

# Selective Targets. Broad Impact.

*Uniquely Powerful Approaches to Tackling the  
Toughest Diseases*

MISSION Phase 1b: KZR-616 for  
the treatment of SLE and LN

*June 2, 2021*

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This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “target,” and similar expressions (as well as other words or expressions referencing future events or circumstances) are intended to identify forward-looking statements. Each of these forward-looking statements involves substantial risks and uncertainties that could cause actual results to differ significantly from those expressed or implied by such forward-looking statements. Forward-looking statements contained in this presentation include, but are not limited to, statements regarding the disruption of our business and clinical trials from the global outbreak of a novel strain of coronavirus (COVID-19), the potential use of our product candidates to treat patients, the association of data with treatment outcomes, the design, timing of initiation, progress, enrollment and scope of clinical trials for our product candidates, the expected timing of program updates and data disclosures, the timing of filing INDs and other regulatory documents, the timing and likelihood of seeking regulatory approval for our product candidates, and the patient prevalence, regulatory pathway and competitive landscape for our product candidates.

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**John Fowler**  
**Chief Executive Officer**



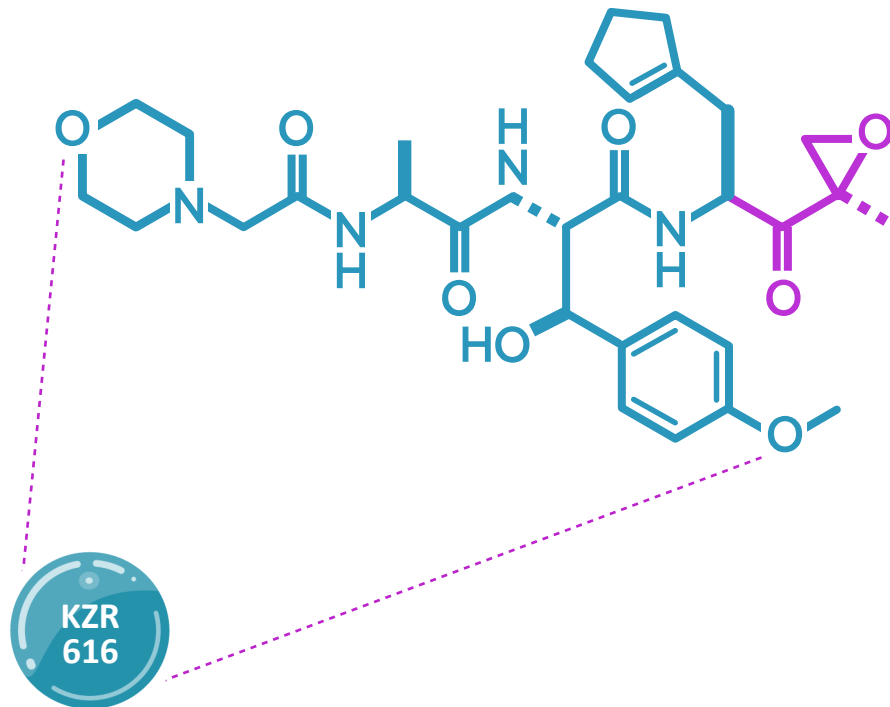
## KEZAR REPRESENTATIVES

Name	Title
John Fowler	Co-Founder and CEO
Christopher Kirk, PhD	Co-Founder and Chief Scientific Officer
Noreen R. Henig, MD	Chief Medical Officer
Celia Economides	SVP, Strategy & External Affairs

# AGENDA

Topic	Speaker
Welcome and KZR-616 Program Overview	John Fowler, CEO
MISSION Phase 1b data	Noreen R. Henig, CMO
Overview of SLE/LN and Experience with KZR-616	Samir V. Parikh, MD, FASN, Assistant Director of Nephrology, Ohio State Wexler Medical Center
Q&A	All

## KZR-616, A FIRST-IN-CLASS SELECTIVE IMMUNOPROTEASOME INHIBITOR, IS DESIGNED TO BE USED AS A CHRONIC THERAPY FOR IMMUNE-MEDIATED DISEASES



Administered once a week subcutaneously,  
amenable to self-administration



Cleared rapidly from the plasma (< 2hours)



Full recovery of immunoproteasome activity  
occurs within 3-7 days



No off-target effects; potential lack of  
immunosuppression<sup>1</sup>



Potential be steroid sparing

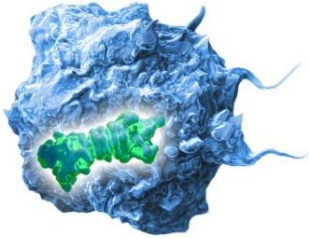


Extensive IP - 2034+.

<sup>1</sup>Muchamuel et al. ACR 2019

# INFLAMMATORY DISORDERS ARE CURRENTLY TREATED ONE CYTOKINE OR CELL AT A TIME BUT INHIBITING THE IMMUNOPROTEASOME COVERS THEM ALL

Macrophages  
Dendritic Cells  
Monocytes

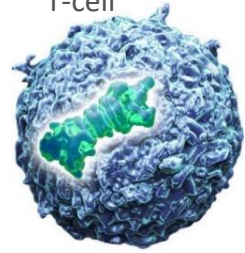


Cytokines  
TNF- $\alpha$   
IL-6  
IL-23



**Humira, et al**  
**Actemra**  
**Skyrizi/Stelara**

T-cell

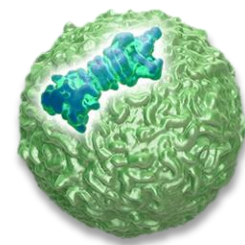


Cytokines  
IL-17



**Orencia**  
**Xeljanz**  
**Cosentyx/Taltz**

B-cell



**Rituxan/Gazyva**  
**Benlysta**



# PROOF OF PRINCIPLE STUDIES INDICATE THAT TARGETING THE IMMUNOPROTEASOME HAS THE POTENTIAL TO TREAT MULTIPLE CHRONIC IMMUNE-MEDIATED DISEASES

Orphan and/or high unmet need\*:

	Clinical Data w/Dual Proteasome Inhibitors	Pre-clinical Data w/ KZR-616/ONX-0914*
Lupus Nephritis (LN)	✓	✓
Myositis	✓	✓
Antibody-mediated transplant rejection	✓	✓
Graft vs host disease (GVHD)	✓	✓
Myasthenia Gravis (MG)	✓	✓
Autoimmune cytopenias	✓	
IGA Nephropathy (IgAN)	✓	
IgG4-4 related disease	✓	
Pemphigoid	✓	
CIDP	✓	
ANCA-associated vasculitis (AAV)	✓	

*\*partial list*

Large market:

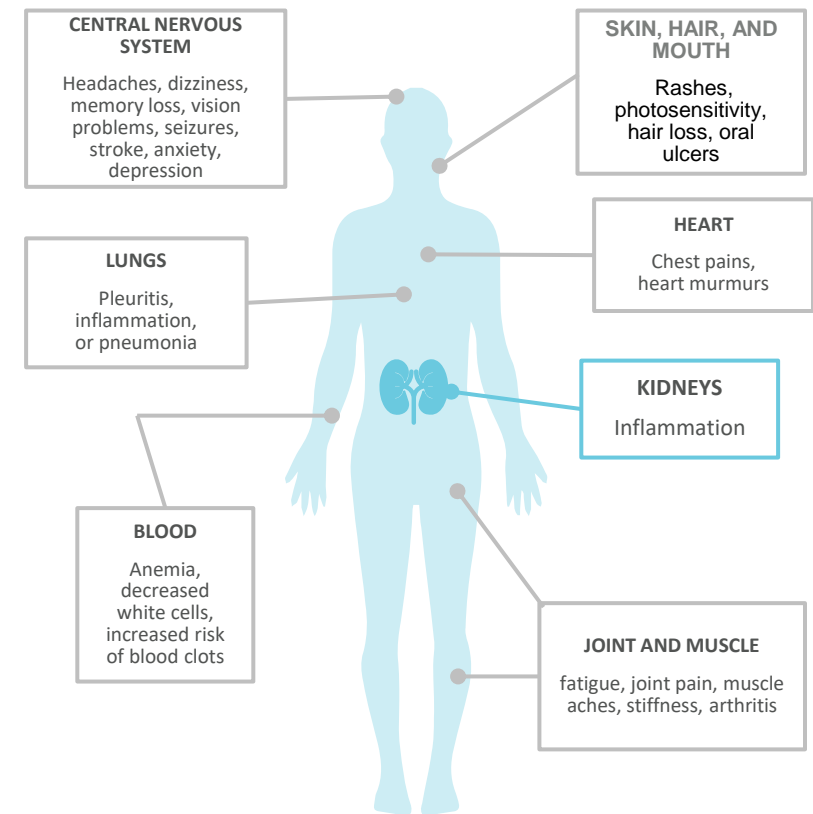
Rheumatoid Arthritis (RA)	✓	✓
Systemic Lupus Erythematosus (SLE)	✓	✓
Multiple Sclerosis (MS)		✓
Crohn's Disease (CD)		✓
Type 1 Diabetes		✓

\*ONX-914 is a predecessor compound to KZR-616



# SIGNIFICANT UNMET TREATMENT NEED REMAINS IN SLE/LN

- **There is no cure for SLE or LN<sup>1</sup>**
- **Few medications have FDA-approved indications for SLE/LN**
- **SLE/LN are heterogenous diseases with multiple underlying pathways**
- **Current SOC treatments for SLE/LN have serious AE profiles<sup>2</sup>**
- **Patients experience refractory disease despite maximized SOC treatments**



<sup>1</sup>Parikh SV, et al. *Am J Kidney Dis.* 2020;76(2):265-281. <sup>2</sup>Tesar V, et al. *Nephrol Clin Pract.* 2014;128:205-215. <sup>3</sup>Wilkinson L, et al. *Endocr Connect.* 2018;7(12):R328-R349. <sup>4</sup>Hoover PJ, et al. *Kidney Int.* 2016;90(3):487-492.

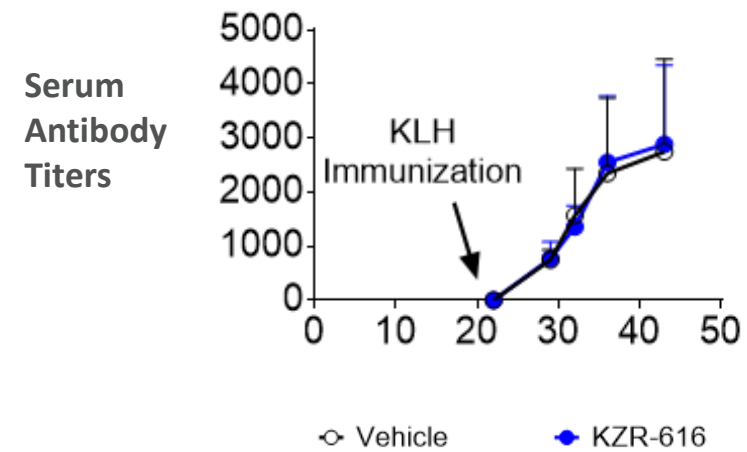
**Abbreviations:** AE, adverse event; FDA, Food and Drug Administration; LN, lupus nephritis; SLE, systemic lupus erythematosus; SOC, standard of care.

# KZR-616 HAS DEMONSTRATED A LACK OF IMMUNOSUPPRESSION IN ANIMAL MODELS

- In animals, inhibition of the immunoproteasome does not make viral infections worse
- There is no depletion of white blood cells (e.g. lymphopenia) in animals receiving KZR-616 for up to 9 months

- Normal antibody responses upon immunization in animals treated with KZR-616 suggests that vaccinations will be effective in patients receiving KZR-616

 Anti-KLH IgG Levels



Data on file.

## KZR-616 CLINICAL PROGRAM OVERVIEW

KZR-616 is currently the only agent with FDA Orphan Drug Designation in both DM and PM

Phase	Name/Indication	Status
Phase 1	Healthy Volunteers (frozen formulation)	Complete
Phase 1	Female Healthy Volunteers (lyophilized formulation)	Complete
Phase 1b/2	MISSION/ (SLE +/- LN, LN)	Ph 1 – Complete; Ph 2 - Ongoing
Phase 2	PRESIDIO (DM/PM)*	Ongoing
Extension Study	Extension for MISSION in LN	Planned
Extension Study	Extension for PRESIDIO in DM/PM	Ongoing

# MISSION Phase 1b Clinical Data

Noreen R. Henig, MD  
Chief Medical Officer



# PHASE 1B MISSION TRIAL DESIGN – SAFETY, TOLERABILITY, AND DOSE FINDING STUDY IN SLE PATIENTS WITH AND WITHOUT NEPHRITIS



\*Cohorts 2b/2c/3 use lyophilized formulation; prophylactic oral electrolyte solution, non-sedating antihistamines, and antiemetics and/or dose escalation.

## Endpoints:

1: Safety.

2: Recommended Phase 2 doses, Plasma PK.

## Exploratory:

Efficacy, PD, Biomarkers, Pharmacogenomics.

