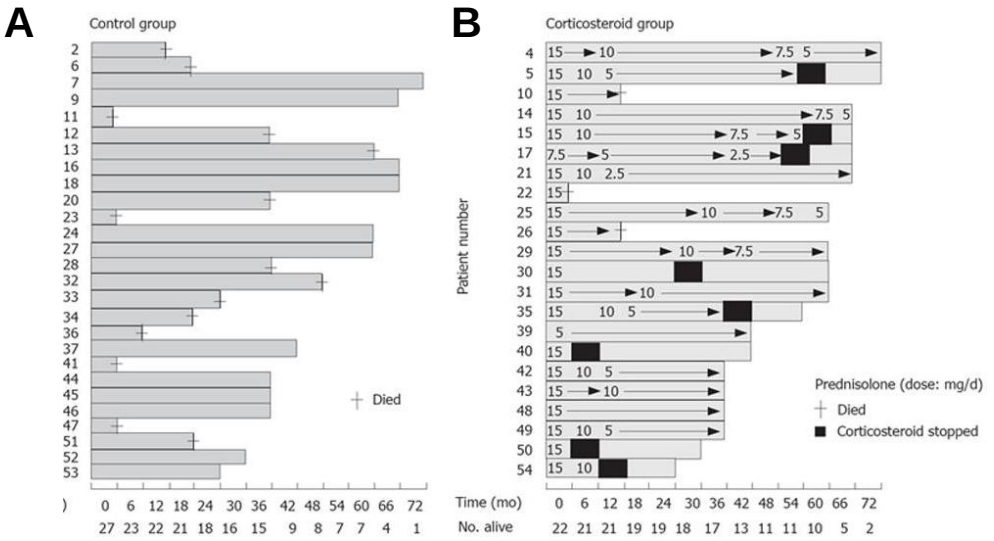


Jan Waldenstrom (1950):

Corticosteroids 1953
Azathioprine 1964

2 novel non-steroid agents

1971



12/27 — 19/22

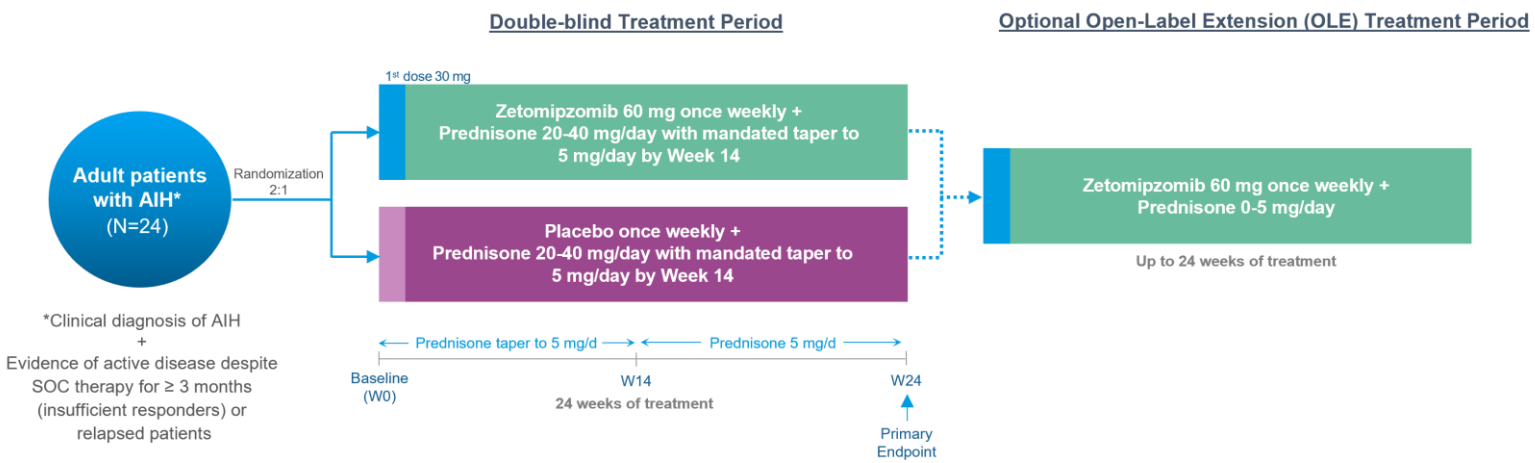
Corticosteroids 2023
Azathioprine 2023

Cook GC, et al. Q J Med. 1971;40:159–185.

Clinical Trial Considerations for Autoimmune Hepatitis

- **Very few clinical trials completed since initial landmark studies in AIH**
- **Incredible need for improved both first and second line treatment regimens**
- **Future clinical trials should address patient and clinical unmet needs**
  - *Hard to control disease*
  - *Loss of remission*
  - *Steroid dependency*
  - *Poor quality of life*
  - *Diverse populations*
- **Non-invasive liver tissue assessments should be explored as endpoints in clinical trials**

PORTOLA Trial Evaluates the Safety and Efficacy of Zetomipzomib in Patients with AIH



KEY ENDPOINTS

Primary Efficacy

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

Primary Safety

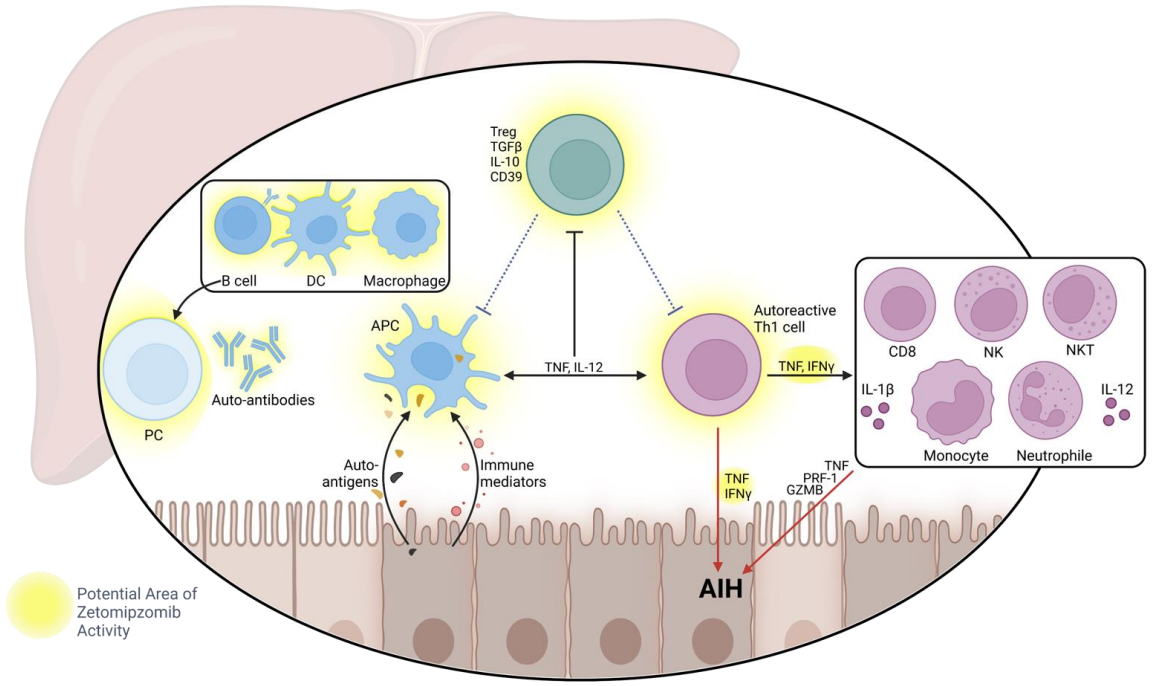
- Proportion of patients who experience adverse events and severe adverse events

PORTOLA KEY DIFFERENTIATORS:

- Protocol-mandated steroid taper by W14
- Allows for 3 months of prior standard of care for insufficient responders
- Permits background medication of AZA, tacrolimus, MMF, 6-MP, CSA
- Use of FibroScan® to assess changes in liver stiffness (exploratory)
- Use of GTI, a glucocorticoid toxicity-monitoring instrument (exploratory)
- Open-label extension study for up to an additional 6 months to evaluate longer-term safety, tolerability and efficacy (disease flare)

Abbreviations: AZA, azathioprine; CSA, cyclosporine; GTI, Glucocorticoid Toxicity Index; MMF, mycophenolate mofetil; 6-MP, mercaptopurine.

