



September 3, 2025

**BIOGEN**  
**THEMATIC PIPELINE SEMINAR**  
**LUPUS**

# FORWARD-LOOKING STATEMENTS

This presentation and the discussions during the related conference call contain forward-looking statements relating to, among others: our journey to build a new Biogen with an aim of long-term sustainable growth in our commercial portfolio; the potential and expansion of our late-stage pipeline to support long-term growth; our potential to deliver medicines to patients of lupus; the potential benefits, safety and efficacy of litlemab and dapirolizumab pegol (DZP, developed in collaboration with UCB); the growth potential of lupus treatments into a larger multi-billion dollar market; the potential for lupus treatments to be a pillar of Biogen's long-term growth; the anticipated benefits, risks and potential of our collaboration arrangements with UCB and other partners; the innovation of our lupus and other pipeline products; the potential of Biogen's pipeline in early-stage development, including fzelartamab in lupus nephritis and BLIB142; how our proven track record in MS positions us to succeed in lupus; the risks and uncertainties associated with drug development and commercialization; our strategy and plans; potential of, and expectations for, our commercial business and pipeline programs; clinical development programs, clinical trials, and data readouts and presentations; regulatory discussions, submissions, filings, and approvals and the timing thereof; the potential benefits, safety, and efficacy of our and our collaboration partners' products and investigational therapies; actions to improve the risk profile and productivity of our R&D pipeline, collaborations, and business development activities; expected strong cash flow and our future financial and operating results and financial guidance. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "estimate," "expect," "forecast," "goal," "guidance," "hope," "intend," "may," "objective," "outlook," "plan," "possible," "potential," "predict," "project," "prospect," "should," "target," "will," "would," and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements. Given their forward-looking nature, these statements involve substantial risks and uncertainties that may be based on inaccurate assumptions and could cause actual results to differ materially from those reflected in such statements. These forward-looking statements are based on management's current beliefs and assumptions and on information currently available to management. Given their nature, we cannot assure that any outcome expressed in these forward-looking statements will be realized in whole or in part.

We caution that these statements are subject to risks and uncertainties, many of which are outside of our control and could cause future events or results to be materially different from those stated or implied in this document, including, among others, factors relating to: our substantial dependence on revenue from our products and other payments under licensing, collaboration, acquisition or divestiture agreements; uncertainty of long-term success in developing, licensing, or acquiring other product candidates or additional indications for existing products; expectations, plans and prospects relating to product approvals, approvals of additional indications for our existing products, sales, pricing, growth, reimbursement and launch of our marketed and pipeline products; the potential impact of increased product competition in the biopharmaceutical and healthcare industry, as well as any other markets in which we compete, including increased competition from new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways; our ability to effectively implement our corporate strategy; the successful execution of our strategic and growth initiatives, including acquisitions; the drivers for growing our business; difficulties in obtaining and maintaining adequate coverage, pricing, and reimbursement for our products; the drivers for growing our business, including our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks associated with current and potential future healthcare reforms; risks related to commercialization of biosimilars, which is subject to such risks related to our reliance on third-parties, intellectual property, competitive and market challenges and regulatory compliance; failure to obtain, protect, and enforce our data, intellectual property, and other proprietary rights and the risks and uncertainties relating to intellectual property claims and challenges; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events, restrictions on use with our products, or product liability claims; risks relating to technology, including our incorporation of new technologies such as artificial intelligence into some of our processes; risks related to use of information technology systems and potential impacts of any breakdowns, interruptions, invasions, corruptions, data breaches, destructions and/or other cybersecurity incidents of our systems or those of connected and/or third-party systems; problems with our manufacturing capacity, including our ability to manufacture products efficiently or adequately address global bulk supply risks; risks relating to management, personnel and other organizational changes, including our ability to attracting, retaining and motivating qualified individuals; risks related to the failure to comply with current and new legal and regulatory requirements, including judicial decisions, accounting standards, and tariff or trade restrictions; the risks of doing business internationally, including geopolitical tensions, acts of war and large-scale crises; risks relating to investment in our manufacturing capacity; risks relating to the distribution and sale by third parties of counterfeit or unfit versions of our products; risks relating to the use of social media for our business, results of operations and financial condition; fluctuations in our operating results; risks related to investment in properties; risks relating to access to capital and credit markets to finance our present and future operations and business initiatives and obtain funding for such activities on favorable terms; risks related to indebtedness; the market, interest, and credit risks associated with our investment portfolio; risks relating to share repurchase programs; change in control provisions in certain of our collaboration agreements; fluctuations in our effective tax rate and obligations in various jurisdictions in which we are subject to taxation; environmental risks; and any other risks and uncertainties that are described in other reports we have filed with the U.S. Securities and Exchange Commission, which are available on the SEC's website at [www.sec.gov](http://www.sec.gov).

These statements speak only as of the date of this presentation and the discussions during this conference call and are based on information and estimates available to us at this time. Should known or unknown risks or uncertainties materialize or should underlying assumptions prove inaccurate, actual results could vary materially from past results and those anticipated, estimated or projected. Investors are cautioned not to put undue reliance on forward-looking statements. A further list and description of risks, uncertainties and other matters can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and in our subsequent reports on Form 10-Q and Form 10-K, in each case including in the sections thereof captioned "Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in our subsequent reports on Form 8-K. Except as required by law, we do not undertake any obligation to publicly update any forward-looking statements whether as a result of any new information, future events, changed circumstances or otherwise.

# CALL PARTICIPANTS



**Priya Singhal, M.D.,  
M.P.H.**

Head of Development



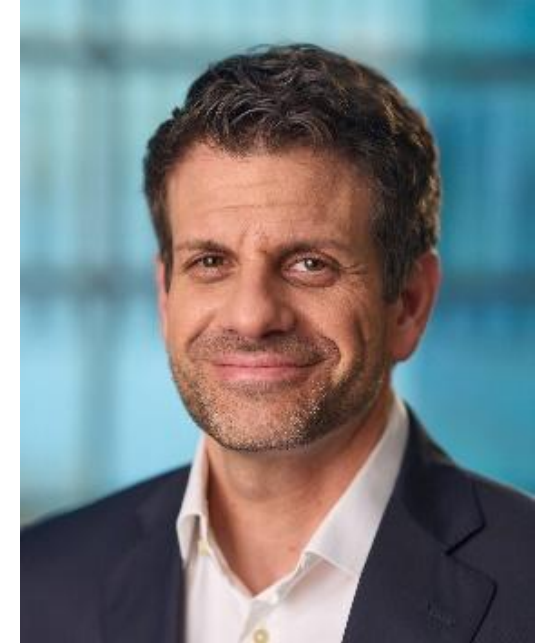
**Daniel Quirk, M.D.,  
M.P.H., M.B.A.**

Chief Medical Officer, Head  
of Medical Affairs



**Diana Gallagher,  
M.D.**

Head of Clinical Development,  
MS&I and AD



**Adam Meyers,  
M.B.A., M.S.**

Head of Immunology and  
New Disease Areas Franchise

# AGENDA

Opening Remarks

Priya Singhal, M.D., M.P.H.  
Head of Development

Lupus Overview

Daniel Quirk, M.D., M.P.H., M.B.A.  
Chief Medical Officer, Head of Medical Affairs

*Late-stage Lupus Programs:*  
Dapirolizumab Pegol in SLE

Diana Gallagher, M.D.  
Head of Clinical Development, MS&I and AD

Q+A

All participants

*Late-stage Lupus Programs:*  
Litifilimab in SLE And CLE

Diana Gallagher, M.D.  
Head of Clinical Development, MS&I and AD

Concluding Remarks

Priya Singhal, M.D., M.P.H.  
Head of Development

Q+A

All participants

# OPENING REMARKS



Priya Singhal, M.D., M.P.H.

