



NEW PATHWAYS TO  
SMARTER MEDICINE™

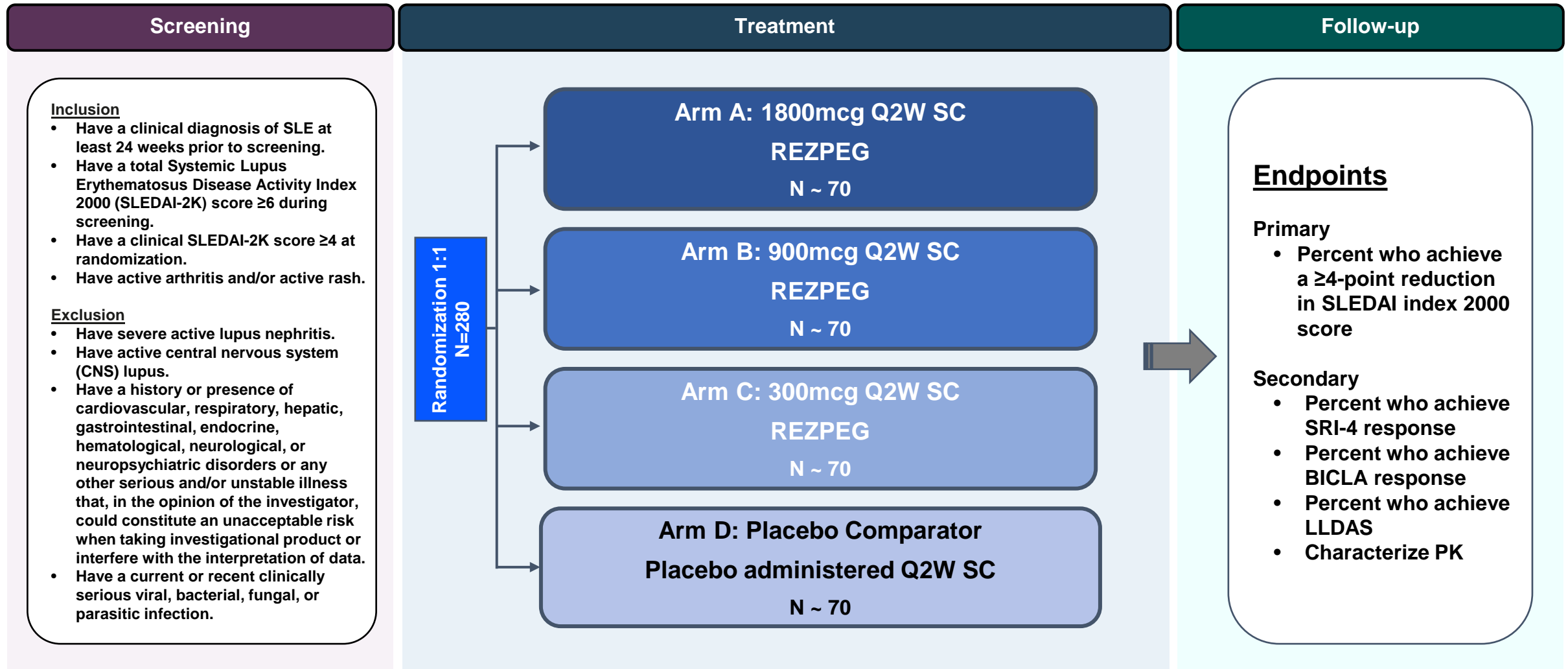
**Phase 2 ISLAND Study of  
REZPEG in SLE**  
*Topline Data Results*

**February 23, 2023**

---

*This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, unaudited year-end cash and investments and sufficiency of working capital and future availability of clinical trial data. Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 4, 2022. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.*

# REZPEG Phase 2 ISLAND Study Schematic



# ISLAND Phase 2 Study: Prespecified Criteria that Lilly Used for Phase 3 Decision-Making

- Primary endpoint (SLEDAI-2K) was not chosen as critical success factor
  - No drug has been approved in lupus on SLEDAI-2K
  - SRI-4 endpoint used as basis for approval in 2011
  - **BICLA endpoint used as basis for approval in 2021**
- Each dose level considered independently
- Criteria:
  - SRI-4: 17-22% low threshold range; >22% high threshold
  - BICLA: 10-16% low threshold range; **>16% high threshold**
    - Most recent endpoint supporting approval of anifrolumab
- Study was not statistically powered for these secondary clinical endpoints