Zetomipzomib Potential in the AIH Treatment Landscape



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

- Immunoproteasome expression is increased in liver cells of patients with chronic active hepatitis or cirrhosis
- Zetomipzomib targets multiple effector cells involved in AIH pathophysiology
- The PORTOLA study evaluates zetomipzomib as a possible new therapeutic in AIH as a:
  - Potential immunomodulatory rather than immunosuppressive with no predicted off-target effects
  - Potential steroid-sparing agent

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ZETOMIPZOMIB AUTOIMMUNE HEPATITIS UPDATE

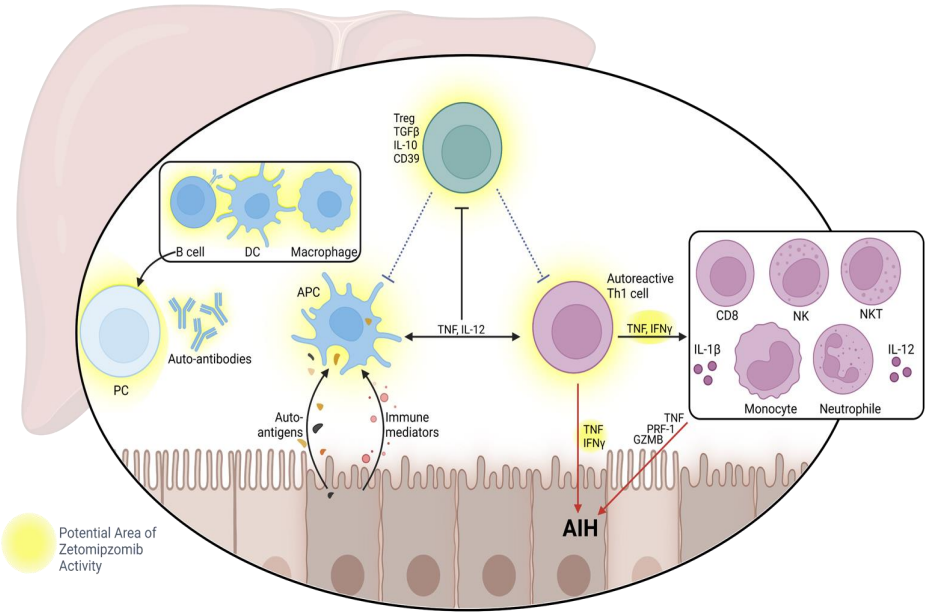
Noreen R. Henig, MD
Chief Medical Officer

Newest Clinical Program for Zetomipzomib: Autoimmune Hepatitis

Significant Need for Treatments That Reduce Use of Chronic Immunosuppression

- AIH can affect 100,000 - 200,000 individuals in the U.S.(1)
- High risk of relapse after treatment withdrawal(2)
- Inadequate response to standard therapies(3)
- High dependency on steroids(3)
- Significant toxicity associated with long-term immunosuppression and steroid use(2)
- Lack of therapy that addresses AIH pathophysiology

Zetomipzomib Targets Multiple Immune Effector Cells Involved in AIH



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

1 Linzay CD *et al*. Autoimmune Hepatitis. [Updated 2022 Aug 22]. In: StatsPearls [Internet]. Treasure Island (FL): StatsPearl Publishing;2022 Jan -.
2. Mack *et al*. *Hepatology*. 2020;72(2):671-722.
3. Autoimmune Hepatitis Association. Data on File.

Abbreviations: *AIH, autoimmune hepatitis.*

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

Autoimmune Hepatitis

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

FDA Clearance of IND

Clinical Development

PORTOLA

Phase 2a Placebo-Controlled Trial in Adults with AIH

(N=24)

Topline Data Expected in Mid-2025

Clinical Goals

- ✓ Control of liver inflammation and ALT reduction with reduced steroid use
- ✓ Patient benefit
- ✓ Strong safety and tolerability

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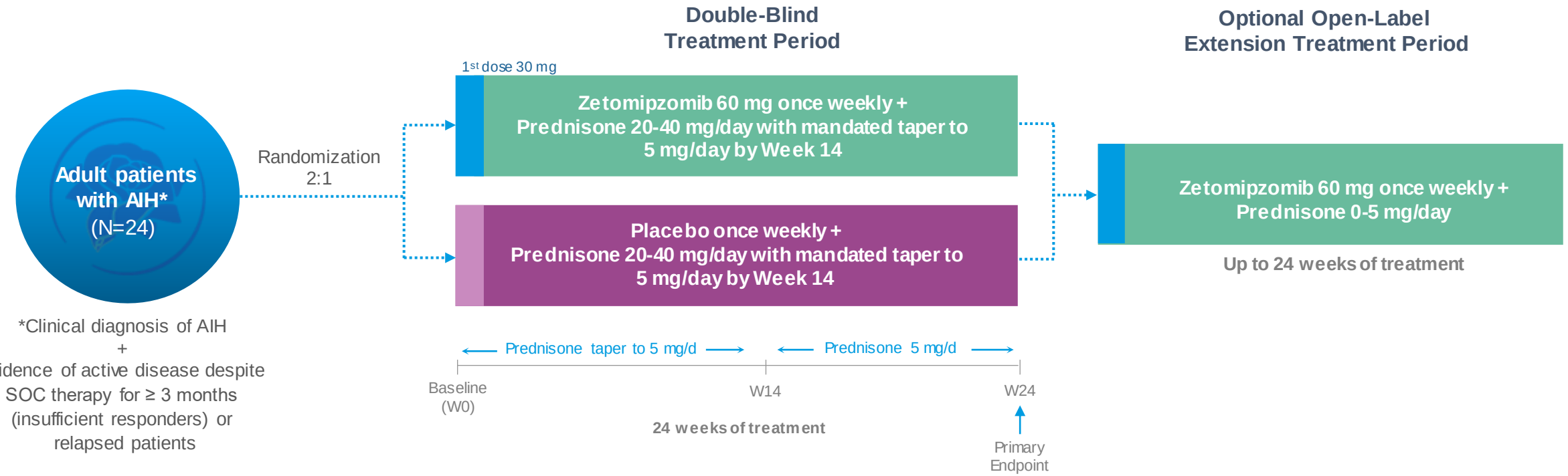
Abbreviations: *AIH, autoimmune hepatitis; IND, Investigational New Drug; MOA; mechanism of action.*