Head of Development

# WE ARE ON A JOURNEY WITH THE AIM OF BUILDING THE NEW BIOGEN

## Strategic Objectives

### Maximize the profitability of the legacy MS business



### Continue to build momentum of ongoing drug launches

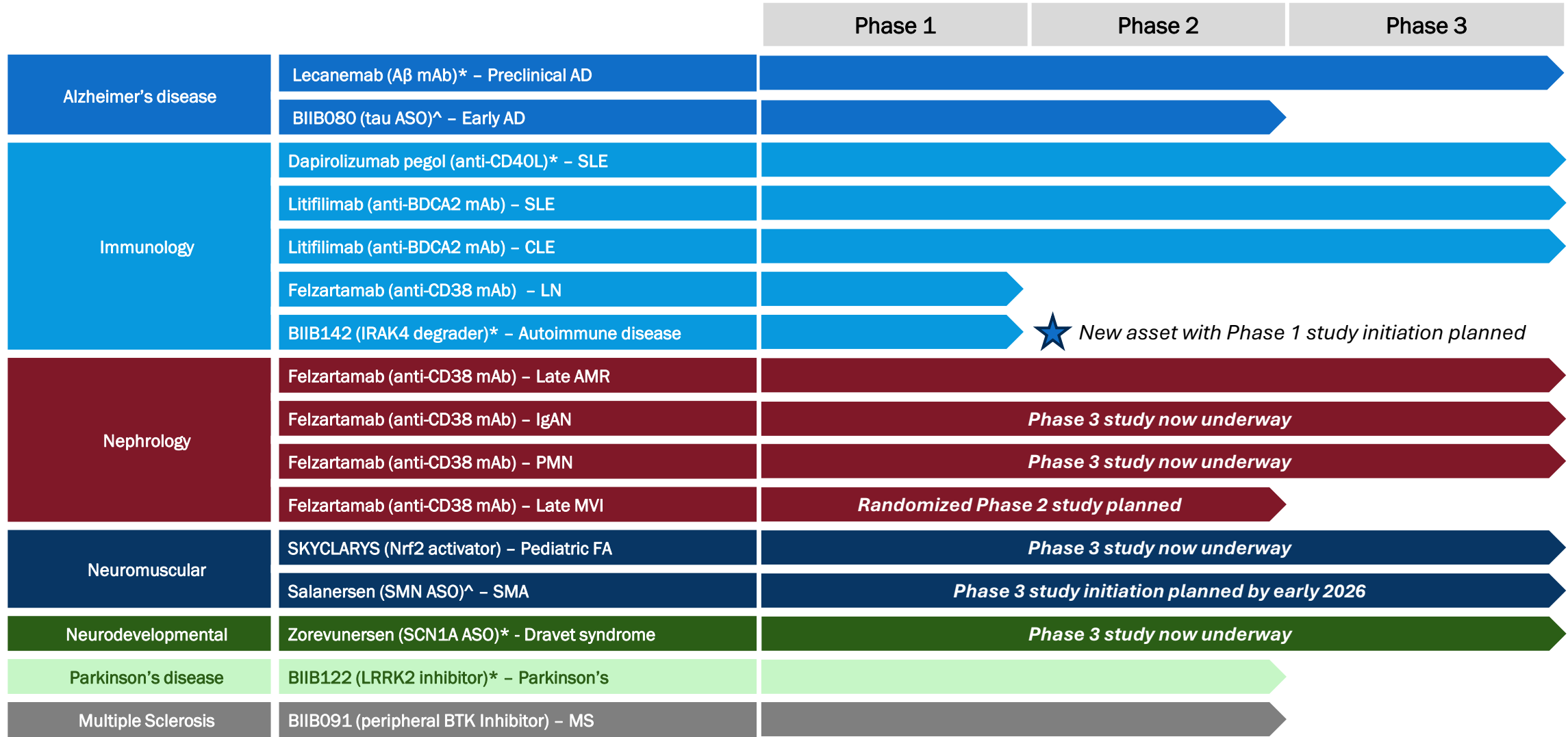


### Advance our high conviction late-stage pipeline to support long-term growth

<b>Dapirolizumab Pegol</b> * (SLE)	<b>BIIB080</b> <sup>^</sup> (Early AD + dementia)
<b>Litifilimab</b> (SLE + CLE)	<b>Zorevunersen</b> * (Dravet syndrome)
<b>Felzartamab</b> (AMR + IgAN + PMN + MVI + LN)	<b>Salanersen</b> <sup>^</sup> (SMA)
<b>Other Pipeline</b>	<b>Potential Opportunities for Business Development</b>

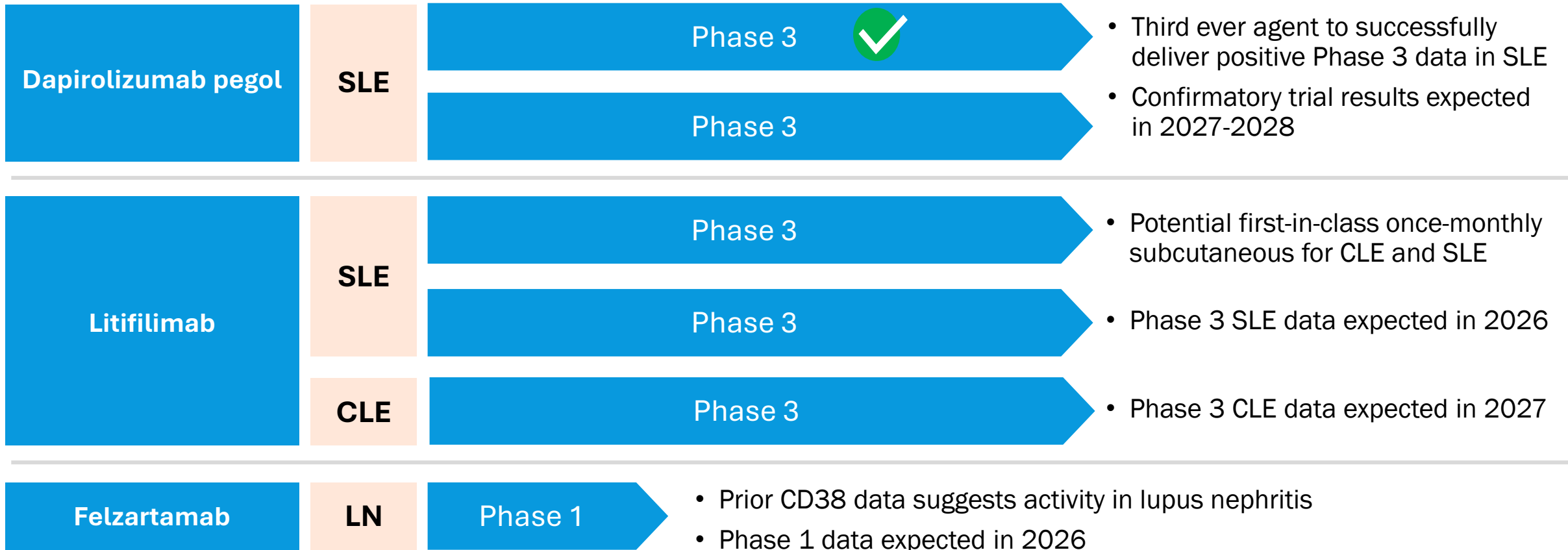
*Expected strong cash flow supports a balance sheet that allows for investment to augment growth*