Phase 3: 12% of patients had placebo-adjusted SRI-4 response with belimumab<sup>1</sup>

Phase 3: Range of 16 to 17% of patients had placebo-adjusted BICLA response with anifrolumab<sup>2</sup>

- Range of 6 to 18% placebo-adjusted SRI-4 response

# ISLAND Phase 2 Protocol: Definition of Secondary Clinical Endpoints

## SRI-4 (Systemic Lupus Erythematosus Responder Index)<sup>1</sup>

- SLEDAI:  $\geq 4$ -point reduction from baseline
- PGA: No worsening
- BILAG: No worsening

## BICLA (British Isles Lupus Assessment Group-based Composite Lupus Assessment)<sup>1</sup>

- SLEDAI: No worsening from baseline
- PGA: No Worsening
- BILAG: Improvement
- BILAG: No Worsening

**SLEDAI (Systemic Lupus Erythematosus Disease Activity Index):** Global index for the assessment of lupus disease activity in the preceding 10 days. It consists of 24 weighted clinical and laboratory variables of nine organ systems.<sup>1</sup>

**SLEDAI-2K:** SLEDAI-2K allows persistent active disease in alopecia, mucous membrane ulcers, rash, and proteinuria to be scored.<sup>1</sup>

**LLDAS (Lupus Low Disease Activity State):** The LLDAS was designed to reflect low SLE disease activity rather than changes in lupus activity. It can, therefore, be considered a more clinically relevant outcome in SLE studies compared with the SLE Responder Index (SRI)-4.<sup>3</sup>

**BILAG (British Isles Lupus Assessment Group):** The BILAG index is a clinical measure of lupus disease activity. It is valid, reliable and sensitive to change. Scoring in the BILAG index is based upon the physician's intention to treat. A flare of active lupus is defined as a new A or B score in at least one system.<sup>2</sup>

**PGA (Physician Global Assessment):** Visual analogue score (VAS) that reflects the clinician's judgment of overall Systemic Lupus Erythematosus (SLE) disease activity. The aim of this systematic literature review (SLR) is to describe and analyze the psychometric properties of PGA.<sup>4</sup>

# ISLAND Phase 2 Protocol: Definition of Study Populations

- **Modified ITT**: Randomized and received at least one dose of study medication
- **Modified ITT and BICLA Evaluable**: Randomized, received at least one dose of study medication and had 1 BILAG A and/or 2 BILAG B at baseline
- **Per Protocol Population**: All randomized patients who do not commit an Important Protocol Deviation (IPD) that could potentially compromise efficacy results
- **Safety Population**: Received at least 1 dose of study intervention and did not discontinue the study for the reason “lost to follow-up” at the first post baseline visit

# ISLAND Phase 2 Study: Study Populations

n (%)	Placebo (n=74)	REZPEG 300mcg (n=74)	REZPEG 900mcg (n=70)	REZPEG 1800mcg (n=73)	REZPEG All Doses (n=217)	Total (n=291)
Modified Intent to Treat (mITT)	74 (100%)	74 (100%)	70 (100%)	73 (100%)	217 (100%)	291 (100%)
Per Protocol (PP)	57 (77.0%)	58 (78.4%)	55 (78.6%)	52 (71.2%)	165 (76.0%)	222 (76.3%)
Modified Intent to Treat (mITT) BICLA Evaluable	60 (81.1%)	59 (79.7%)	56 (80.0%)	60 (82.2%)	175 (80.6%)	235 (80.8%)
Per Protocol (PP) BICLA Evaluable*	48 (84.2%)	46 (79.3%)	44 (80%)	41 (78.8%)	131 (79.4%)	179 (80.6%)
Safety Population	74 (100%)	74 (100%)	70 (100%)	73 (100%)	217 (100%)	291 (100%)

# ISLAND Phase 2 Study: Baseline Demographics

Demographic	Placebo (n=74)	REZPEG 300mcg (n=74)	REZPEG 900mcg (n=70)	REZPEG 1800mcg (n=73)
Age (yrs)	42	40	41	40
Female (%)	91%	93%	91%	93%
BMI (kg/m <sup>2</sup> )	27	26	26	27
<b>Race (%)</b>				
White	62%	60%	64%	67%
Asian	22%	27%	20%	21%
Black/African American	7%	8%	6%	4%
<b>Geographical Region (%)*</b>				
Latin America	27%	27%	29%	27%
North America	22%	20%	20%	21%
Europe	14%	14%	17%	15%
Japan	5%	8%	4%	8%