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



KEY ENDPOINTS

Primary Efficacy

- 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

NCT05569759

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

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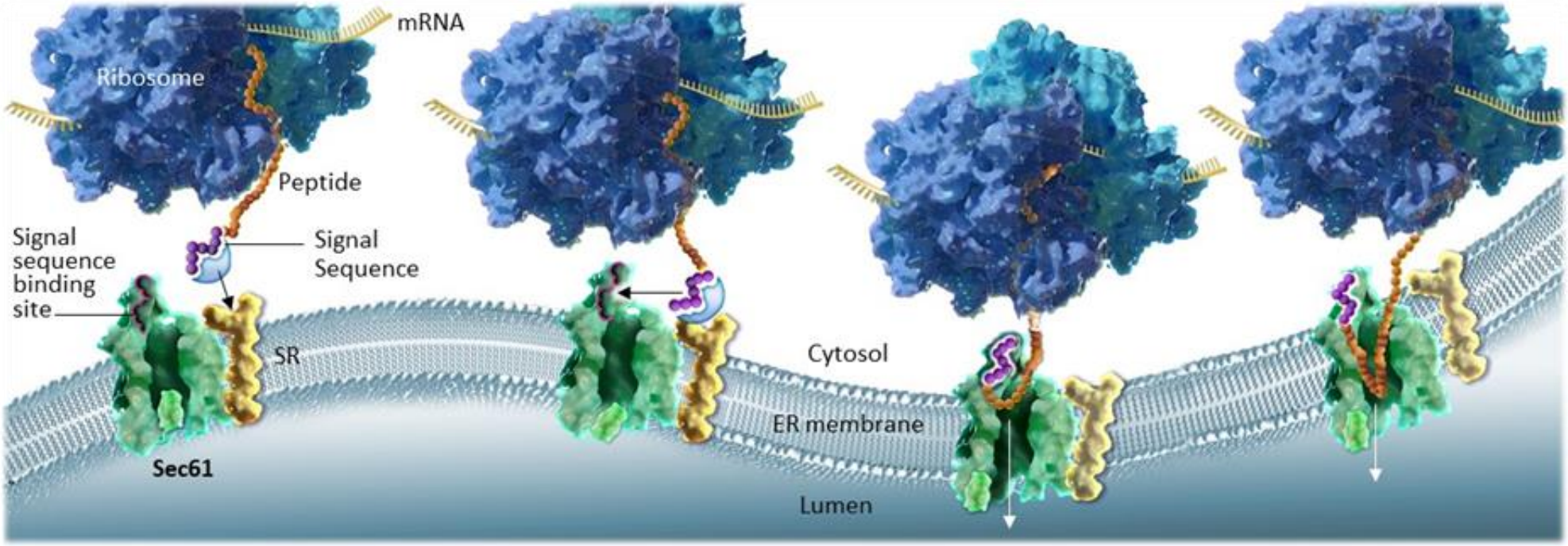
PROTEIN SECRETION PLATFORM RESEARCH UPDATE

Neel K. Anand, PhD
Senior Vice President,
Research & Discovery

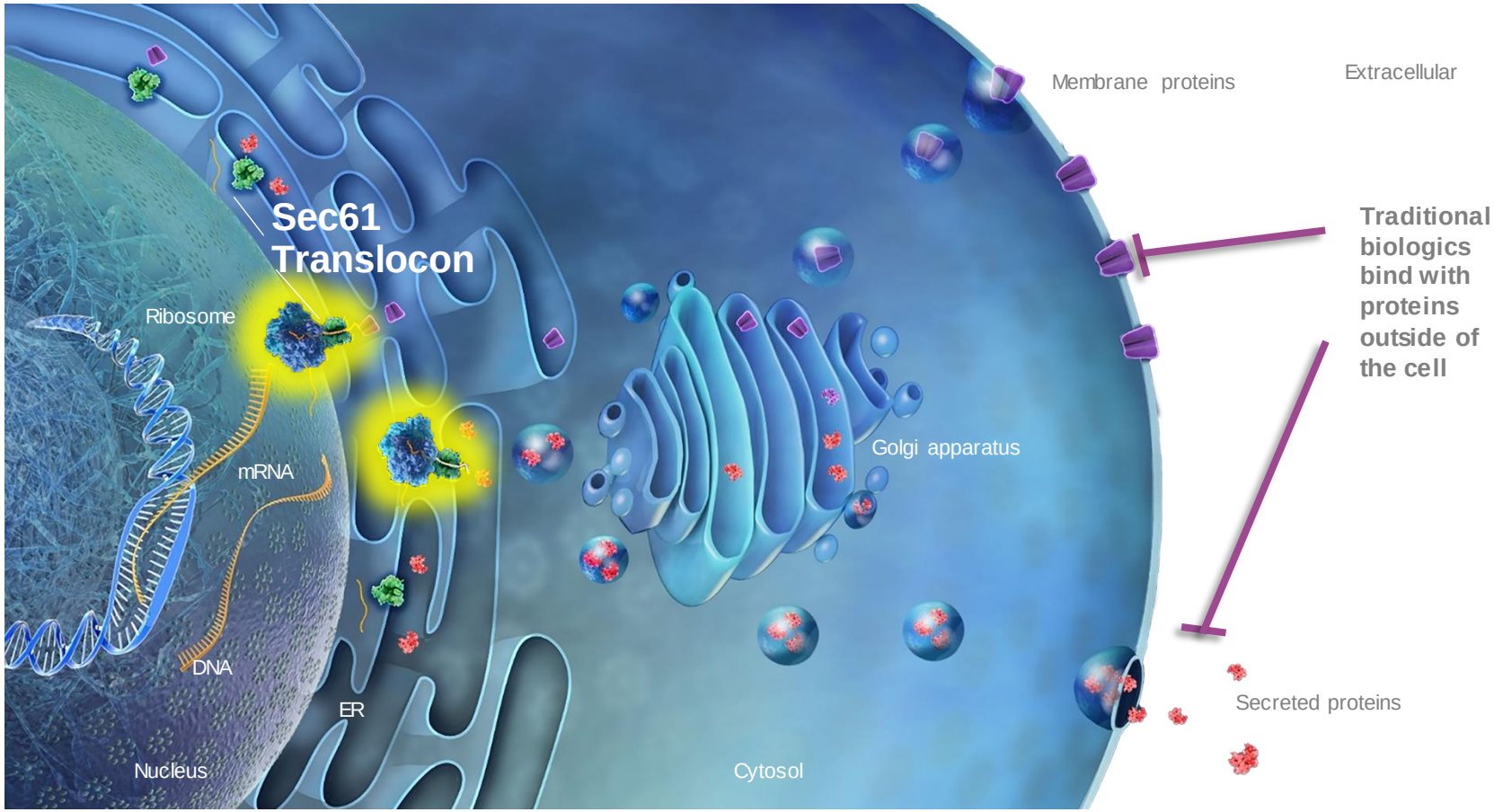
The Sec61 Translocation Channel (Translocon) is the Initiation of the Protein Secretion Pathway and a Novel Drug Target

- 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**



Sec61 Translocon is a Master Regulator for Secretion or Membrane Expression of Most Validated Targets for Biologics

Biologics target proteins after they have been made and released.
Sec61 inhibition blocks these proteins before they are made.