# PIPELINE NOW INCLUDES MULTIPLE HIGH SCIENTIFIC CONVICTION LATE-STAGE ASSETS



\*Collaboration program; ^ Licensed from Ionis Pharmaceuticals, Inc. AD = Alzheimer's disease; AMR = antibody mediated rejection; ASO = antisense oligonucleotide; CLE = cutaneous lupus erythematosus; FA = Friedreich ataxia; IgAN = IgA nephropathy; LN = lupus nephritis; LRRK2 = leucine rich repeat kinase 2; MS = multiple sclerosis; MVI = microvascular inflammation in kidney transplant patients; PMN = primary membranous nephropathy; SLE = systemic lupus erythematosus; SMA = spinal muscular atrophy

# OUR IMMUNOLOGY PORTFOLIO IS ANCHORED BY TWO PHASE 3 LUPUS ASSETS



Note: Dapirolizumab pegol is being developed in collaboration with UCB  
 CLE = cutaneous lupus erythematosus; LN = lupus nephritis; SLE = systemic lupus erythematosus

# OPPORTUNITY TO DELIVER MEANINGFUL NEW MEDICINES FOR PATIENTS WITH LUPUS

*We believe lupus is a highly underserved market with significant potential for market expansion*

**Lupus is estimated to affect millions of patients globally\***  
Low treatment rates due to heterogeneity and lack of treatment options

## Dapirolizumab pegol

- One of only three drugs with positive Phase 3 data
- Compelling data across fatigue, reduction in flares and fewer steroids
- May support use in pregnant women due to limited placental crossing
- Confirmatory Phase 3 data expected 2027/2028

## Litifilimab

- Exciting Phase 2 data in both SLE and CLE published in NEJM
- Compelling data on skin, joint and overall disease control
- Monthly SC autoinjector
- First Phase 3 data expected next year

**Phase 1 study underway for Felzartamab in LN**

Note: Dapirolizumab pegol is being developed in collaboration with UCB

\*Lupus Facts and Statistics. Lupus Foundation of America, [www.lupus.org/resources/lupus-facts-and-statistics](http://www.lupus.org/resources/lupus-facts-and-statistics). Accessed 20 Aug. 2025

CLE = cutaneous lupus erythematosus; LN = lupus nephritis; NEJM = New England Journal of Medicine; SC = subcutaneous; SLE = systemic lupus erythematosus

# WE BELIEVE OUR PROVEN TRACK RECORD IN MS POSITIONS US TO SUCCEED IN LUPUS

## Characteristics of MS also associated with Lupus<sup>1</sup>

- Heterogeneous disease and symptoms
- Younger, predominantly female
- Associated with flares, remission, and relapse
- Driven by underlying immunologic pathology

~30 years in neuro-immunology pioneering the development of MS treatments



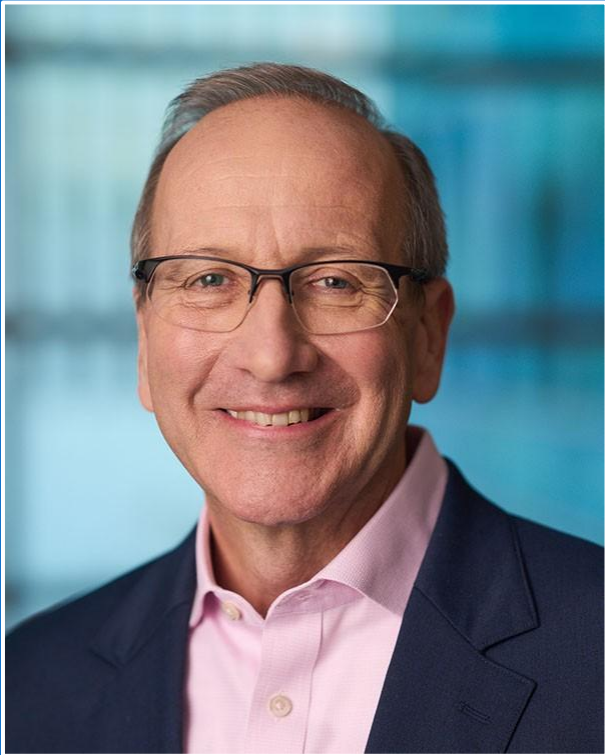
*Today, MS represents a ~\$24B global market<sup>2</sup>*

1. Dai, X., Fan, Y. & Zhao, X. Systemic lupus erythematosus: updated insights on the pathogenesis, diagnosis, prevention and therapeutics. Sig Transduct Target Ther 10, 102 (2025) 2. Total 2024 global sales revenue of MS products; Data sourced from IQVIA Analytics Link  
MS = multiple sclerosis

# WE HAVE AN OPPORTUNITY TO DELIVER EXCITING NEW MEDICINES FOR PATIENTS WITH LUPUS

- We have two Phase 3 assets that have demonstrated strong clinical data in lupus
- Lupus has the potential to grow into a larger multi-billion dollar market with new approved treatment options
- We believe our proven track record in multiple sclerosis positions us to succeed in lupus

# LUPUS OVERVIEW



**Daniel Quirk, M.D., M.P.H.,  
M.B.A.**

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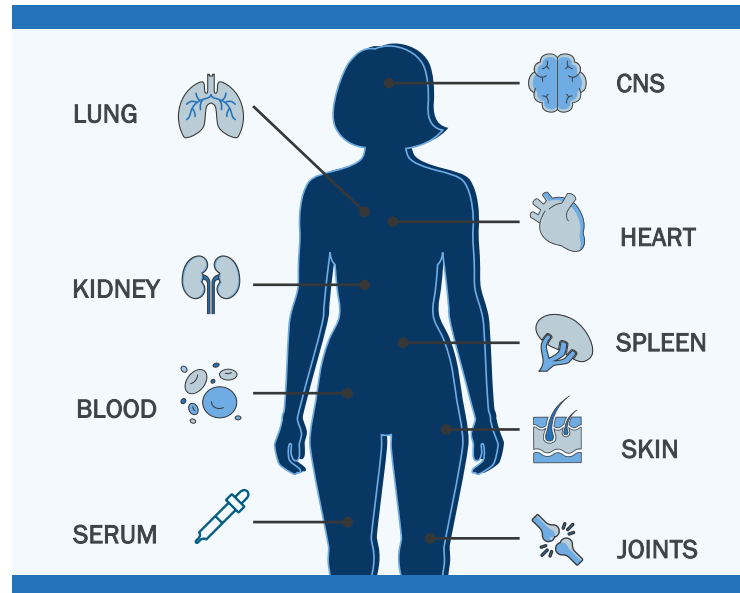
Chief Medical Officer, Head of Medical Affairs

# LUPUS IS A VERY COMPLEX, HETEROGENEOUS SET OF DISEASES

## Complex biology

- Involves both the adaptive and innate immune systems
- Tissue damage caused by multiple factors

## Multiple organs impacted

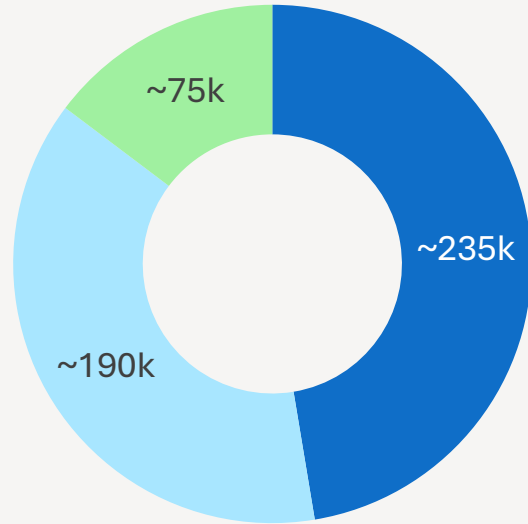


## Variability in patient experience

- Symptoms vary by patient
- Response to therapy is highly variable between patients
- Ambiguity of symptoms can lead to delays in diagnosis