# ISLAND Phase 2 Study: REZPEG Country Enrollment

Country, n	Placebo (n=74)	REZPEG 300mcg (n=74)	REZPEG 900mcg (n=70)	REZPEG 1800mcg (n=73)	Total (n=291)
Argentina	8	12	11	13	44
United States	9	14	9	11	43
India	10	12	8	8	38
Ukraine	10	8	7	10	35
Mexico	12	8	9	7	36
Japan	4	6	3	6	19
Poland	0	5	7	4	16
Puerto Rico	7	1	5	3	16
Romania	6	4	2	2	14
Other*	8	4	9	9	30

\*Other countries enrolling 5 patients or less each include Australia, Canada, Czech Republic, Germany, Hungary, Israel, Korea, Russia, Spain and Taiwan

# ISLAND Phase 2 Study: Baseline Disease Characteristics

Disease Characteristic	Placebo (n=74)	REZPEG 300mcg (n=74)	REZPEG 900mcg (n=70)	REZPEG 1800mcg (n=73)
<b>SLEDAI 2K Mean Score</b>	9.9	9.7	9.1	9.9
<b>SLEDAI-2K</b>				
< 10	42%	39%	59%	47%
≥ 10	58%	61%	41%	53%
<b>Mucocutaneous Involvement (Yes)</b>	99%	99%	94%	100%
<b>Musculoskeletal Involvement (Yes)</b>	97%	97%	96%	97%
<b>Renal Involvement (Yes)</b>	8%	4%	3%	11%
<b>Immunologic Involvement (Yes)</b>	53%	53%	40%	49%
<b>Tender Joint Count (Mean)</b>	10.7	11.0	10.6	10.2
<b>Swollen Joint Count (Mean)</b>	6.7	6.7	6.7	5.9
<b>CLASI* Total Activity Score</b>	5.1	6.0	5.7	6.6

# Treatment Discontinuations

Event, n (%)	Placebo (n=74)	REZPEG 300 mcg (n=74)	REZPEG 900 mcg (n=70)	REZPEG 1800 mcg (n=73)
<b>Discontinued</b>	<b>9 (12.2%)</b>	<b>18 (24.3%)</b>	<b>13 (18.6%)</b>	<b>29 (39.7%)</b>
Adverse Event	0	1 (1.4%)	6 (8.6%)**	10 (13.7%)
Death	0	0	1 (1.4%)	0
Lack of Efficacy	0	2 (2.7%)	1 (1.4%)	0
Physician Decision	0	0	0	1 (1.4%)
Withdrawal by Subject*	7 (9.4%)	13 (17.6%)	3 (4.3%)	16 (21.9%)
Lost to Follow-up	0	1 (1.4%)	1 (1.4%)	1 (1.4%)
Other*	2 (2.7%)	1 (1.4%)	1 (1.4%)	1 (1.4%)