- Target of Sec61 Inhibitors

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®)

Kezar Has Developed Robust Drug Discovery Capabilities to Understand the Biology and Druggability of the Protein Secretion Pathway

Primary Screen

Target Protein Signal Peptide (e.g. PD-1) | **Luciferase Enzyme**

Cell Based Inducible Reporter

Luminescent Readout

- > 200 Target Signal Peptides
- Therapeutic Targets and Anti-targets
- Amenable to HTS
- Validated with Sec61 and Signal Peptide mutagenesis studies

Compound Evaluation

Functional Cell Assays

- Pharmacological activity confirmation
- Comparison to SOC

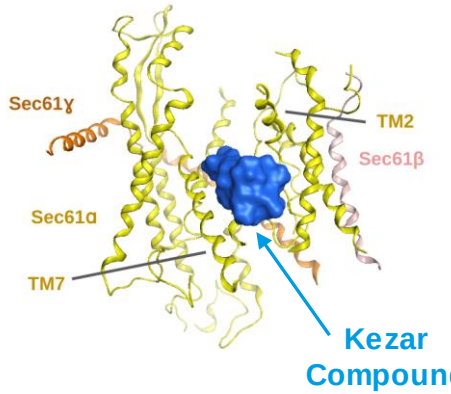
Genomics/ Proteomics

- Differentiate Sec61 client sensitivity per cell type
- Indication profiling

In Vivo Studies

- PK/PD
- Efficacy
- Toxicity

Cryo-EM Structure Elucidation



Overview of Protein Secretion Inhibition | Overview of KZR-261 | Overview of KZR-540 (PD-1)

Sec61 Translocon Can Be Targeted Broadly or Selectively to Develop Unique Therapeutics

Multi-Target

Single Target

Multi-Protein Secretion Inhibitors

- Inhibition of **multiple** secreted/membrane proteins
- Potential combination therapy in a single molecule
- **Multiple potential oncology indications (tumor agnostic)**

KZR-261: 1st clinical candidate

Subset Protein Secretion Inhibitors

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

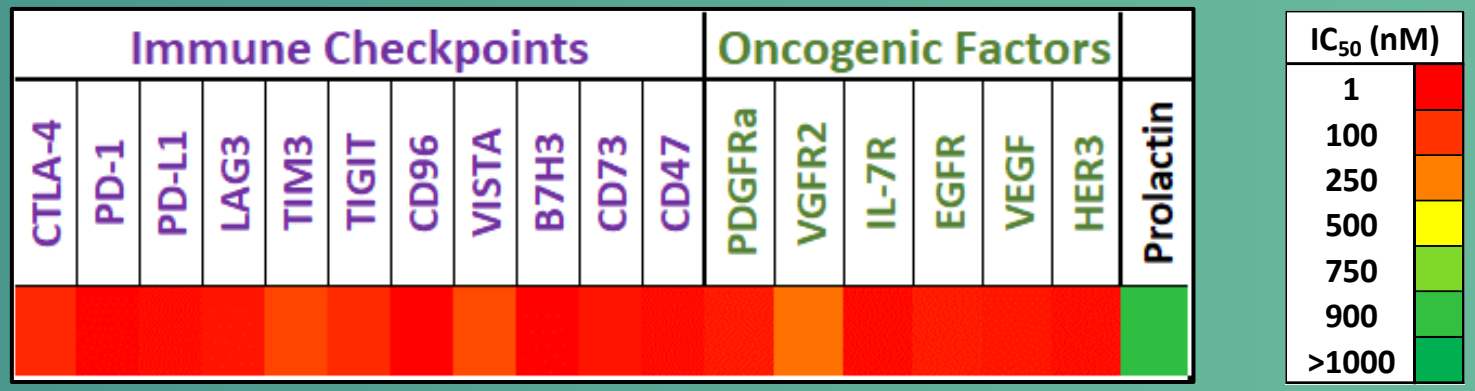
Single Protein Secretion Inhibitors

- Inhibition of a **single** secreted/membrane protein
  - Data presented at SITC 2022
- Non-cytotoxic agents
- **Many potential indications**

KZR-540: Lead compound

KZR-261: Combination Therapy in a Single Small Molecule

***In vitro* Protein Secretion Assays**



Direct Effects on Tumor Cells

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

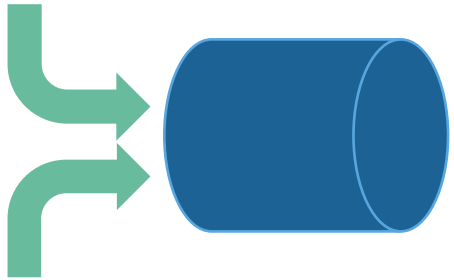
Tumor Microenvironment Modulation

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

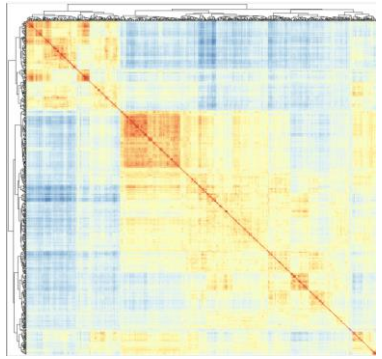
Phase 1 Trial Ongoing

Bioinformatic Workflow to Identify Sensitive Tumor Types

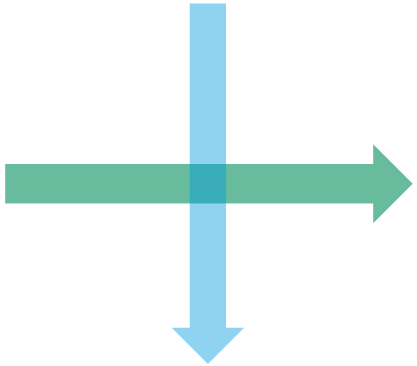
450+ cell lines
treated with KZR-261 Analog