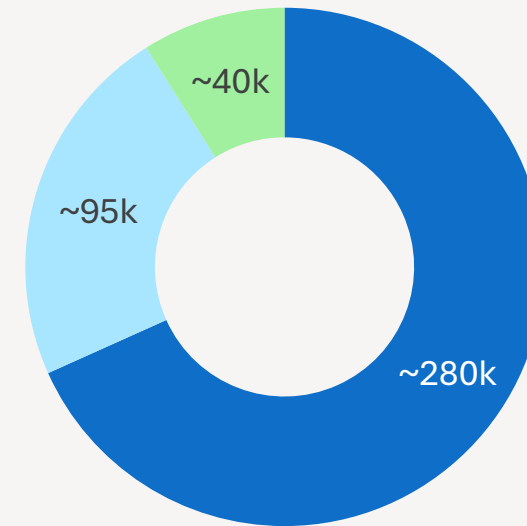
# LUPUS IS COMPOSED OF DISTINCT DISEASES WITH SLE AND CLE BEING THE MOST COMMON

## SLE



- Relapsing-remitting disease course with flares that can cause severe organ damage
- Patients experience fatigue, pain
- Multiple organs involved – skin, joints, brain, heart, lungs, kidneys

## CLE



- Skin-based form of lupus with symptoms including rash, pain, hair loss, itch and photosensitivity
- Scarring and skin atrophy sometimes occur
- Patients also experience depression, anxiety and fatigue
- Can occur in either the presence or absence of SLE



Other indications include lupus nephritis, drug-induced lupus erythematosus and neonatal lupus

# SLE

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## SYSTEMIC LUPUS ERYTHEMATOSUS

# SLE IS A CHRONIC SYSTEMIC AUTOIMMUNE DISEASE WITH A BROAD RANGE OF CLINICAL MANIFESTATIONS

## Typical symptoms

- **Joint involvement** observed in **>90%** of patients<sup>1</sup>
- **Skin manifestations** in up to **85%** of patients<sup>7</sup>
- Symptoms from other organs including kidney, lung, heart, and spleen, and/or **CNS** and serum

## Patient Population

- ~235k patients in the U.S.\*
- Disproportionately affects **younger women** (15-55 years of age) and those who are **Black, Asian, Hispanic, or of Native American descent**<sup>4-5</sup>

## Health impact

- Uncontrolled SLE associated with **mortality rates 2-3x higher** than those in the general population<sup>2</sup>
- At diagnosis, SLE associated with **higher risk of comorbidities** including depression, anemia, CV disease, cancer, neurological disease, and **organ damage**<sup>3</sup>

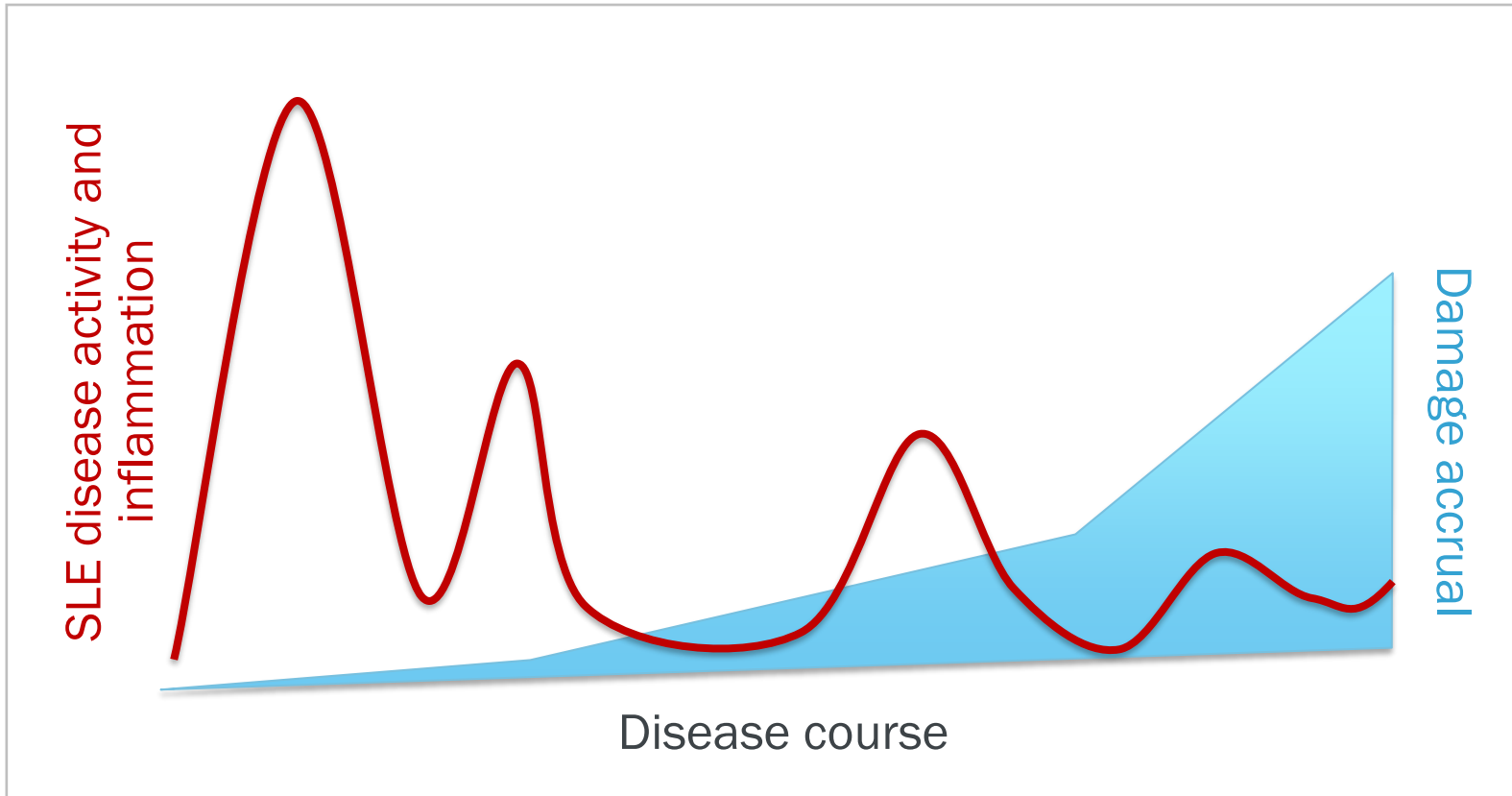
## SLE significantly reduces patients' quality of life

- **Fatigue** is reported by **50–86%** of patients with SLE - many describe it as their **most debilitating symptom**<sup>6-12</sup>
- Often accompanied by cognitive difficulties - commonly described as “brain fog” - that **significantly impairs daily functioning and productivity**