# Treatment Emergent Adverse Events (TEAEs) Reported in $\geq 5\%$ of Patients

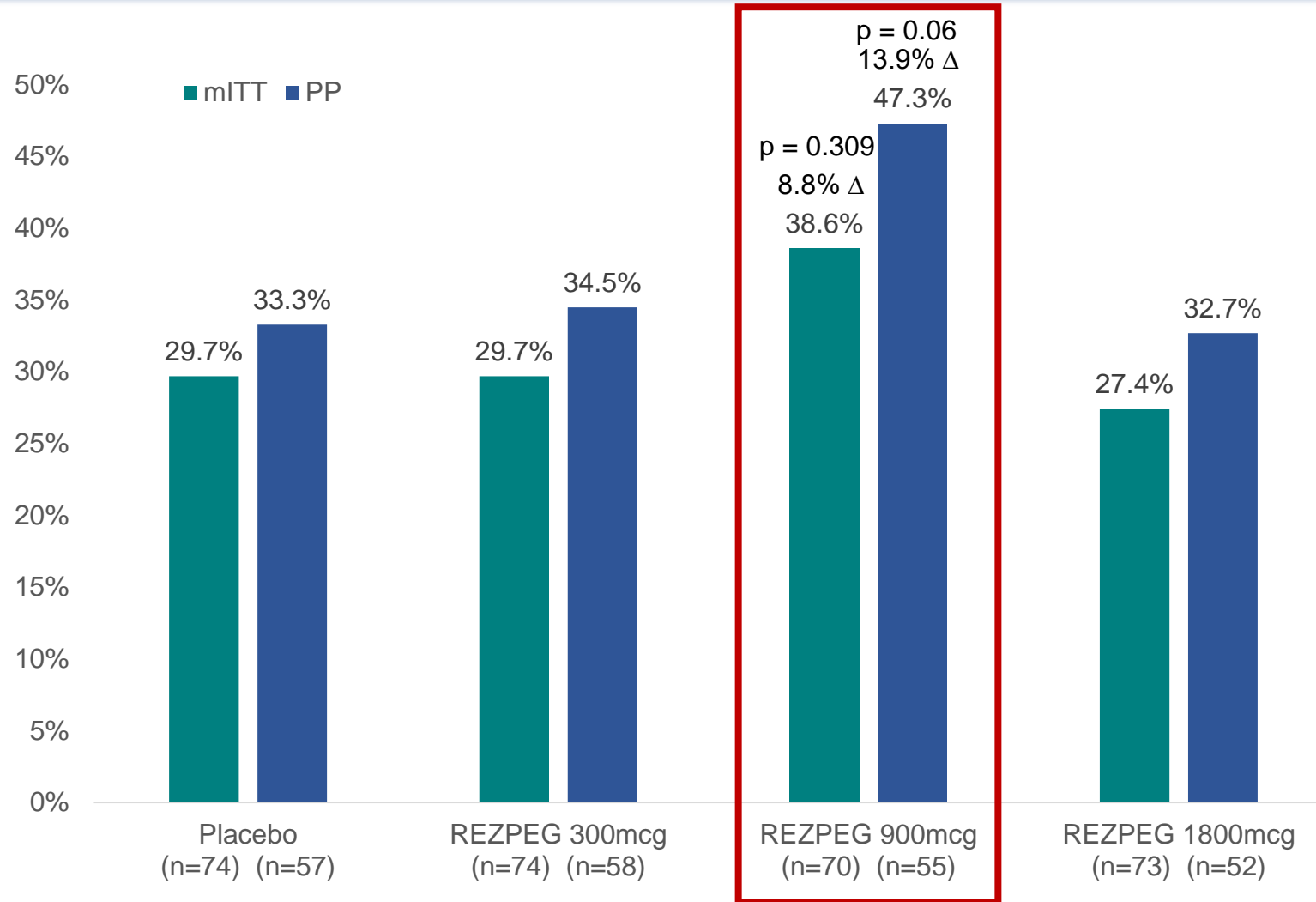
Event, n (%)	Placebo (n=74)	REZPEG 300 mcg (n=74)	REZPEG 900 mcg (n=70)	REZPEG 1800 mcg (n=73)
Subjects with $\geq 1$ Treatment Emergent Adverse Events (AEs)	21 (28.4%)	26 (35.1%)	29 (41.4%)	36 (49.3%)
Treatment Emergent AEs occurring in $\geq 5\%$ of subjects				
Any infections and infestations	22 (29.7%)	21 (28.4%)	23 (32.9%)	20 (27.4%)
Pyrexia	0	3 (4.1%)	8 (11.4%)	11 (15.1%)
Injection site reaction	0	2 (2.7%)	5 (7.1%)	11 (15.1%)
Fatigue	0	3 (4.1%)	1 (1.4%)	6 (8.2%)
Pain	1 (1.4%)	1 (1.4%)	4 (5.7%)	2 (2.7%)
Arthralgia	1 (1.4%)	5 (6.8%)	1 (1.4%)	5 (6.8%)
Diarrhea	1 (1.4%)	5 (6.8%)	2 (2.9%)	1 (1.4%)
Alanine aminotransferase increase	2 (2.7%)	0	0	4 (5.5%)
Dizziness	1 (1.4%)	4 (5.4%)	0	0
Anemia	0	0	2 (2.9%)	4 (5.5%)
AEs leading to treatment discontinuation	0	1 (1.4%)	6 (8.6%)*	10 (13.6%)
Serious Adverse Events (SAEs)	5 (6.8%)	2 (2.7%)	7 (10%)	3 (4.1%)
Serious Adverse Events (SAEs) Related to Study Medication	2 (2.7%)	1 (1.4%)	1 (1.4%)	0
Deaths	0	0	1 (1.4%)^	0