# KEY ATTRIBUTES OF KZR-616 SUPPORT ADVANCEMENT INTO PHASE 2 TRIALS

Based on data from 2 HV Studies and MISSION Phase 1b data in SLE patients (n>100)



## Safety & Tolerability

- Well-tolerated for 13 weeks of treatment
- Majority of TEAEs are injection site reactions and manageable
- Safety concerns associated with immunosuppressive agents or dual proteasome inhibitors were not observed



## Efficacy & Biomarkers

- Improvement across all measured parameters of disease activity
- Rapid and sustained immunomodulatory gene expression changes
- Reduction in key biomarkers of disease activity



## PK & PD

- Consistent PK and PD across subjects and with repeat dosing
- Highly selective immunoproteasome inhibition with target levels of >80% met at doses  $\geq$  30mg

*Furie et al, EULAR 2021*

**Abbreviations:** HV, healthy volunteers; TEAEs, treatment-emergent adverse events, PK, pharmacokinetics; PD, pharmacodynamics

# PHASE 1B - KZR-616 DEMONSTRATES A FAVORABLE SAFETY AND TOLERABILITY PROFILE FOR USE IN CHRONIC DISEASES



Measures, N% of patients	Cohort 1 (n=8)	Cohort 2 (n=5)	Cohort 2a (n=14)	Cohort 2b (n=6)	Cohort 2c (n=8)	Cohort 3 (n=6)	All patients Cohorts 1-3 (n=47)
Target dose, mg	45	60	60	60	60	75	45-75
Mean compliance, %	69.2	52.3	70.3	92.3	100.0	76.9	76.9
≥1 Treatment Emergent Adverse Event (TEAE)	8 (100.0)	5 (100.0)	12 (85.7)	4 (66.7)	7 (87.5)	3 (50.0)	39 (83.0)
Most Common TEAEs							
Injection Site Erythema	5 (62.5)	2 (40.0)	5 (35.7)	2 (33.3)	6 (75.0)	0 (0)	20 (42.6)
Nausea	2 (25.0)	4 (80.0)	5 (35.7)	1 (16.7)	4 (50.0)	3 (50.0)	19 (40.4)
Vomiting	1 (12.5)	5 (100.0)	3 (21.4)	1 (16.7)	2 (25.0)	1 (16.7)	13 (27.7)
Infections and Infestations TEAEs	1 (12.5)	0 (0)	5 (35.7)	2 (33.3)	2 (25.0)	1 (16.7)	11 (23.4)
Serious TEAEs	0 (0)	1 (20.0)	2 (14.3)	1 (16.7)	0 (0)	0 (0)	4 (8.5)
TEAEs leading to discontinuation	3 (37.5)	3 (60.0)	2 (14.3)	0 (0)	0 (0)	2 (33.3)	10 (21.3)
Patients receiving prednisone	5 (62.5)	5 (100.0)	10 (71.4)	4 (66.7)	5 (62.5)	3 (50.0)	31 (66.0)

Cohorts 2b, 2c, and 3 received a lyophilized formulation of KZR-616, prophylactic oral electrolyte solution, nonsedating antihistamines, and antiemetics and/or dose escalation. Furie et al, EULAR 2021 and Data on File.

**Abbreviations:** TEAE, treatment-emergent adverse event

# PHASE 1B: KZR-616 DEMONSTRATED IMPROVEMENT ON EXPLORATORY EFFICACY MEASURES OF DISEASE ACTIVITY ACROSS ORGAN SYSTEMS

Patients Completing Study, Evaluable Patient Population\* (n=35)

Instrument	Improvement	Baseline Mean, SD	EOT -W13 Mean, SD	EOS -W25 Mean, SD
SLEDAI-2K	+	9.1 (2.8)	6.6 (2.6)	7.1 (2.5)
CLASI-A	+	4.3 (4.1)	2.3 (3.0)	2.3 (3.2)
Tender Joint Count	+	11.1 (6.3)	4.8 (4.7)	5.8 (5.1)
Swollen Joint Count	+	7.6 (5.6)	2.5 (3.7)	2.3 (2.7)
Physician Global Assessment Score	+	57.0 (21.7)	39.7 (23.5)	38.2 (17.6)
Patient Global Assessment Score	+	58.3 (23.2)	38.2 (24.1)	42.7 (20.0)
HAQ-pain	+	58.5 (21.2)	43.1 (26.0)	41.7 (23.6)

\*Intent to treat (ITT) that did not withdraw before week 13

**Abbreviations:** BL=Baseline; EOT=End of Treatment; EOS=End of Study; W13=week 13; W25=week 25; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; HAQ, Health Assessment Questionnaire; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000

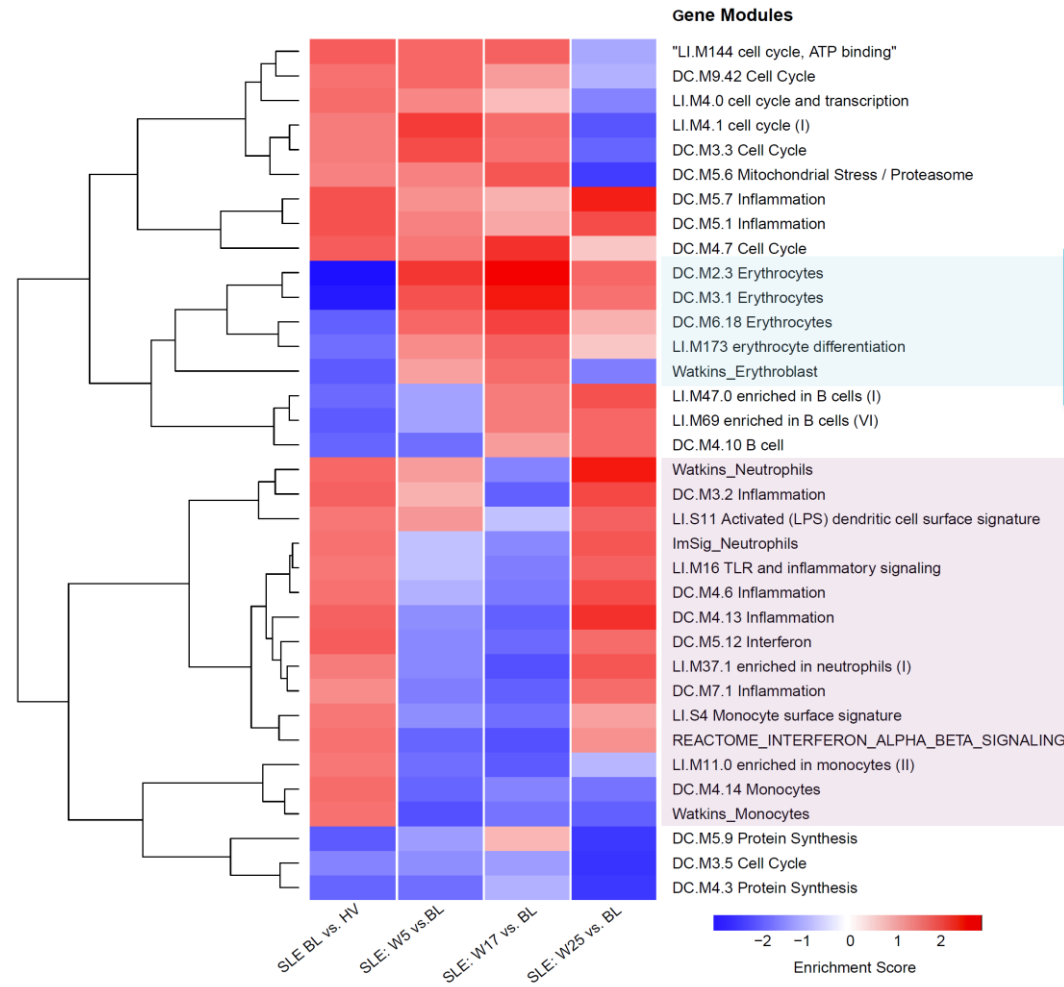
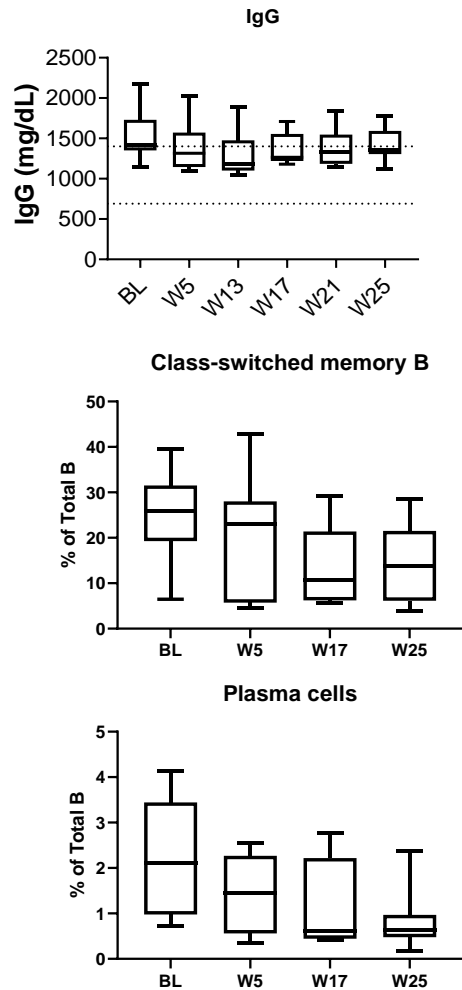