**SLE patients are typically treated by rheumatologists with ~6k practicing in the U.S. today<sup>^</sup>**

\* Based on Biogen 2025 Global Lupus Epidemiology Research ^ Mannion ML, Xie F, FitzGerald JD, et al. Changes in the workforce characteristics of providers who care for adult patients with rheumatologic and musculoskeletal disease in the United States. Arthritis Rheumatol. 2024 July;76(7). 1. Data reported from multiple studies with up to 500 patients. HR-QoL, health-related quality of life; SF-36, 36-Item Short Form Survey. 2. Barber MR, et al. Nat Rev Rheumatol 2021; 17:515-532 3. Fanouriakis A, et al. Ann Rheum Dis 2021;80:14-25 4. Barber MR et al. Rheumatology [Oxford];2023;62:i4-i9; 5. Manson JJ, Rahman A. Orphanet J Rare Dis 2006;1:6; Olesinska M & Saletra A. Reumatologia. 2018;56:45-54; 4. McElhone K, et al. Lupus. 2006;15:633-43; 5. Bruce IN, et al. Ann Rheum Dis. 1999;58:379-81; 6. Zonana-Nacach A, et al. Lupus. 2000;9:101-9; 7. Krupp LB, et al. J Rheumatol. 1990;17:1450-2; 8. Wysenbeek AJ, et al. Br J Rheumatol. 1993;32:633-5; 9. Taylor J, et al. Rheumatology (Oxford). 2000;39:620-3  
CNS = central nervous system; CV = cardiovascular; SLE = systemic lupus erythematosus

# SLE IS CHARACTERIZED BY PHASES OF FLARES FOLLOWED BY LOW DISEASE ACTIVITY OR REMISSION



- SLE disease activity commonly fluctuates
- ~25% of patients flare within 1–2 years after achievement of low disease activity or remission<sup>1</sup>
- Increased organ damage occurs as the disease progresses
- Disease is managed by therapy escalation and tapering

# A CONVERSATION WITH DR. KAREN COSTENBADER, MD, MPH

Karen Costenbader, MD, MPH is Professor of Medicine at Harvard Medical School and holds the Michael E. Weinblatt, MD Endowed Chair in Rheumatology in the Division of Rheumatology, Inflammation and Immunity at Brigham and Women's Hospital in Boston, Massachusetts, where she serves as Director of the Lupus Program and Chief of the Section of Clinical Sciences. Dr. Costenbader's research investigates the epidemiology and pathogenesis of systemic lupus erythematosus and rheumatoid arthritis in particular. She is an experienced research mentor for medical students, residents, graduate students in epidemiology, and rheumatology fellows and junior faculty, having trained over 50 doctoral and post-doctoral fellows and faculty. She is PI of the Lupus Registry containing data on more than 3,000 patients. She is currently the Deputy Editor of Arthritis & Rheumatology. She has served as the Chair of the NIH's 'Arthritis, Musculoskeletal and Skin Disease' Study Section, Chair of the Medical and Scientific Advisory Council for the Lupus Foundation of America, and as Faculty Director of the Office of Research Careers at the Brigham and Women's Hospital.



# SIGNIFICANT OPPORTUNITY TO EXPAND TREATMENT AND BENEFIT MORE PATIENTS WITH SLE

- Disproportionately affects women aged 15-55 and people who are Black, Asian, Hispanic or Native American
- Characterized by flares with potential for severe organ damage followed by periods of remission or low disease activity
- Most patients experience joint pain and skin involvement; quality of life severely impacted including with symptoms of fatigue
- Pregnant women often stop treatment
- Lack of treatment options and heterogenous patient population limit biologic treatment rates today

# CLE

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# CUTANEOUS LUPUS ERYTHEMATOSUS

# CLE PRIMARILY MANIFESTS IN THE SKIN AND MUCOSAL TISSUES, WHICH CAN OCCUR WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

## Typical symptoms

- Photosensitivity
- Hair loss
- Pain
- Rash
- Itch
- Scarring
- Dyspigmentation

## Health impact

- CLE associated with **higher risk of comorbidities** including hypertension, dyslipidemia, anxiety disorder, obesity, depression, T2D, and other conditions<sup>6</sup>

## Patient Population

- ~280k patients in the U.S.\*
- Disproportionately **women**<sup>1</sup>
- People who are **Black or Hispanic have a higher risk of developing CLE**. Black and Asian patients typically have greater disease severity<sup>2-3</sup>
- **CLE is a distinct disease**, but up to one-third of patients with CLE have, or will have, SLE<sup>4-5</sup>

## CLE significantly reduces patients' quality of life

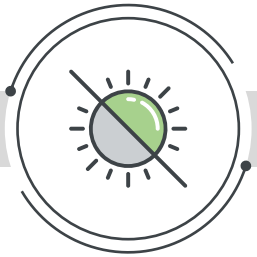
- 70% of patients report **painful skin**<sup>7</sup>
- Patients report **fatigue** at 13x rates of healthy individuals<sup>8</sup>
- Significant impact on **emotional and mental health**<sup>9</sup>

CLE patients are typically treated by dermatologists but are referred to a rheumatologists if they also have SLE

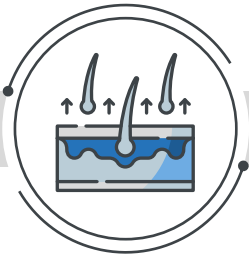
\* Based on Biogen 2025 Global Lupus Epidemiology Research. 1. Petersen MP, et al. Lupus. 2018;27:1424-1430. 2. Izmirly P, et al. Lupus Sci Med. 2019;6:e000344. 3. Verma SM, et al. Br J Dermatol. 2014;170:315-321 4. Petersen MP, et al. Lupus. 2018;27(9):1424-1430. 5. Vera-Recabarren MA, et al. Clin Exp Dermatol. 2010;35:729-735. 6. Merola JF, et al. Poster presented at EADV 2024 (Abstract 841). 7. Ogunsanya ME, et al. Lupus. 2020;29:1691-1703 8. Tarazi M, et al. Br J Dermatol. 2019;180:1468-1472 9. Klein R, et al. J Am Acad Dermatol. 2011;64:849-858  
CLE = cutaneous lupus erythematosus; SLE = systemic lupus erythematosus ; T2D = type 2 diabetes

# CLE IS DISTINCT DISEASE ASSOCIATED WITH SKIN MANIFESTATIONS

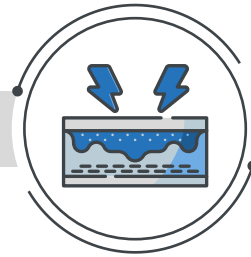
## Chronic Skin Manifestations



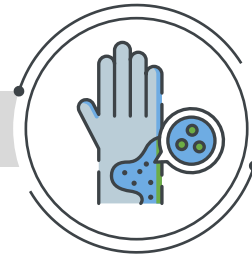
Photosensitivity<sup>2</sup>



Hair loss<sup>3</sup>



Pain<sup>2</sup>



Rash<sup>1</sup>



Itch<sup>2</sup>



Disfiguring scars<sup>1,2,4</sup>



Dyspigmentation<sup>1,2</sup>



Image 1: erythema; image 2: erythema, scale, infiltration; image 3: alopecia; image 4: erythema, scale, edema; CLE = cutaneous lupus erythematosus. Images obtained for use with consent.