# ISLAND Phase 2 Study: PK/PD Observations

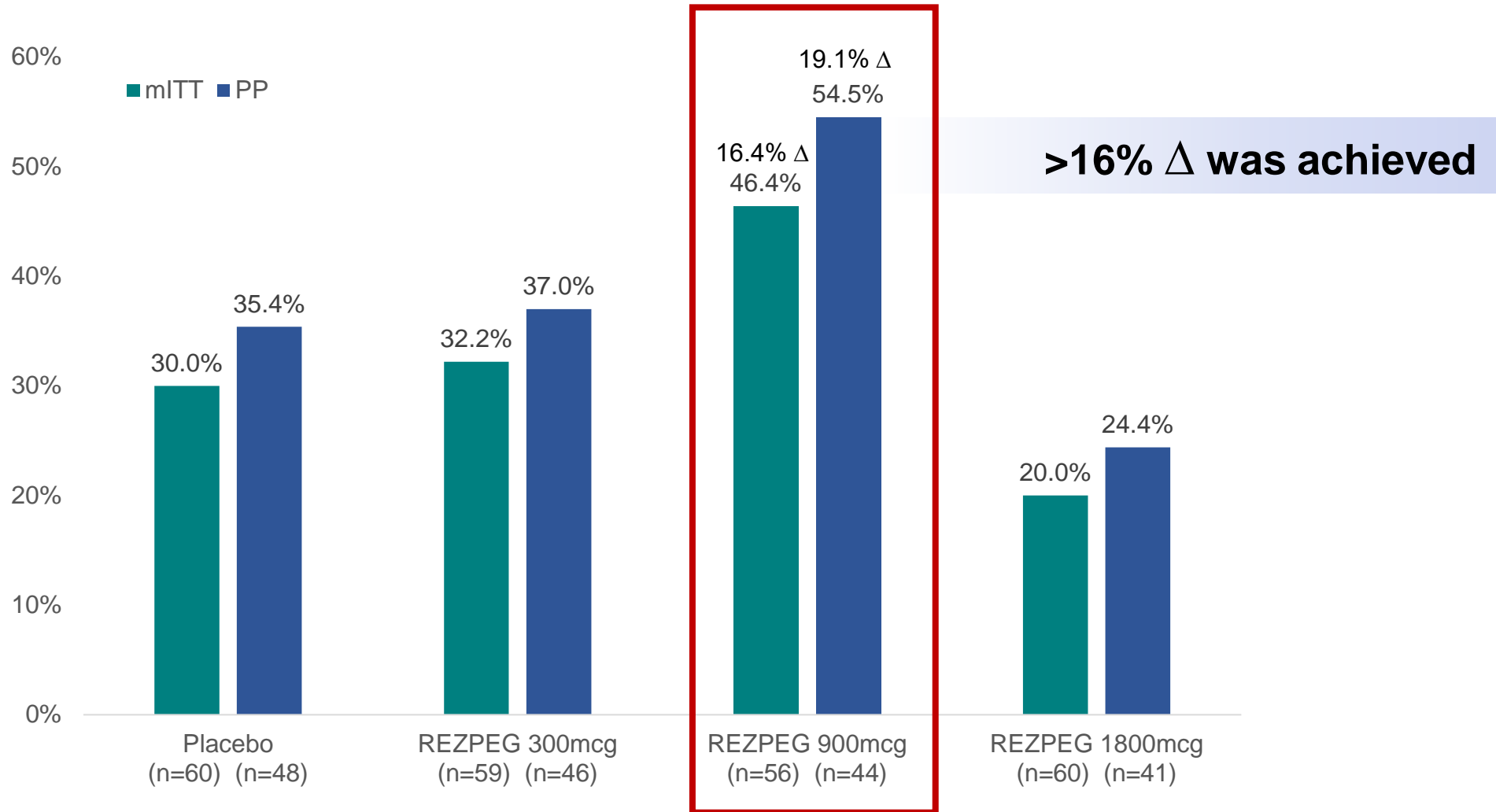
---

- PK is approximately dose proportional over 300 to 1800mcg range and exposure levels are consistent with prior studies
- Activated Treg increases observed in dose dependent manner consistent with prior studies
- No changes to Tcon (CD4 and CD8) cells and consistent with prior studies
- NK cell increases observed in dose-dependent manner over time especially at 1800mcg dose consistent with prior studies