## KZR-616 TREATMENT RESULTS IN BIOMARKER CHANGES IN PATIENTS WITH SLE

- Whole blood RNASeq data from MISSION Phase 1b patients support potential broad immunomodulatory activity of KZR-616
- Immune gene modules have higher expression in patients with SLE relative to HV and are downregulated after KZR-616 treatment
- KZR-616 treatment upregulates erythrocyte gene modules which are suppressed in patients with SLE compared to HVs
- Platelets and RBCs remain stable after 13 weeks of treatment with KZR-616 in SLE Patients
- Anti-dsDNA antibody titers reduced over time in 8 patients with elevated levels at baseline
- Reduced circulating plasma cells were observed and likely account for reduction in autoantibodies
- Total IgG levels were unchanged following treatment with KZR-616
- Complement levels can be suppressed in SLE patients with active disease. C3 normalized in 5 /10 patients and C4 normalized in 4 / 6 patients with low levels at baseline.

**Abbreviations:** HV, healthy volunteers; IgG, immunoglobulin G; SLE, systemic lupus erythematosus.

# KZR-616 TREATMENT DECREASES IGG LEVELS AND B-CELL SUBSETS AND AFFECTS MULTIPLE INFLAMMATORY GENE EXPRESSION MODULES IN PATIENTS WITH SLE



Erythrocyte gene modules have lower expression in patients with SLE relative to HVs and are upregulated after treatment

These immune gene modules have higher expression in patients with SLE relative to HV and are downregulated after KZR-616 treatment

Gene list from Berthier, CC et al. *J Immunol.* 2012;189(2):988-1001.

Abbreviations: BL, baseline; HVs, healthy volunteers; IgG, immunoglobulin G; SLE, systemic lupus erythematosus.

## PHASE 1B - ALL PATIENTS EXPERIENCED SIGNIFICANT REDUCTION IN ANTI-DSDNA LEVELS

### Patients Completing Study w/Elevated anti-dsDNA at BL\*

Individual	Mean anti-dsDNA level, IU/mL (baseline)	% Change from baseline, week 13 (end of treatment)	% Change from baseline, week 25 (end of study)
Patient A	1015	-64.0	-82.0
Patient B <sup>a</sup>	87	-20.7	-33.3
Patient C	32	-6.3	-18.8
Patient D <sup>b</sup>	134	-60.4	-54.5
Patient E <sup>a</sup>	90	-76.7	-68.9
Patient F <sup>b</sup>	98	-46.9	-45.9
Patient G	29	-17.2	-24.1
Patient H <sup>a</sup>	162	-42.6	-33.3

\*Elevated levels of anti-dsDNA antibodies are highly specific markers of SLE disease activity (>20 IU/mL considered elevated)

<sup>a</sup>History of nephritis. <sup>b</sup>Active nephritis.

Abbreviation: anti-dsDNA, anti-double-stranded DNA antibody

# SUMMARY OF MISSION PHASE 1B RESULTS



## Safety

No significant adverse events, off target effects or systemic toxicities

Low rate of serious ( $\geq$  Grade 3) infections (2.2%) suggest lack of immunosuppression with KZR-616



## Efficacy

Improvement across all exploratory measured parameters of disease activity.