1. Drenkard C, et al. *Front Med (Lausanne)* 2022;9:897987; 2. Ogunsanya ME, et al. *Int J Womens Dermatol* 2018;4:152-158; 3. Ogunsanya ME, et al. *Br J Dermatol* 2017;176:52-61; 4. Drenkard C, et al. *Arthritis Care Res* 2019;71:95-103

# A CONVERSATION WITH DR. JOSEPH MEROLA, MD, MMSc, FAAD, FACR

Joseph F. Merola, M.D. MMSc, FAAD FACR  
Dermatologist, Rheumatologist  
Medical and Scientific Board, Lupus Foundation  
President Elect, Rheumatology – Dermatology Society



# THERE IS A CLEAR OPPORTUNITY TO IMPROVE TREATMENT OPTIONS FOR CLE PATIENTS

- Disproportionately affects women and people who are Black or Hispanic
- Characterized by skin manifestations that are often painful and sometimes disfiguring
- Quality of life severely impacted including body-image concerns and symptoms of fatigue
- There are no FDA approved treatments for patients with CLE

# OUR LATE-STAGE SLE PROGRAMS



**Diana Gallagher**

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Head of Clinical Development,  
MS&I and AD

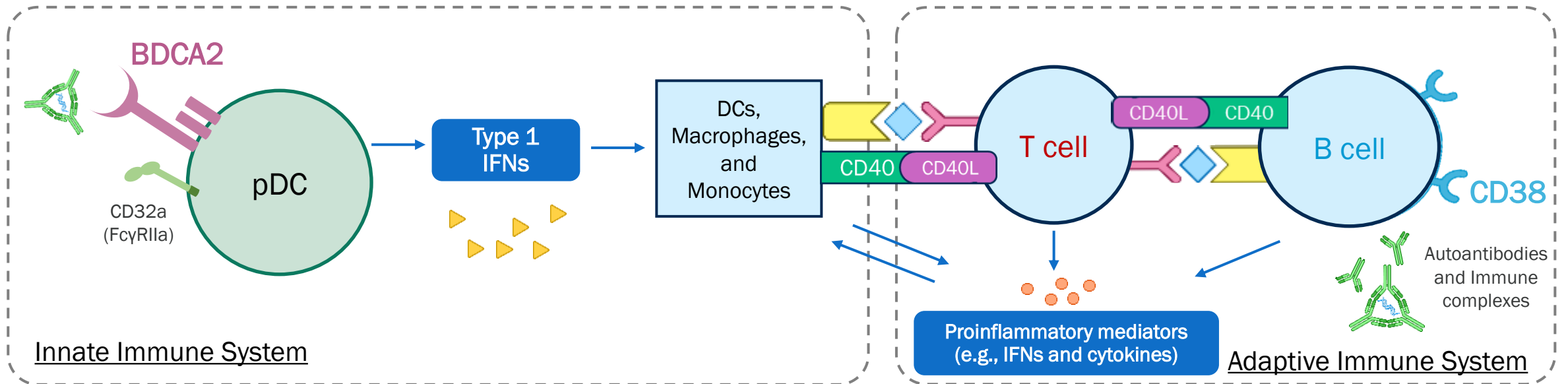
# BIOLOGY OF LUPUS INVOLVES SEVERAL REINFORCING PATHWAYS THAT PROVIDE DISTINCT OPPORTUNITIES FOR INTERVENTION

**Key Immune Cells**

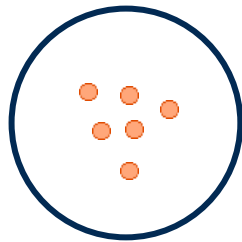
**pDCs** (plasmacytoid Dendritic Cells) produce excess IFN-I and other cytokines and activate antigen presenting dendritic cells

**T-cells** cause direct tissue damage and secrete proinflammatory signals and activate B-cells via CD40

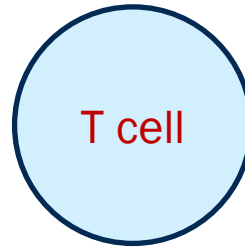
**B-cells** generate autoantibodies that cause inflammation and tissue damage



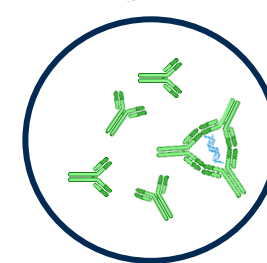
**Tissue damage caused by**



**1. Cytokines**  
Promote inflammation and immune cell activation

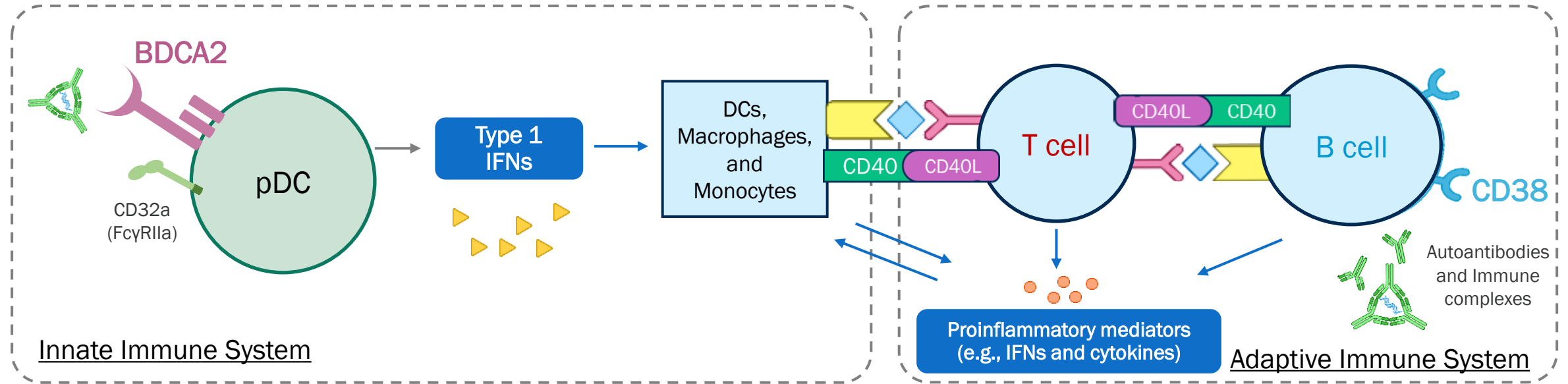


**2. T-cell infiltration**  
Direct tissue damage and release of proinflammatory cytokines



**3. Auto-antibodies and immune complexes**  
Trigger inflammation and activate the complement system

# OUR PIPELINE SPANS MULTIPLE POINTS OF INTERVENTION IN THE LUPUS CASCADE



## Immune Cells

- **Litifilimab** – pDCs
- **Felzartamab** – B-cells
- **Belimumab** – B-cells
- **CAR-T and bi-specifics** – T-cells & B-cells
- **Obinutuzumab** – B-cells

## Cytokines

- **Litifilimab** – (upstream) Type 1 IFN
- **Anifrolimab** – Type 1 IFN
- **TYK2** – (upstream) Type 1 IFN

## Intercellular Signaling

- **Dapirolizumab pegol** – CD40L

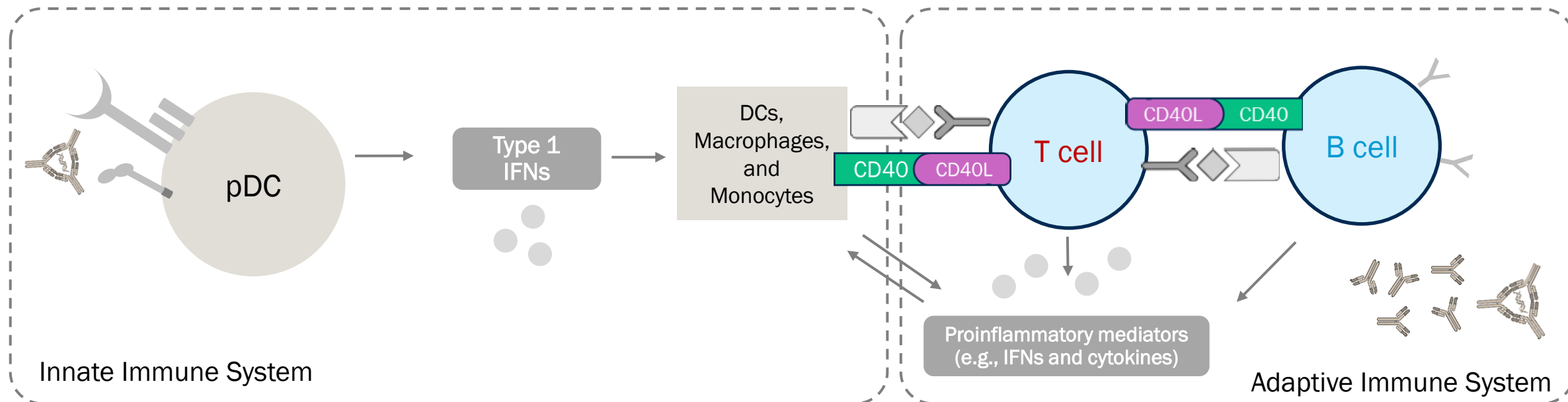
Note: Dapirolizumab pegol is being developed in collaboration with UCB  
 Graphic is intended to be a simplified schematic and does not include all cell types, or signaling pathways implicated in the pathogenesis of lupus. List of therapies is non-exhaustive.  
 DC = dendritic cell; IFN = interferon