# SLEDAI-2K: Primary Endpoint (mITT and PP) at Week 24



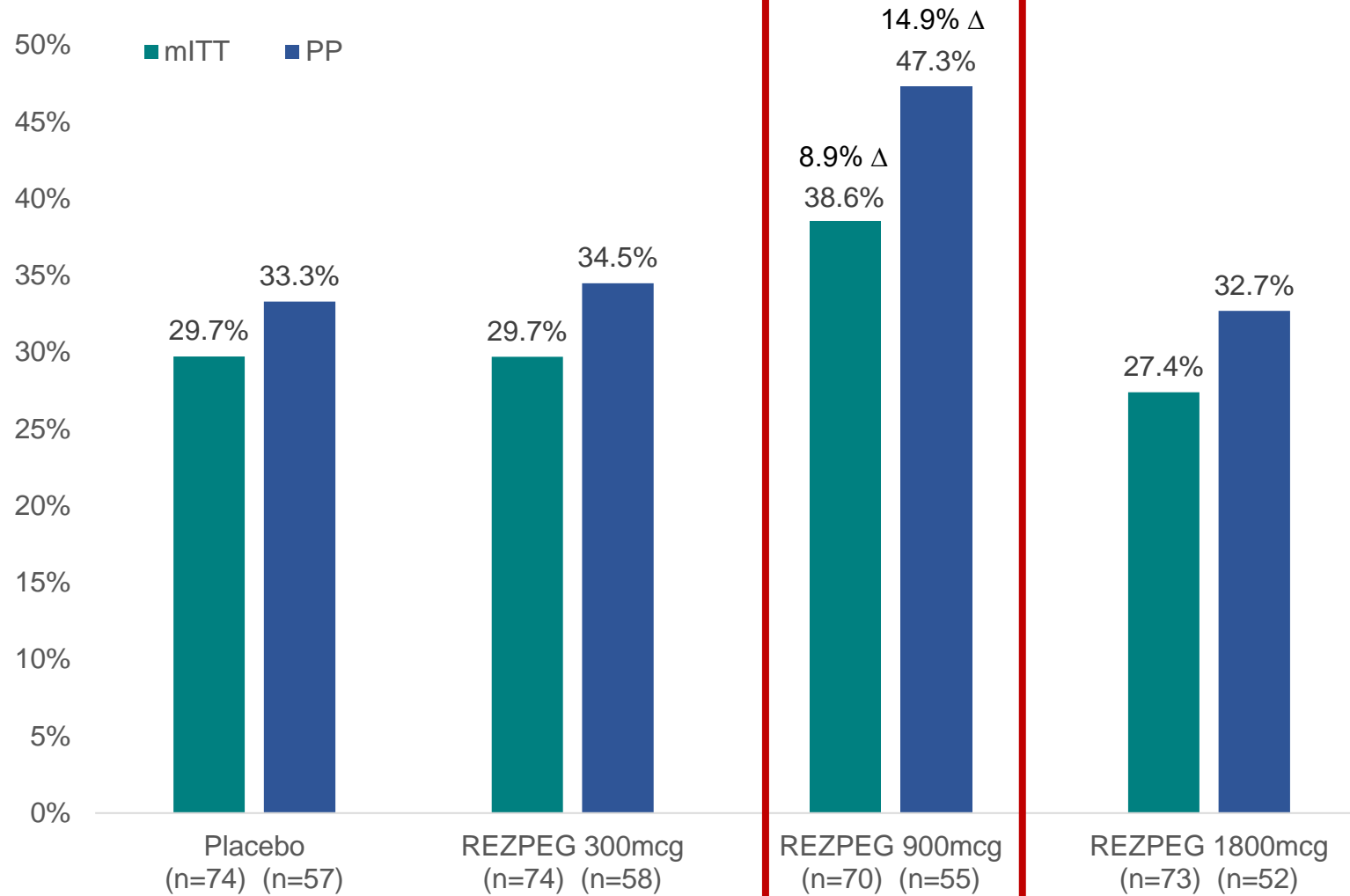
# BICLA Clinical Secondary Endpoint at Week 24



19.2% of patients enrolled into the study not eligible for BICLA baseline measurements

mITT analysis was a secondary analysis and PP was exploratory analysis

# SRI-4 Clinical Endpoint at Week 24



*mITT analysis was a secondary analysis and PP was exploratory analysis*



# ISLAND Phase 2 Study: Prespecified Criteria that Lilly Used for Phase 3 Decision-Making

- Primary endpoint (SLEDAI-2K) was not chosen as critical success factor
  - No drug has been approved in lupus on SLEDAI-2K
  - SRI-4 endpoint used as basis for approval in 2011
  - **BICLA endpoint used as basis for approval in 2021**
- Each dose level considered independently
- Criteria:
  - SRI-4: 17-22% low threshold range; >22% high threshold
  - BICLA: 10-16% low threshold range; **>16% high threshold**
    - Most recent endpoint supporting approval of anifrolumab
- Study was not statistically powered for these secondary clinical endpoints