## Tolerability

Well-tolerated for 13 weeks of treatment

Majority of treatment emergent adverse events (TEAEs) have been mild or moderate



## PK, PD, Dosing

Highly selective immunoproteasome inhibition at doses  $\geq$  30mg

Up to 75mg weekly dosing is well tolerated

Doses of 45mg and 60mg identified as doses for Phase 2 clinical trials

## URINARY CD163 IS A BIOMARKER THAT CORRELATES STRONGLY WITH ACTIVE INFLAMMATION IN LN

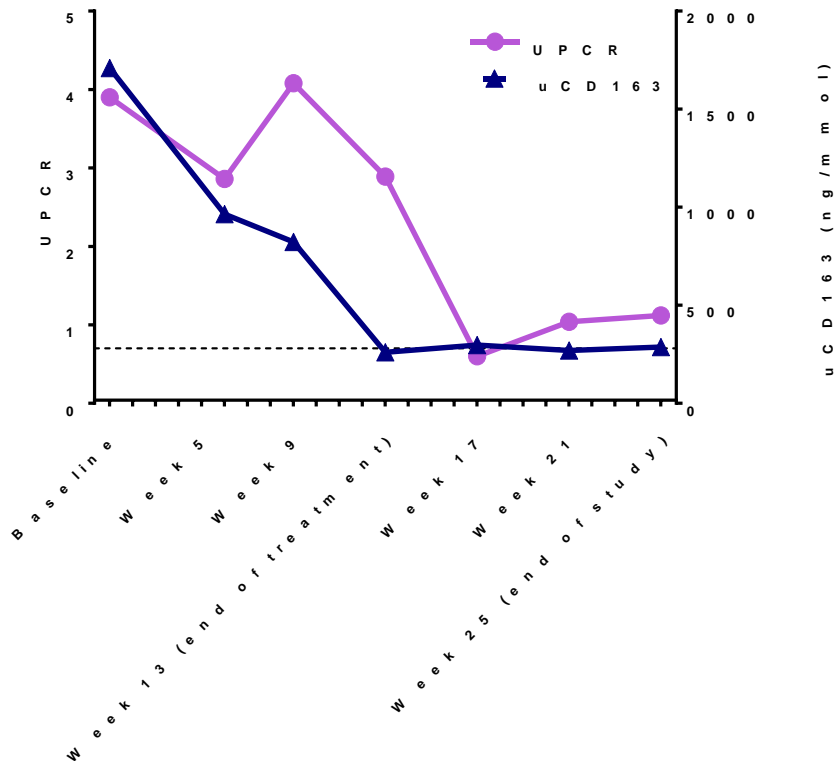


- CD163 is a transmembrane protein primarily expressed by M2c macrophages
- Urinary excretion, but not plasma levels, of uCD163 correlate highly with active inflammation of the glomeruli of patients with inflammatory kidney disease
- uCD163 gene expression is increased in glomeruli from patients with active LN
- Elevated uCD163 levels in LN correlate with number of infiltrating glomerular macrophages and are a sign of active disease
- uCD163 is significantly elevated in active LN when compared with healthy controls, inactive SLE, or active non-renal lupus

Mejia-Vilet J, et al. *JASN*. 2020;31(6):1335-1347.

**Abbreviations:** LN, lupus nephritis; uCD, urine CD; UPCR, urine protein to creatine ratio.

# RAPID REDUCTION IN DISEASE ACTIVITY OBSERVED FROM #1 OF 2 PATIENTS WITH LN

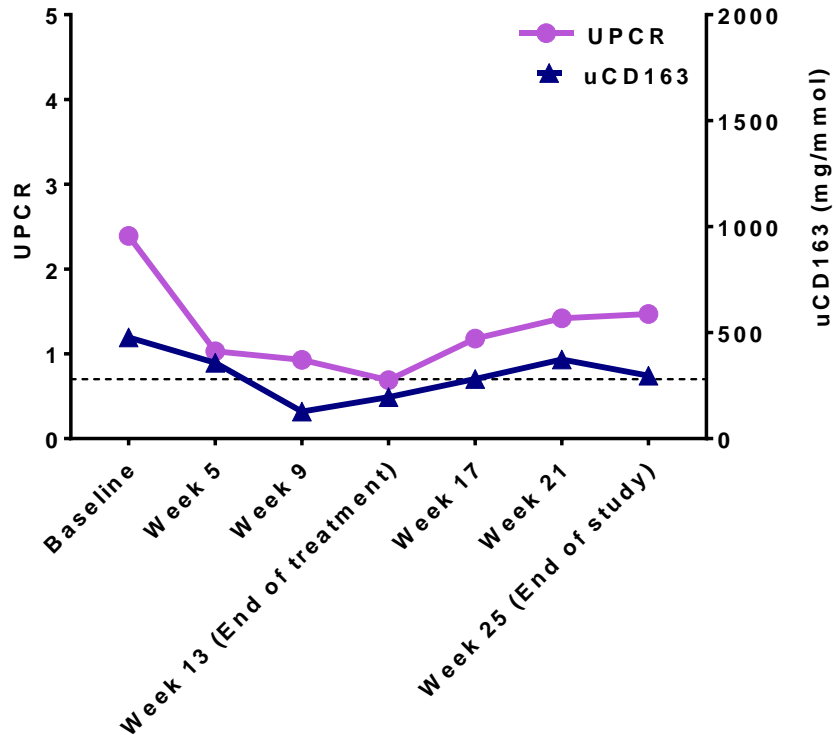


	<u>SLEDAI-2K</u>	<u>anti-dsDNA(IU/ml)</u>
		<u>% Δ</u>
<b>BL</b>	17	134
<b>W13</b>	8	-60.4
<b>W25</b>	8	-54.5

- Class IV/V
- Nephrotic Range
- 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 antibody titers at week 13
- Overall reduction in uCD163 preceded reduction in UPCR
- Drug holiday due to AE W2-4 & W11

**Abbreviations:** anti-dsDNA, anti-double-stranded DNA antibody; LN, lupus nephritis; MMF, mycophenolate mofetil; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urine protein to creatine ratio; uCD163, urinary CD163

# RAPID REDUCTION IN DISEASE ACTIVITY OBSERVED FROM #2 OF 2 PATIENTS WITH LN



	<u>SLEDAI-2K</u>	<u>anti-dsDNA(IU/ml)</u> % Δ
<b>BL</b>	14	98
<b>W13</b>	8	-46.9
<b>W25</b>	NA	-45.9

- Class III
- Baseline stable treatment regimen of MMF (2 g), hydroxychloroquine, and prednisone (10 mg/d)
- Nephrotic range
- >50% reduction in UPCR at week 5
- Reduction in uCD163 tracks with reduction UPCR
- Improved symptom scores at week 5
- Reduced anti-dsDNA antibody titers at week 5

**Abbreviations:** anti-dsDNA, anti-double-stranded DNA antibody; LN, lupus nephritis; MMF, mycophenolate mofetil; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urine protein to creatine ratio.