# **DAPIROLIZUMAB PEGOL IN SLE**

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**FC-FREE PEGYLATED ANTIGEN-BINDING FRAGMENT**

# CD40L IS A KEY TARGET TO DISRUPT CD40 SIGNALING AND INTERRUPT THE IMMUNOLOGIC CASCADE IN SLE

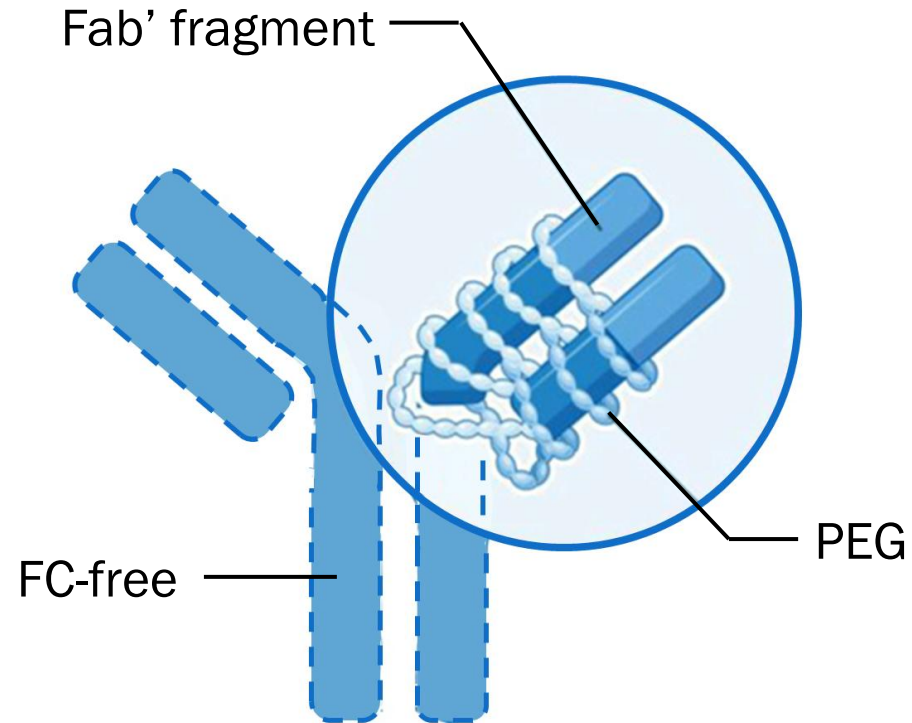


- When CD40 binds to CD40L it signals the cell to activate
- Therefore, preventing binding CD40 to CD40L blocks the downstream signaling that activates multiple cells in the SLE cascade (e.g. T-cells, B-cells, pDCs)

Note: Dapirolizumab pegol is being developed in collaboration with UCB  
Graphic is intended to be a simplified schematic and does not include all cell types expressing CD40 or CD40-CD40L signaling components, including those relevant to lupus such as dendritic cells and antigen presenting cells  
DC = dendritic cell; IFN = interferon; pDC = plasmacytoid dendritic cells; SLE = systemic lupus erythematosus

# DAPIROLIZUMAB PEGOL IS DESIGNED TO DELIVER EFFICACY WITHOUT THE POTENTIAL FOR THROMBOSIS SEEN WITH OLDER CD40L AGENTS

## Dapirolizumab pegol (DZP)



- DZP is a pegylated antibody fragment designed to bind to CD40L
- Lack of functional Fc domain abrogates the potential risk of Fc-mediated platelet activation and aggregation
- Conjugation to PEG provides stability and increases circulation

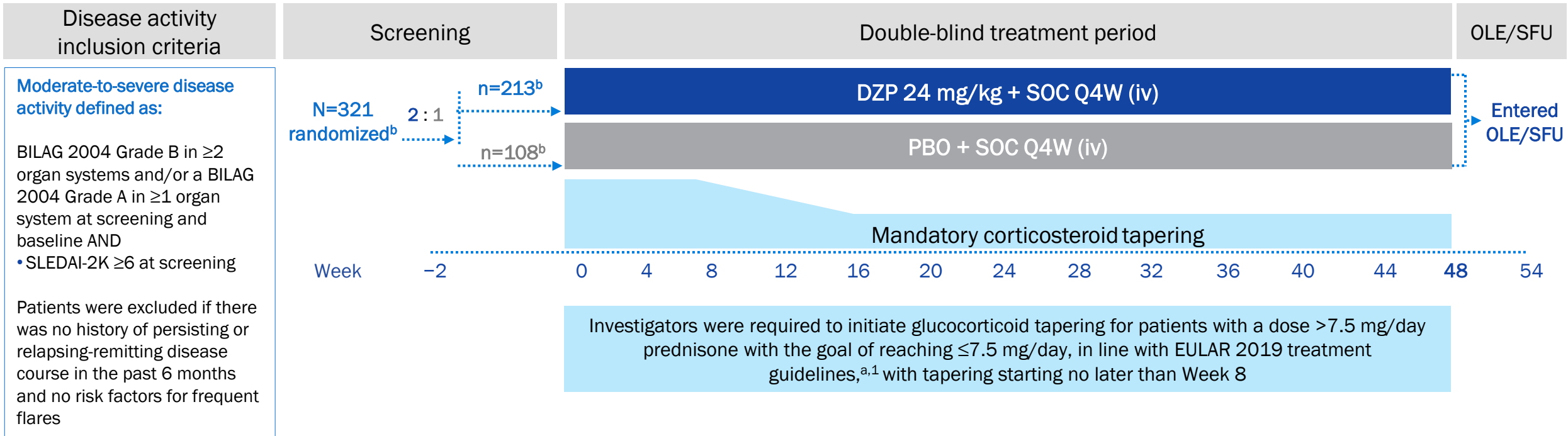
# A PHASE 3 STUDY WAS CONDUCTED TO EVALUATE THE SAFETY AND EFFICACY IN PATIENTS WITH SLE

## Primary objective<sup>1</sup>

BICLA response rate at Week 48

## Key secondary objectives<sup>1</sup>

- Achievement of BICLA response at Weeks 12 & 24
- Achievement of SRI-4 response at Week 48
- Severe BILAG flares through Week 48
- LLDAS  $\geq$  50% postbaseline at Week 48