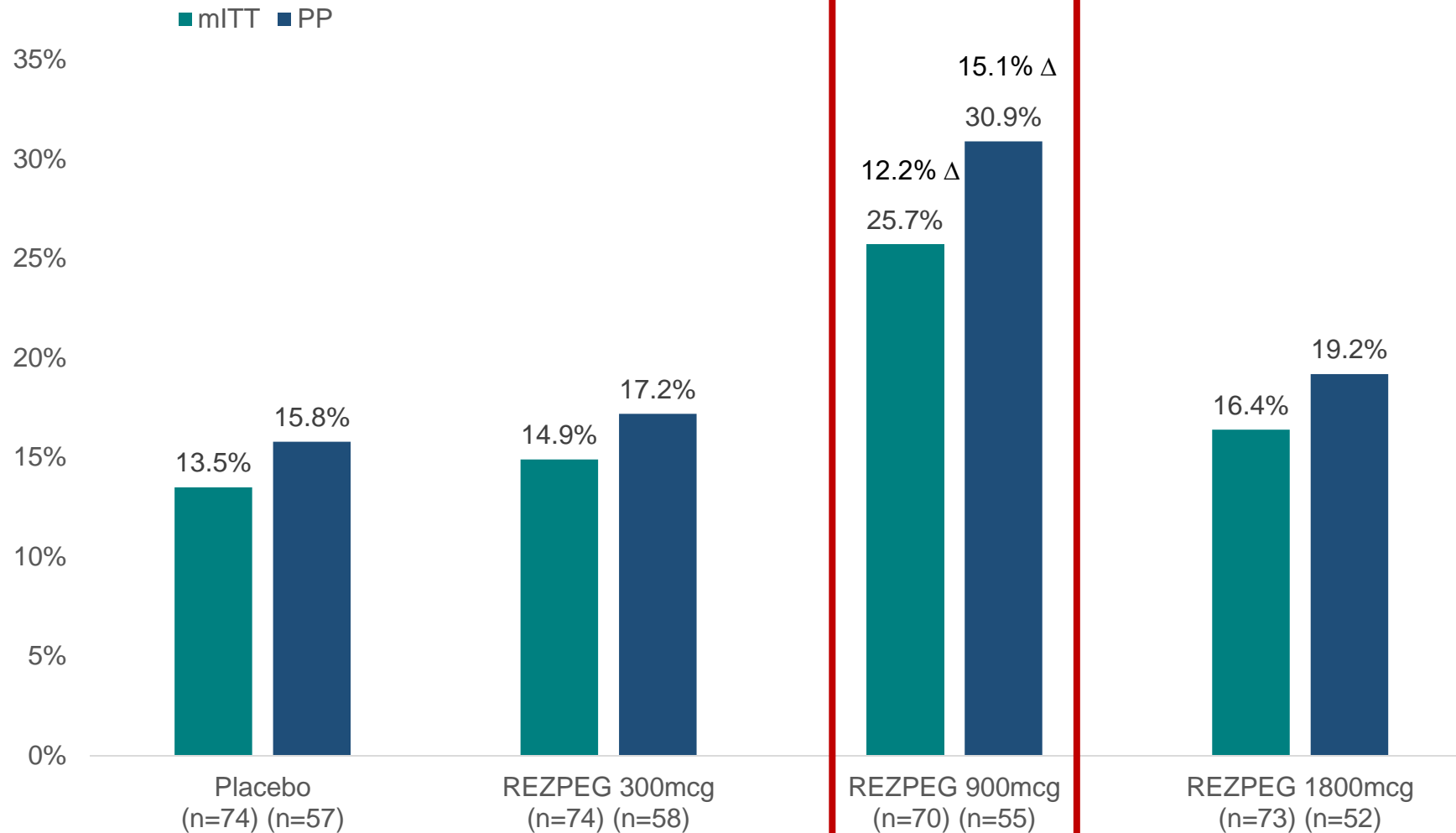
## **REZPEG placebo-adjusted 900mcg dose level:**