7,000 gene modules
assessed



6 gene modules correlating
with sensitivity



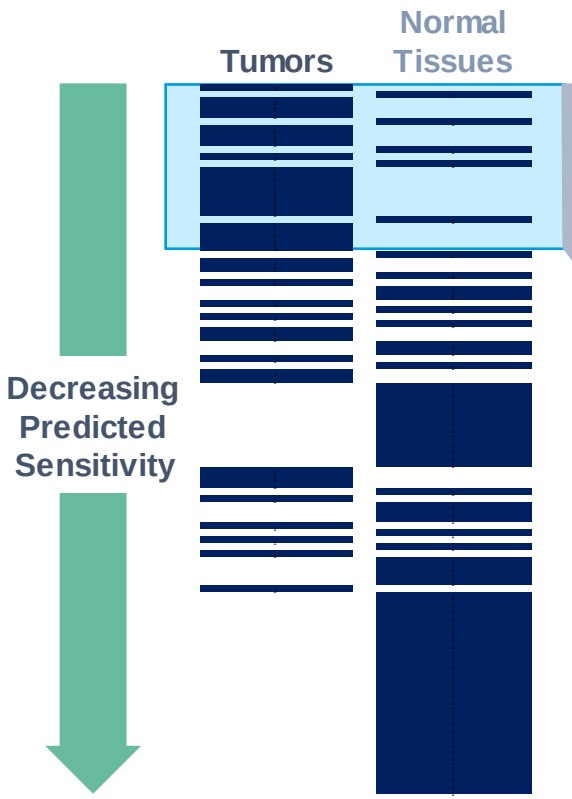
Modules linked
to target biology

- Sec61 clientome
- Vesicular transport
- mRNA translation

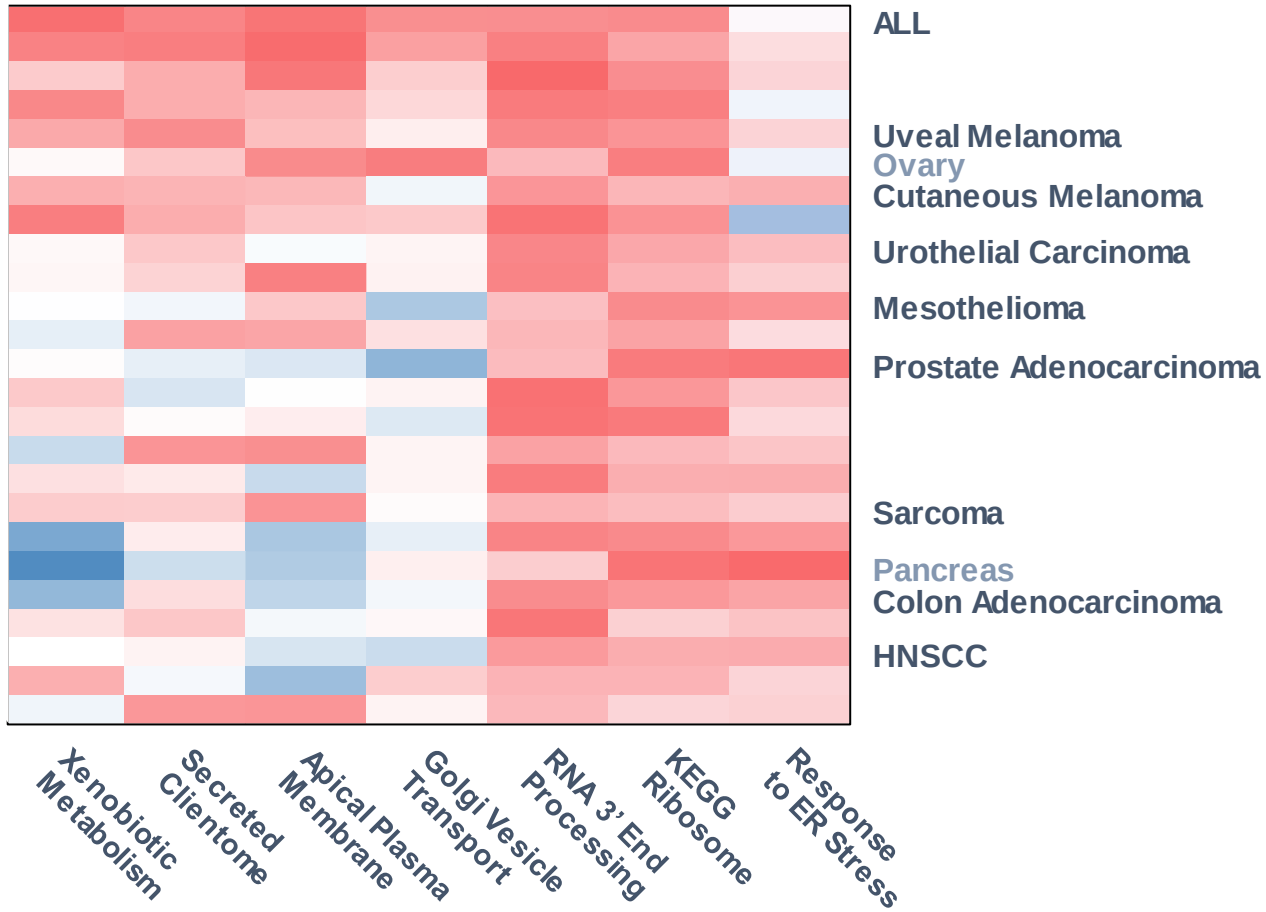
- CCLE (1400+ cancer cell lines)
- TCGA (20K+ primary cancer samples)
- Gtex (50+ normal tissues, 15K+ samples)

This approach identifies only tumor intrinsic factors

Bioinformatics, Preclinical Data and Market Opportunity Informed Multiple Solid and Liquid Tumors as Potential Indications for KZR-261



- Tumors are predicted to be more sensitive than **normal tissues**
- **Pancreas** observed to be a target tissue for tox in preclinical studies



Gene modules correlating with sensitive cell lines

Sec61 Translocon Can Be Targeted Broadly or Selectively to Develop Unique Therapeutics

Multi-Target

Single Target

Multi-Protein Secretion Inhibitors

- Inhibition of **multiple** secreted/membrane proteins
- Potential combination therapy in a single molecule
- **Multiple potential oncology indications (tumor agnostic)**

KZR-261: 1st clinical candidate

Subset Protein Secretion Inhibitors

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

Single Protein Secretion Inhibitors

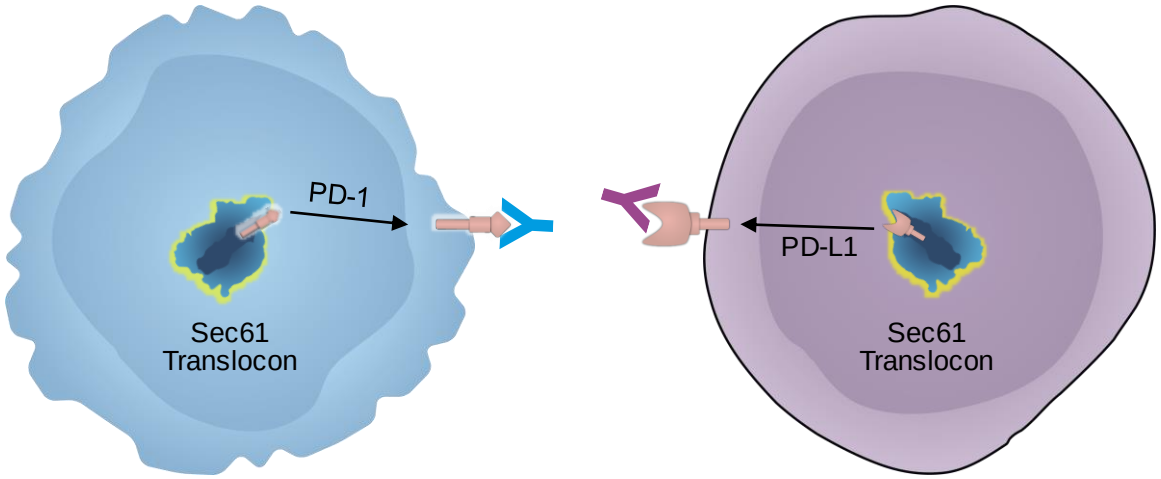
- Inhibition of a **single** secreted/membrane protein
  - Data presented at SITC 2022
- Non-cytotoxic agents
- **Many potential indications**

KZR-540: Lead compound

KZR-540: Oral Small Molecule PD-1 Inhibitor is Potential I/O Partner of Choice for Combination Therapies

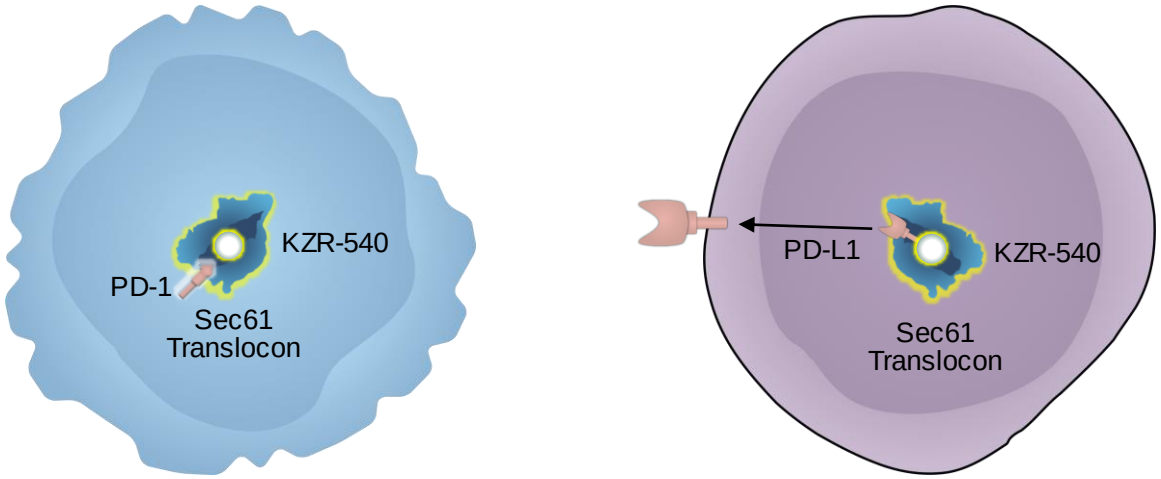
Monoclonal Antibodies (mAbs)