# Unmet Needs in Systemic Lupus Erythematosus and Lupus Nephritis

Samir V Parikh, MD, FASN

Associate Professor, Division of Nephrology

The Ohio State University Wexner Medical Center

June 2, 2021

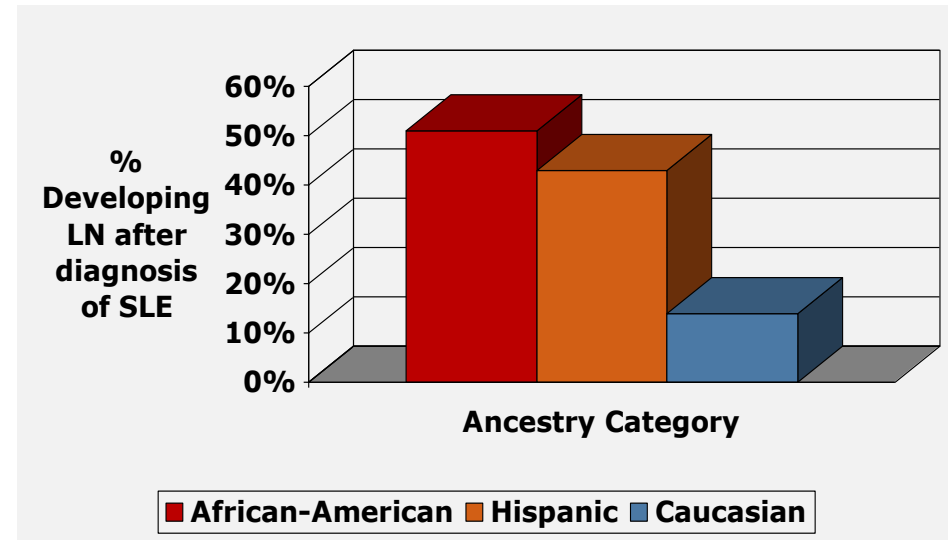


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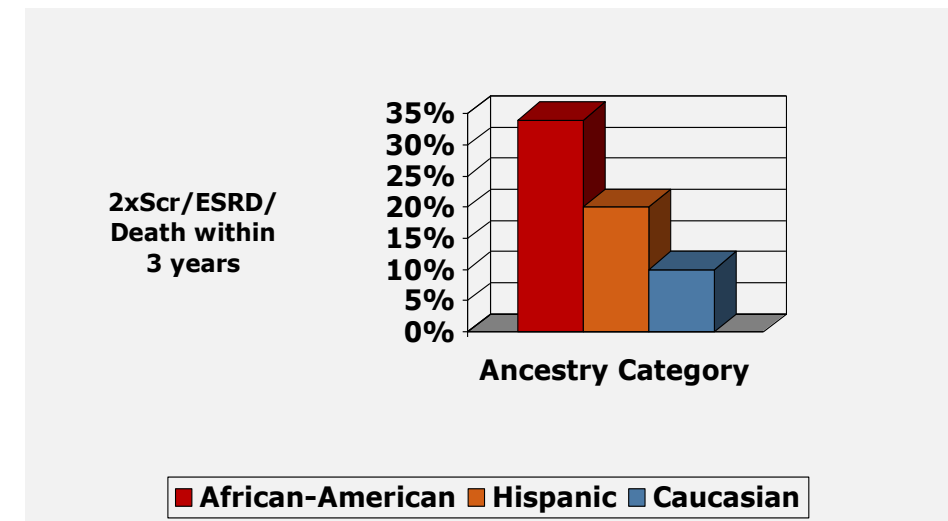


# SLE and LN – Who's at risk

- Approximately **300,000** Adults in US with SLE
- SLE predominantly affects young and predominantly females (9:1)
- Approximately 50% of patients with SLE will develop lupus nephritis (LN)
- 10-30% of patients still progress to ESRD within 15 years of diagnosis
- Kidney involvement is associated with poorest outcomes
- Incidence/Prevalence influenced by age, gender, race





LUMINA Study Group- Lupus 11:152-160, 2002



Contreras G, et al Lupus 14:890-895, 2005

# SLE/LN Impose a Substantial Disease Burden

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- **SLE/LN can severely impair patients' ability to work<sup>1</sup>**
  - Average annual lost economic productivity between \$1,200 and \$20,000<sup>2</sup>
- **Physical, mental, social, and emotional health are adversely affected by SLE/LN<sup>1</sup>**
  - Negative Health Factors: fatigue (24%), joint and muscle pain (24%), and kidney disease (21%)<sup>3</sup> (Per ICER)
  - Poor QoL  Reduced treatment adherence  Disease progression<sup>1</sup>
- **Average annual health care costs for a person with SLE are >\$32,000<sup>2,4</sup>**
  - Inpatient admissions and outpatient visits are the largest drivers of cost<sup>5</sup>
- **According to ICER: Negative Treatment Factors: Side effects (54%), Pill burden (54%), and Cost (42%)<sup>3</sup>**
- **ED visits, hospitalization rates, inpatient LOS, and ambulatory care utilization are greater for patients with LN than for patients with SLE without LN<sup>6</sup>**

<sup>1</sup>Carter EE, et al. *Nat Rev Rheumatol*. 2016;12(10):605-620. <sup>2</sup>Lupus Foundation of America. <https://www.lupus.org/resources/lupus-facts-and-statistics> <sup>3</sup>Clarke AE, et al. *Semin Arthritis Rheum*. 2020;50(4):759-768. <sup>4</sup>Murimi-Worstell IB, et al. *J Rheumatol*. 2021;48. <sup>5</sup>Hammond E, et al. *Ann Rheum Dis*. 2017;76(suppl 2):859-860.

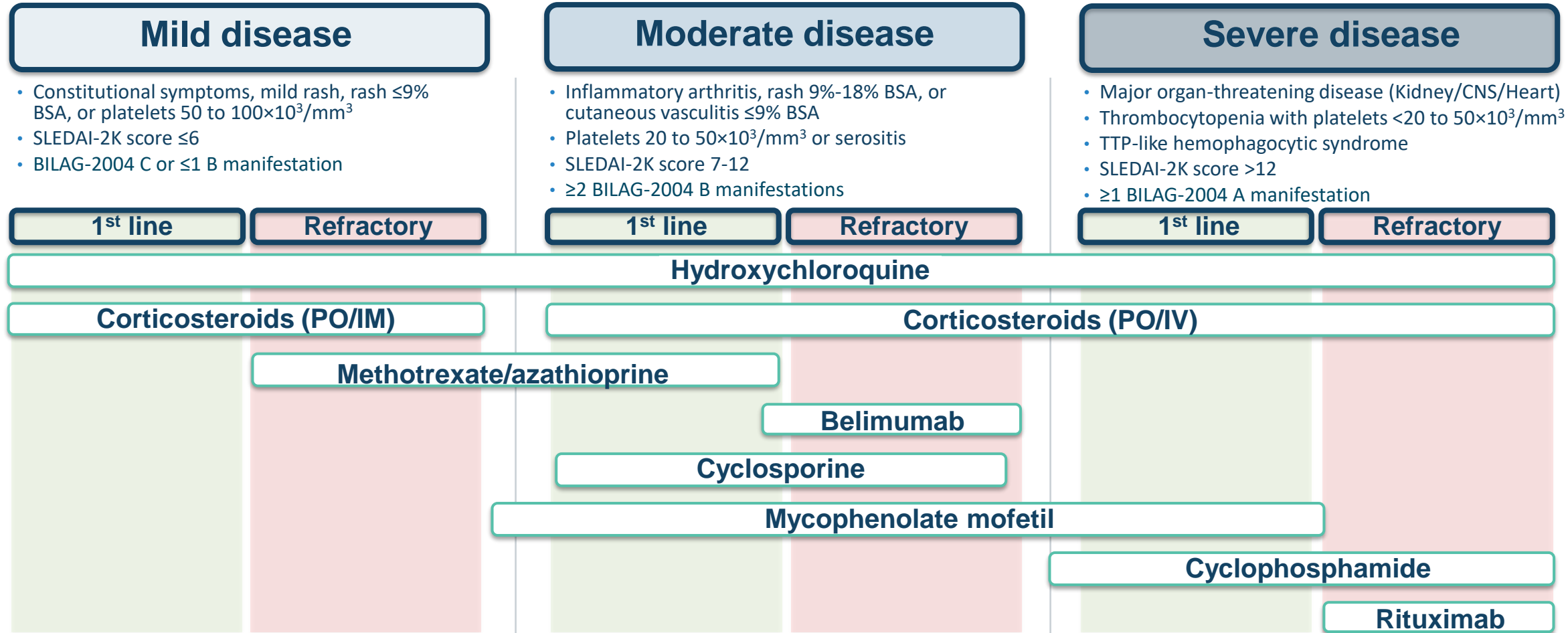
**Abbreviations:** ED, emergency department; LN, lupus nephritis; LOS, length of stay; QoL, quality of life; SLE, systemic lupus erythematosus.