- SRI-4: 8.8% for mITT; 13.9% for PP
- BICLA: 16.4% for mITT; 19.1% for PP

*BICLA components measure different levels of BILAG improvement, and the differences reported between SRI-4 and BICLA may reflect different mechanisms of action and other variables between the two instruments\**

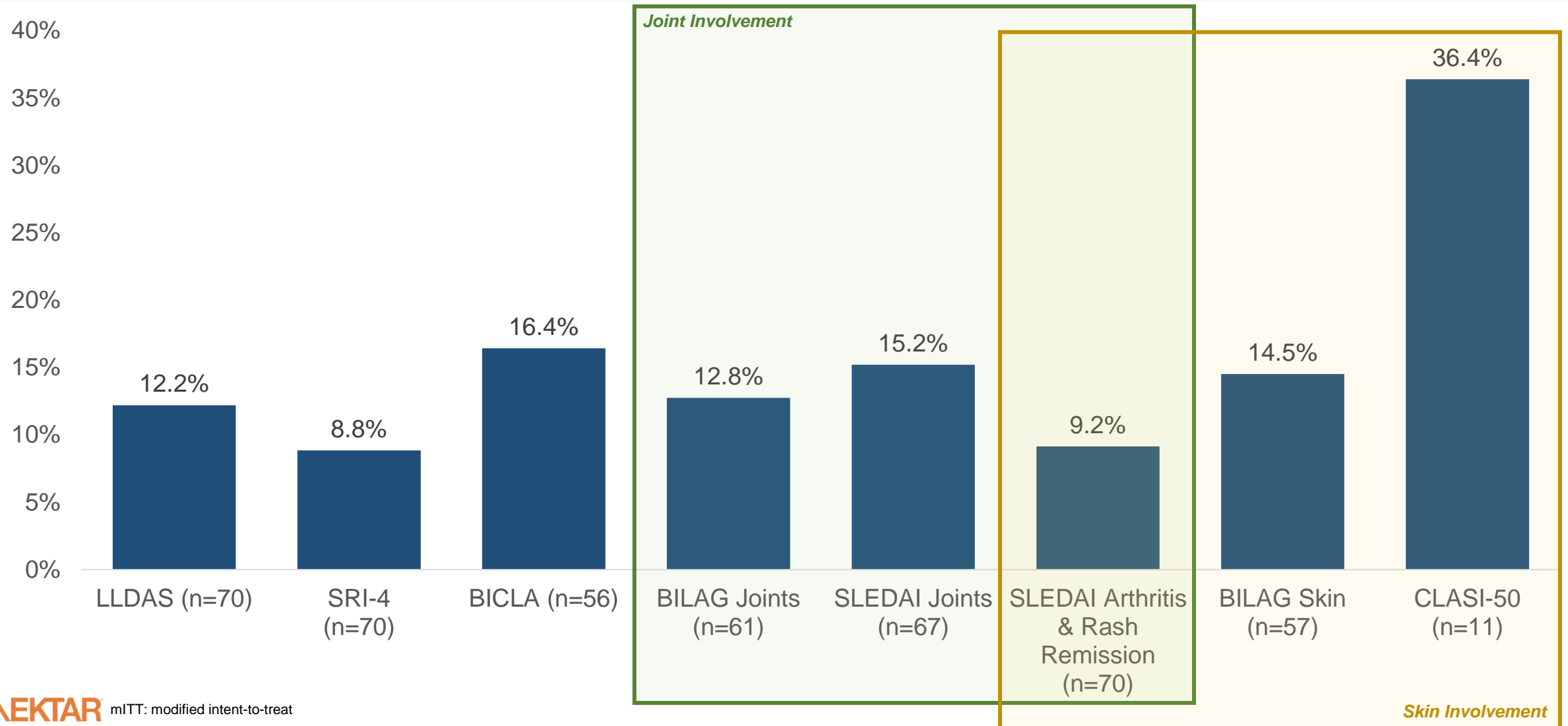
\*[Arthritis Rheumatol.](#) 2021 Nov; 73(11): 2059–2068.  
Published online 2021 Sep 22. doi: [10.1002/art.41778](https://doi.org/10.1002/art.41778)

# LLDAS Clinical Endpoint at 24 Weeks for mITT Population



*mITT analysis was a secondary analysis and PP was exploratory analysis*

# Demonstrated Activity of 900 mcg on multiple endpoints in mITT Population at Week 24 (placebo adjusted)





---

NEW PATHWAYS TO  
SMARTER MEDICINE™

---

## **Q&A Session**