Block expressed PD-(L)1



KZR-540

Block expression of PD-1



POTENTIAL ADVANTAGES OF ORAL PD-1 INHIBITOR, KZR-540:

1

Reduced Treatment Burden

Oral QD dosing regimen anticipated

2

Dose-Modulation

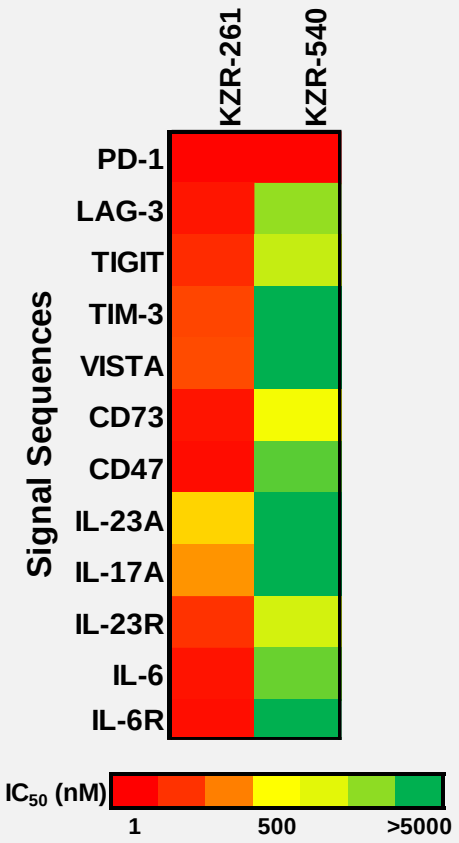
AEs more efficiently controlled by modulating administration

3

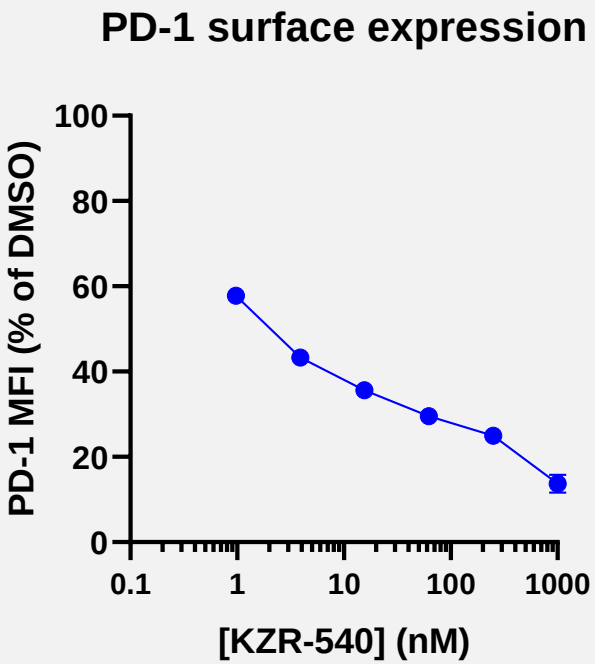
Cost-Benefit Improvement

Lower CoGs and health infrastructure costs

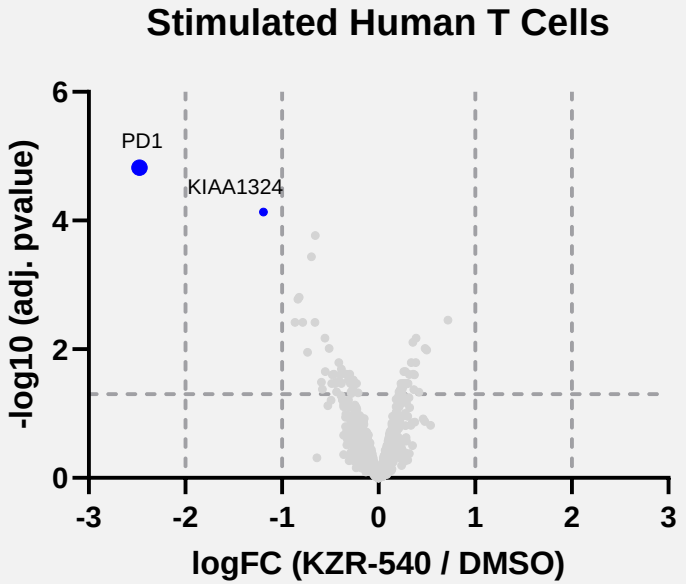
KZR-540: Highly Selective and Robust PD-1 Downregulation *In Vitro*



KZR-540 treatment decreased PD-1 surface expression in human PBMCs



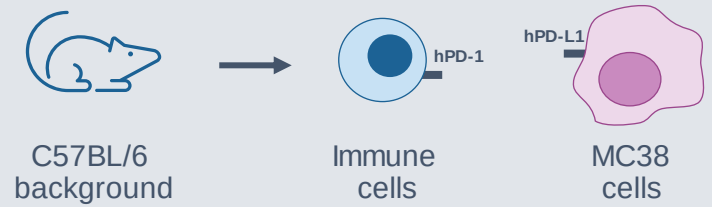
Proteomic analysis demonstrates exquisite selectivity of KZR-540



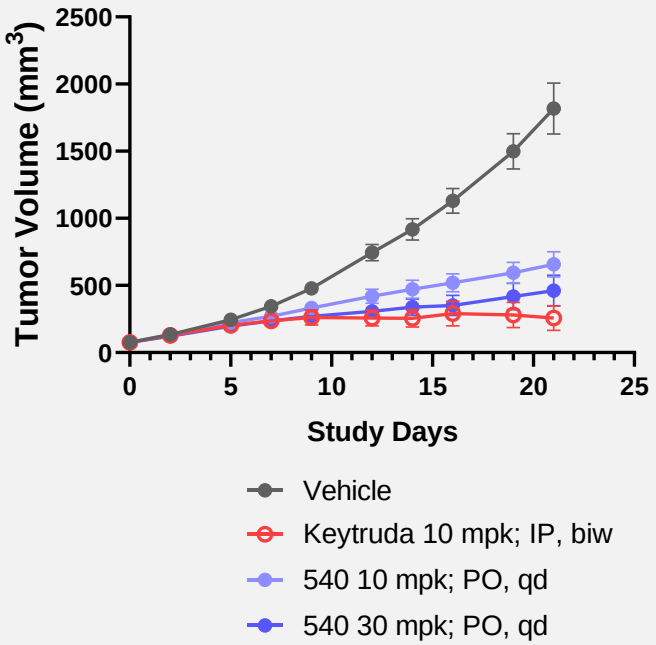
Reporter assay IC_{50}	
PD1	6 nM
KIAA1324	38 nM

Oral Administration of KZR-540 Has Shown Similar Efficacy to Traditional Anti-PD-1 Monoclonal Antibodies