# Lupus Nephritis: Goals of Therapy

- ❖ Treatment includes an initial period of high-intensity immunosuppression to control disease activity, followed by a longer period of treatment to consolidate response and prevent flares



# Treatment of SLE



Fanouriakis A, et al. *Ann Rheum Dis.* 2019;78(6):736-745.

**Abbreviations:** BILAG-2004; British Isles Lupus Assessment Group-2004; BSA, body surface area; IM, intramuscularly; IV, intravenously; PO, by mouth; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2000; TTP, thrombotic thrombocytopenic purpura.

# STANDARD INITIAL THERAPY for PROLIFERATIVE LN:

Proliferative LN: Give IV Methylprednisolone 0.5-1g/d for 1-3 days followed by Oral Prednisone 1mg/kg/d ideal body weight, Maximum 80 mg/d, Taper Over Weeks

PLUS:

IV Cyclophosphamide  
0.5-1g/m<sup>2</sup> Monthly  
for 6 months

Or

PO Cyclophosphamide  
1-1.5mg/kg/d,  
maximum 150 mg/d for  
2-4 months

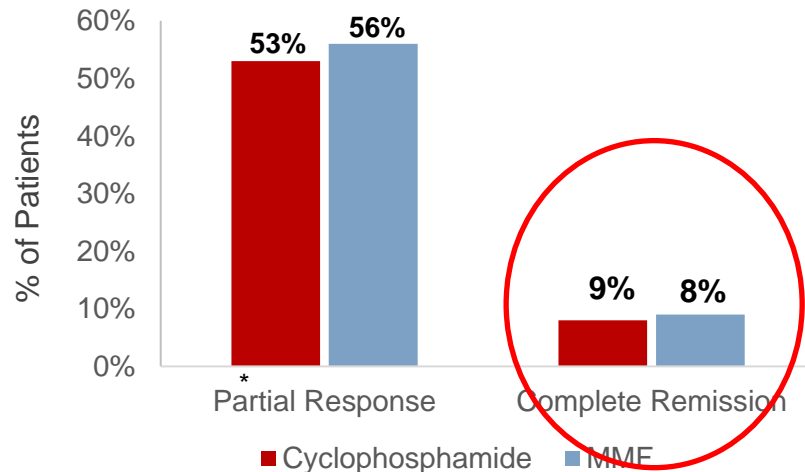
Or

IV Cyclophosphamide  
500 mg every 2 weeks for  
3 months: LOW-DOSE-  
EURO-LUPUS REGIMEN

Or

Oral MMF  
2-3g/d for  
6 months

24 week Partial Response & Complete Remission Rates with Cyclophosphamide and MMF<sup>2</sup>

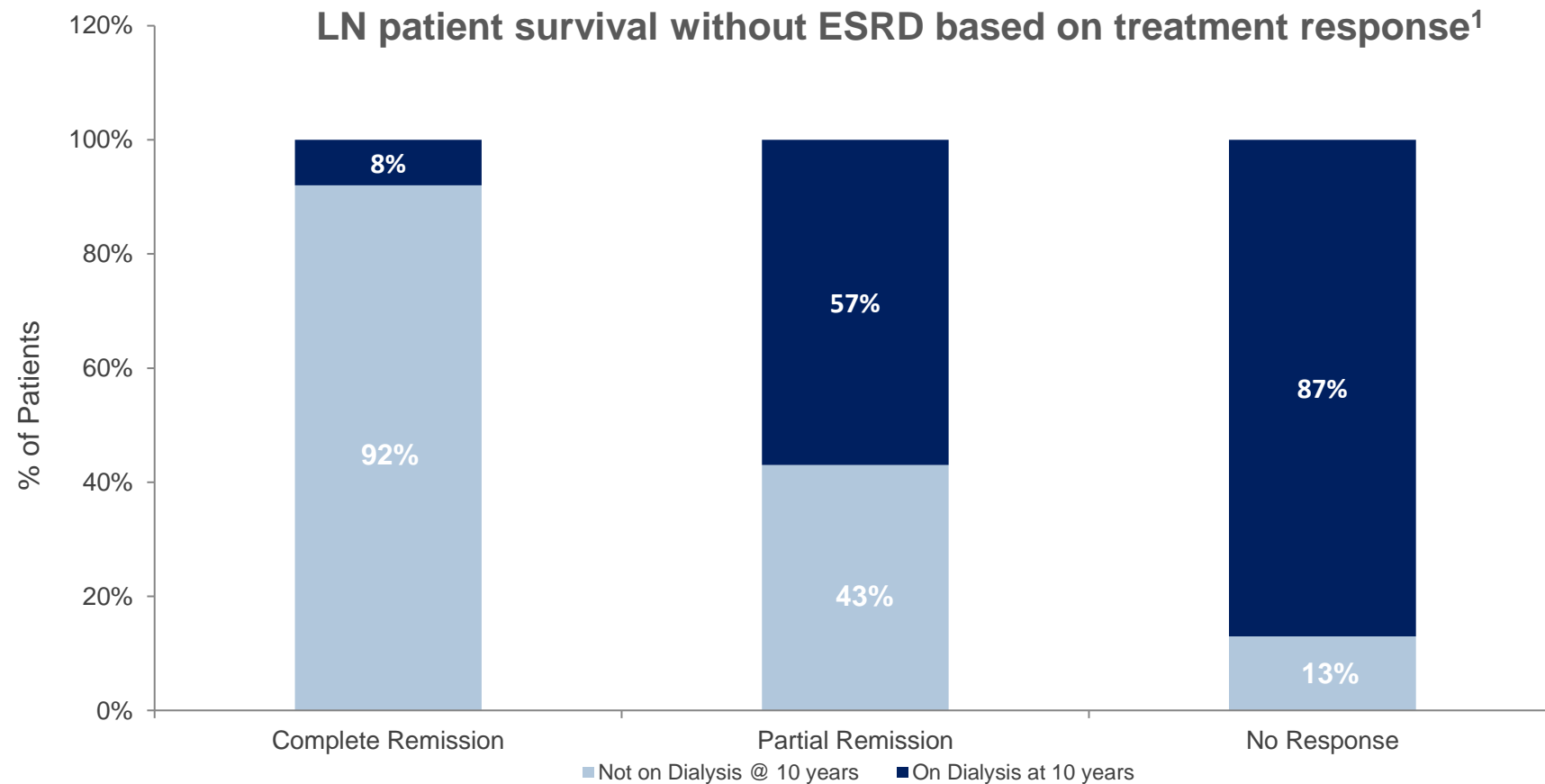


Study	% CRR at 12 Months Placebo Arm
Voclosporin	48 (Phase 2); 41 (Phase 3)
Obinutuzumab	35 (Phase 2)
Belimumab	43 (2-year PERR)