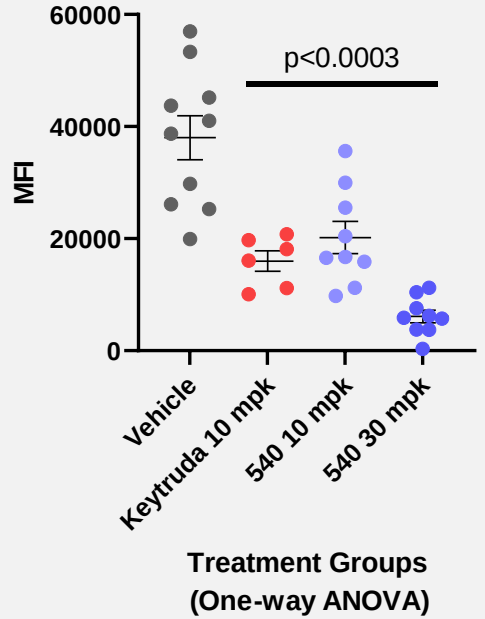
hPD-1 KI mice / hPD-L1 tumor model



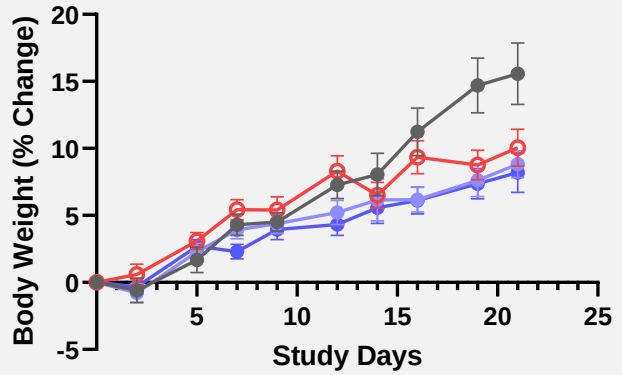
hPD-1 KI mice MC38-hPD-L1



PD-1 expression on tumor infiltrating T cells



Body weights



Kezar's Protein Secretion Platform

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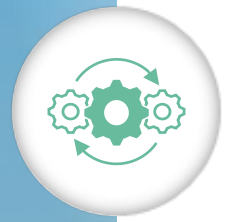

The Sec61 Translocon Protein Secretion Platform

Leadership in research on a unique drug target with multiple therapeutic applications

KZR-261: First Clinical Candidate Targeting Oncogenic Drivers and Multiple Immune Checkpoints

Inhibition of multiple secreted/membrane proteins; potential combination therapy in a single molecule

KZR-540: Novel Oral Small Molecule Inhibitor of PD-1 Expression

Potential I/O partner of choice for all-oral combination therapies

Ability to Develop Small Molecule Therapeutics Against Validated Targets

Unique small molecule replacements for validated biologics across therapeutic areas

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KZR-261 CLINICAL UPDATE

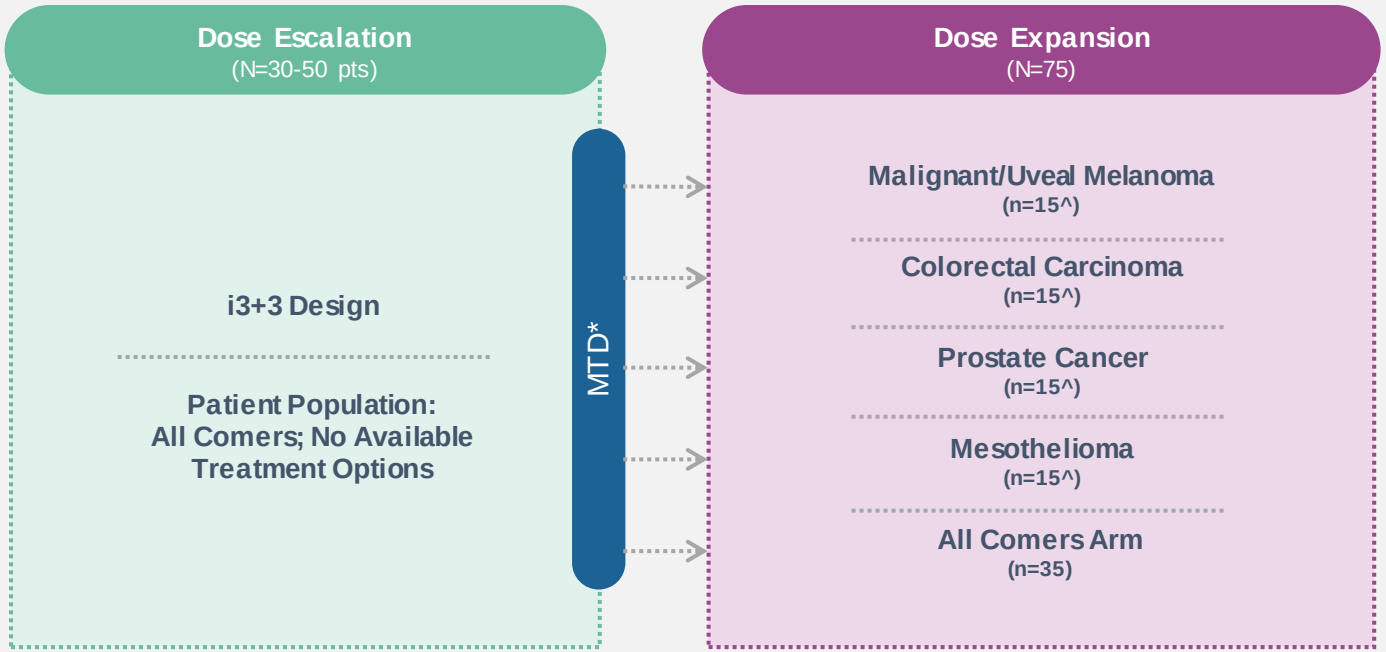
Noreen R. Henig, MD
Chief Medical Officer

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: First-in-Human Trial With Anticipated Dose Escalation Completion in 2H 2023

KZR-261-101 Phase 1 Trial Design



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*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.

Measures & Goals

Key Outcome Measures

- 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

Rapid Dose Escalation

- Cohort 1 (1.8 mg/m^2) – 4 (12 mg/m^2) with rapid escalation without significant safety concerns
- Cohort 5 (18 mg/m^2)
  - Dose approximates MED in preclinical studies
  - 2 patients in 5th cycle
    - 1 melanoma
    - 1 mCRC
- Cohort 6 (27 mg/m^2)
  - Enrolling

Favorable Safety Through First 5 Cohorts

- No consistent patterns of safety signals
- Single DLT at 12 mg/m^2
  - Asymptomatic lipase elevation
- 1 SUSAR (infusion-related reaction) at 18 mg/m^2 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

Next Steps

Topline Data from Dose Escalation expected 2H 2023

Topline Data from Dose Expansion expected starting mid-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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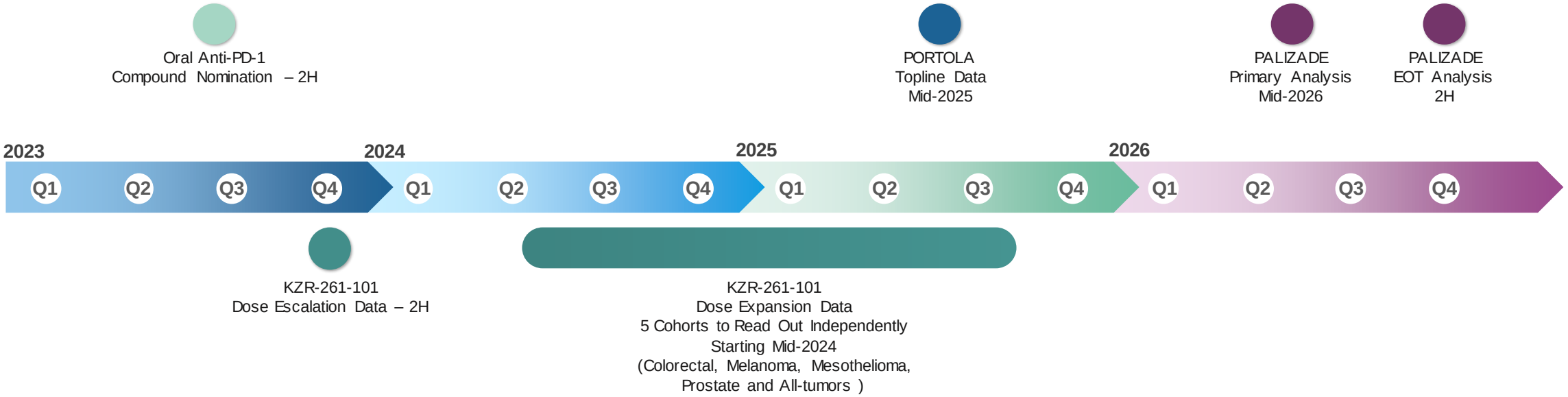
CLOSING REMARKS

John Fowler, MBA
Chief Executive Officer

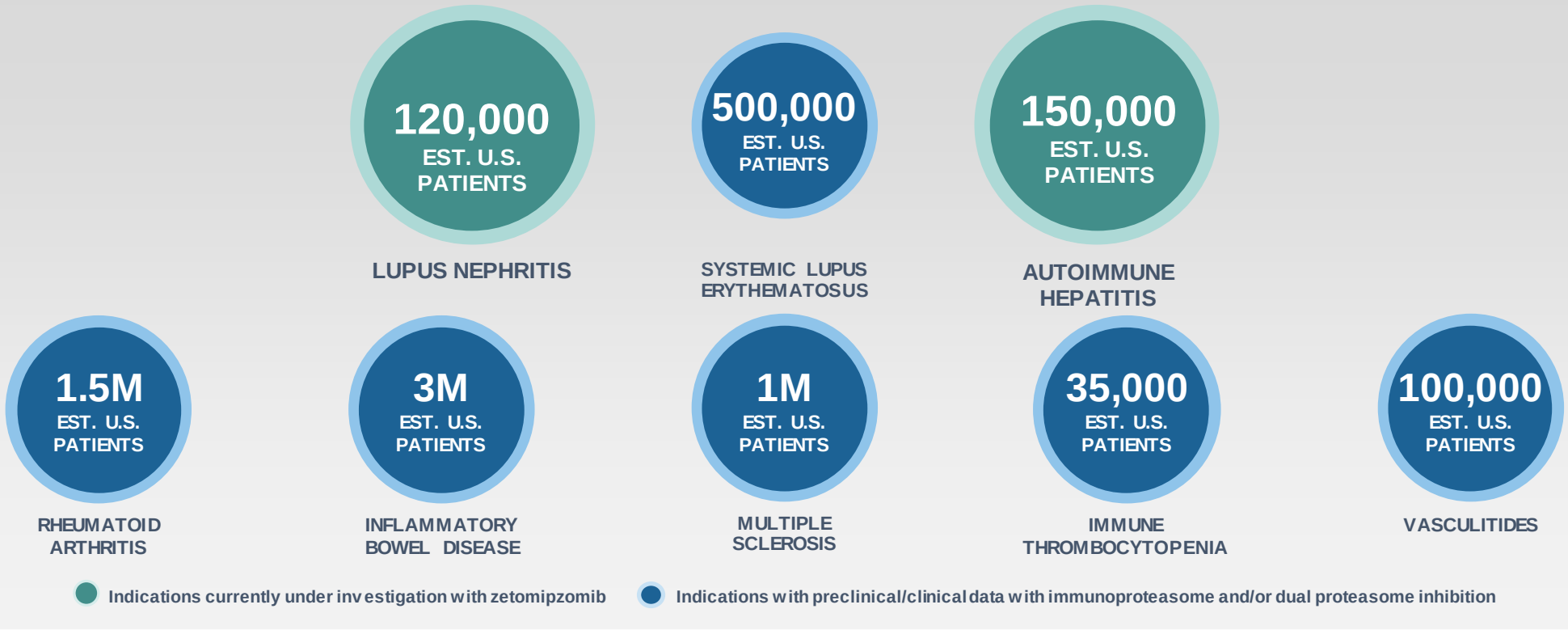
Anticipated Catalysts Across All Programs: Potential Value Creation 2023 – 2027



Zetomipzomib's Pipeline in a Drug: Promising Potential Across Multiple Chronic Autoimmune and Immune-Mediated Diseases

ZETOMIPZOMIB

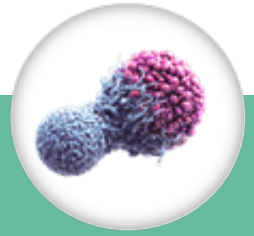
Novel First In Class Compound with Paradigm Shifting Properties



KZR-261: A Differentiated Approach with the Potential For Very Large Market Opportunity

Novel Mechanism of Action

- Novel Sec61 translocon MOA provides opportunity to pursue additional solid tumor indications lacking viable treatment option beyond chemo and traditional I/O agents



Potential to Overcome Chemo Resistance

- Broad activity against anti-proliferation, checkpoint inhibition, and TME modulation allows for the potential to overcome resistance mechanisms

Current Chemotherapy and Checkpoint Inhibitor Market

- Current market for traditional chemotherapy agents generating >$42B[(1)] in sales
- PD-1 / PD-L1 agents have cumulative sales of >$30B[(2)], underscoring the importance for more convenient small molecule additional I/O therapeutics

Patient-Focused

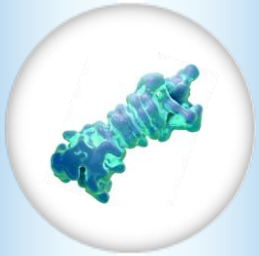
- Patient burden from toxicity profile of multiple lines of therapy or combination therapies remains large
- KZR-261, due to its broad activity, has the potential of combination therapy in a single agent

1. Data Bridge Market Research
2. Expert Market Research

Abbreviations: *I/O, immuno-oncology; MOA, mechanismof action; TME, tumor microenvironment.*

Pursuing Paradigm Shifts in Immunology and Oncology

Selective Immunoproteasome Inhibition: Zetomipzomib (KZR-616)



- Leads to potent immunomodulation without evidence of immunosuppression
- No immediate rebound of symptoms of disease activity
- Steroid sparing potential
- Pipeline in a product potential across several autoimmune indications:
  - MISSION Ph2 (LN) completed in 2022
  - PORTOLA PoC (AIH) initiated in 1H 2023
  - PALIZADE Ph2b (LN) to begin in 1H 2023

Protein Secretion Inhibition: KZR-261 & Discovery Program

- Potential to be first-in-class inhibitor of Sec61 translocon
- Shows broad anti-tumor potential by controlling proliferation, metastasis and immune evasion in preclinical cancer models
- KZR-261-101 dose-escalation ongoing with expected readout in 2H 2023
- More compounds in pre-clinical development for single- and multi-target oncology indications, offering additional upside

Questions & Answers

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