1. Hahn BH, et al. Arthritis Care Res (Hoboken). 2012;64(6):797-808.
2. Appel GB, et al. J Am Soc Nephrol. 2009;20(5):1103-1112
3. Parikh SV et al. J Am Soc Nephrol. 2016

# Early Clinical Response is Critical to Maintaining Long-Term Kidney Health in LN

**Rapid control & reduction of proteinuria in lupus patients may show a reduction in the need for dialysis<sup>1</sup>**



1. Chen YE, et al. Clin J Am Soc Nephrol. 2008;3(1):46-53. Response = 50% reduction in proteinuria; Remission = proteinuria <.33 g/24 hrs..

# Immunosuppressants for SLE/LN

Medication	Mechanism	Common adverse events	
Methotrexate <sup>1</sup>	Inhibits dihydrofolic acid reductase	<ul style="list-style-type: none"> <li>Abdominal distress</li> <li>Leukopenia</li> </ul>	<ul style="list-style-type: none"> <li>Nausea</li> <li>Ulcerative stomatitis</li> </ul>
Azathioprine <sup>2</sup>	Blocks Purine synthesis – Inhibits production of immune cells	<ul style="list-style-type: none"> <li>Leukopenia</li> <li>Malignancy</li> </ul>	<ul style="list-style-type: none"> <li>Serious infections</li> <li>Thrombocytopenia</li> </ul>
Mycophenolate mofetil <sup>4</sup>	Inhibits IMPDH	<ul style="list-style-type: none"> <li>Leukopenia</li> </ul>	<ul style="list-style-type: none"> <li>Serious infections</li> </ul>
Cyclophosphamide <sup>6</sup>	Alkylating Agent, non-selective cytotoxic therapy	<ul style="list-style-type: none"> <li>Fertility Issues</li> <li>BM suppression</li> </ul>	<ul style="list-style-type: none"> <li>Serious infections</li> <li>Alopecia</li> </ul>
Calcineurin Inhibitors (Cyclosporine, Tacrolimus, Voclosporin)	Inhibits calcineurin	<ul style="list-style-type: none"> <li>Hyperglycemia</li> <li>Hypertension</li> <li>Hirsutism</li> </ul>	<ul style="list-style-type: none"> <li>Infection</li> <li>Kidney Toxicity</li> <li>Metabolic Abnormalities</li> </ul>
Belimumab <sup>4</sup>	Inhibits BLYS	<ul style="list-style-type: none"> <li>Depression</li> <li>Serious infections</li> </ul>	<ul style="list-style-type: none"> <li>Suicidal ideation</li> </ul>
Rituximab <sup>5</sup>	Mediates B cell lysis via targeting of CD20 antigen	<ul style="list-style-type: none"> <li>Infusion Reaction</li> <li>Serious infections</li> </ul>	<ul style="list-style-type: none"> <li>Leukopenia</li> <li>Serum Sickness</li> </ul>
<b>Corticosteroids</b>	Anti-Inflammatory	<ul style="list-style-type: none"> <li>Fluid retention</li> <li>Weight Gain</li> <li>Hyperglycemia</li> <li>Hypertension</li> <li>Osteoporosis</li> </ul>	<ul style="list-style-type: none"> <li>Infections</li> <li>Cardiotoxicity</li> <li>Insomnia</li> <li>Mood Changes</li> </ul>

<sup>1</sup>Trexall. Package insert. Teva Women’s Health, Inc.; 2016. <sup>2</sup>Azasan. Package insert. Salix Pharmaceuticals, Inc.; 2019. <sup>3</sup>Sandimmune. Package insert. Novartis Pharmaceuticals; 2020. <sup>4</sup>CellCept. Package insert. Genentech, Inc.; 2019. <sup>5</sup>Myfortic. Package insert. Novartis Pharmaceuticals; 2020. <sup>6</sup>Cyclophosphamide. Package insert. ANI Pharmaceuticals, Inc.; 2019. <sup>7</sup>Prograf. Package insert. Astellas Pharma US, Inc.; 2019. <sup>8</sup>Leflunomide. Package insert. Alembic Pharmaceuticals Inc.; 2019. <sup>9</sup>Lupkynis. Package insert. Aurinia Pharma US, Inc.; 2021.

**Abbreviations:** GFR, glomerular filtration rate; IL, interleukin; IMPDH, inosine monophosphate dehydrogenase; LN, lupus nephritis; SLE, systemic lupus erythematosus; TCGF, T cell growth factor.

# Significant Unmet Treatment Need Remains in SLE/LN

## There is no cure for SLE or LN<sup>1</sup>

- Within 5 years of proliferative LN onset, between 5% and 25% of patients will experience death due to renal disease

## Few medications have FDA-approved indications for SLE/LN

- Belimumab (Benlysta) and voclosporin (Lupkynis) received FDA approval for LN in 2020 and 2021, respectively
- **Even with recent positive trials – Much work remains to be done. Response rates remain unacceptably low.**

## Current SOC treatments for SLE/LN have serious AE profiles<sup>2</sup>

- Possible AEs include infections, organ damage, and malignancies
- AEs contribute to accumulating disease damage and are causes of increased morbidity and mortality
- Long-term maintenance and repeated induction cycles lead to higher cumulative doses and increased risk of AEs

## Patients experience refractory disease despite maximized SOC treatments

- Fewer than 60% of patients with Class III to V LN will achieve a complete response to induction<sup>4</sup>
- Approximately 30% of patients experience relapse of LN increasing risk for developing progressive kidney failure

<sup>1</sup>Parikh SV, et al. *Am J Kidney Dis.* 2020;76(2):265-281. <sup>2</sup>Tesar V, et al. *Nephrol Clin Pract.* 2014;128:205-215. <sup>3</sup>Wilkinson L, et al. *Endocr Connect.* 2018;7(12):R328-R349. <sup>4</sup>Hoover PJ, et al. *Kidney Int.* 2016;90(3):487-492.

**Abbreviations:** AE, adverse event; FDA, Food and Drug Administration; LN, lupus nephritis; SLE, systemic lupus erythematosus; SOC, standard of care.