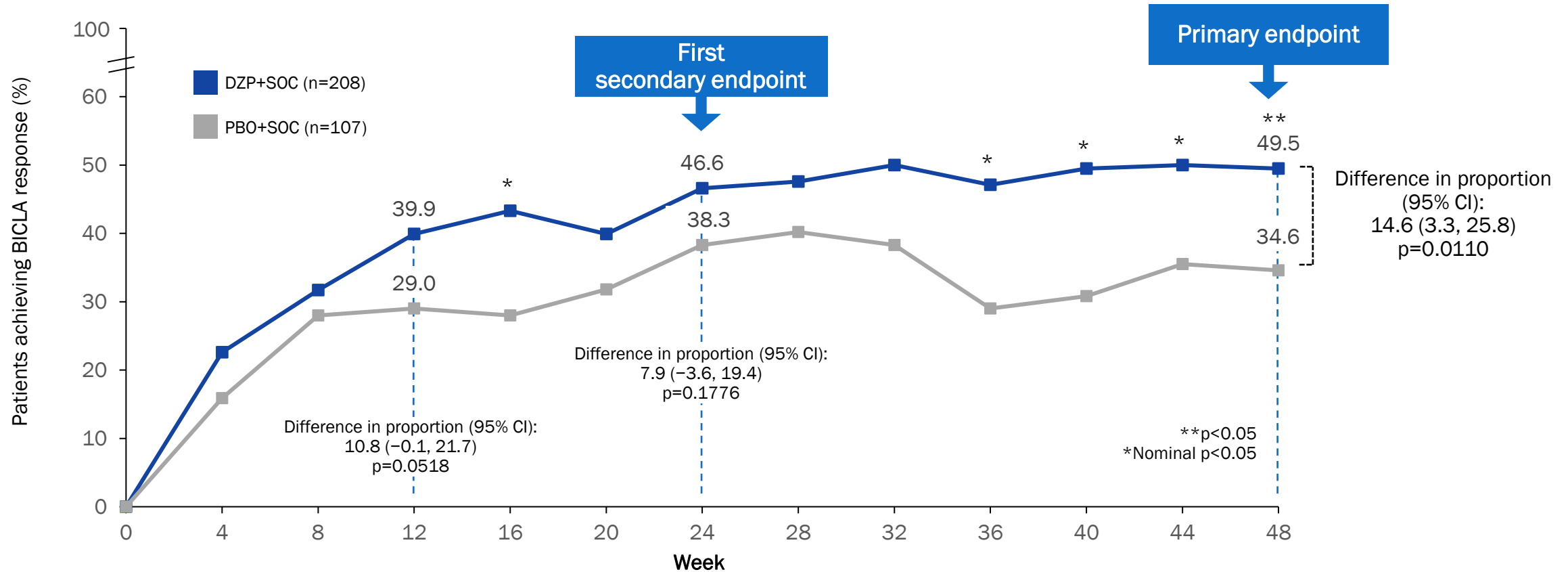


Note: Dapirolizumab pegol is being developed in collaboration with UCB; [a] Guidelines available at the time of study design; [b] Randomized set. 1. Fanouriakis A. Ann Rheum Dis 2019;78:736–45. BICLA = British Isles Lupus Assessment Group-based Composite Lupus Assessment; BILAG = British Isles Lupus Assessment Group; DZP = dapirolizumab pegol; EULAR = European Alliance of Associations for Rheumatology; iv = intravenous; LLDAS = lupus low disease activity state; OLE = open-label extension; PBO = placebo; Q4W = every 4 weeks; SFU = safety follow up; SLE = systemic lupus erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index-2K; SOC = standard of care; SRI-4 = SLE responder index-4.



# DAPIROLIZUMAB PEGOL IS ONLY THE 3<sup>RD</sup> AGENT TO MEET THE PRIMARY ENDPOINT IN A GLOBAL PHASE 3 STUDY

*Dapirolizumab significantly improved disease activity in moderate to severe SLE*

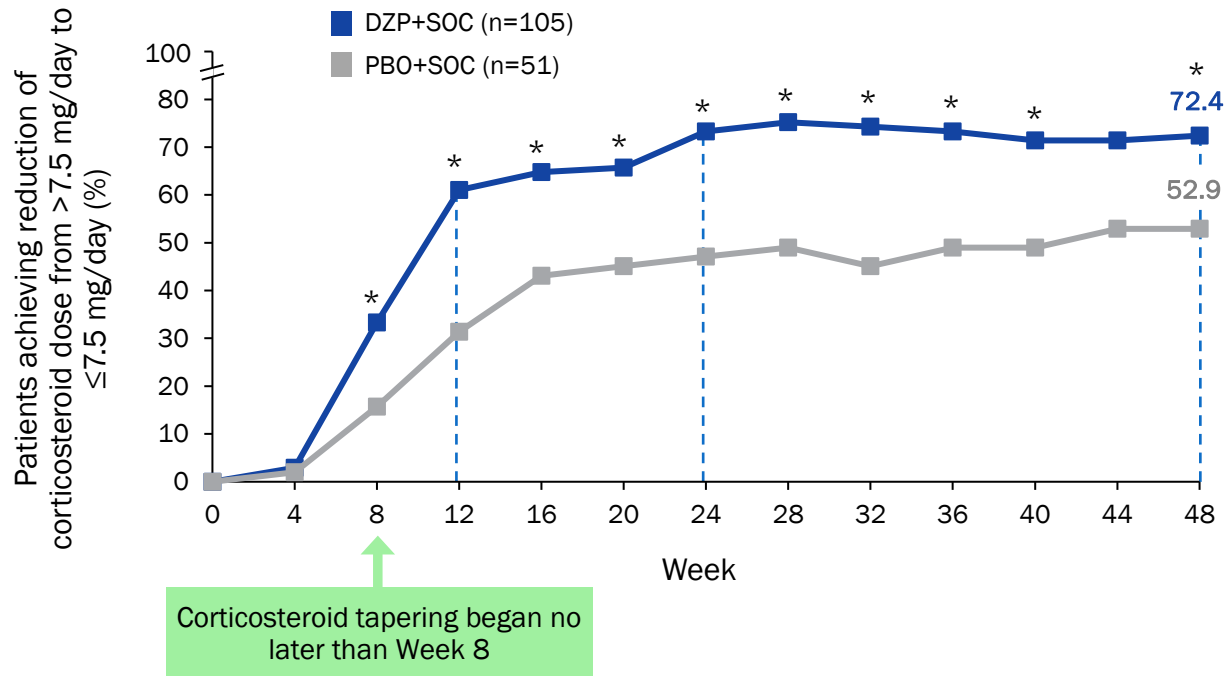


Note: Dapirolizumab pegol is being developed in collaboration with UCB; Full analysis set. Secondary endpoints were controlled for multiplicity using a hierarchical testing procedure. As the second step of the hierarchical testing was BICLA response at Week 24 and the p value was >0.05 for this time point, all other secondary endpoints cannot be considered statistically significant. A composite strategy was used for intercurrent events (escape treatment, premature withdrawal from the study, or permanent discontinuation of study medication while remaining in the study) and patients were assigned as a non-responder from the day after the intercurrent event occurred. After intercurrent event handling, any remaining missing data were handled using NRI. Difference in proportion responding between DZP+SOC and PBO+SOC, 95% CI for difference in proportions, and p-values were estimated and tested using the CMH risk difference estimate controlling for stratification factors (pooled region [North America vs Western Europe/Asia-Pacific vs Latin America/Eastern Europe], baseline disease activity pattern [chronic active vs acute flaring], and baseline SLEDAI-2K score [ $<10$  vs  $\geq 10$ ]). [a] Of all randomized patients. BICLA = British Isles Lupus Assessment Group-based Composite Lupus Assessment; CI = confidence interval; CMH = Cochran-Mantel-Haenszel; DZP = dapirolizumab pegol; NRI = non-responder imputation; PBO = placebo; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index-2K; SOC = standard of care.

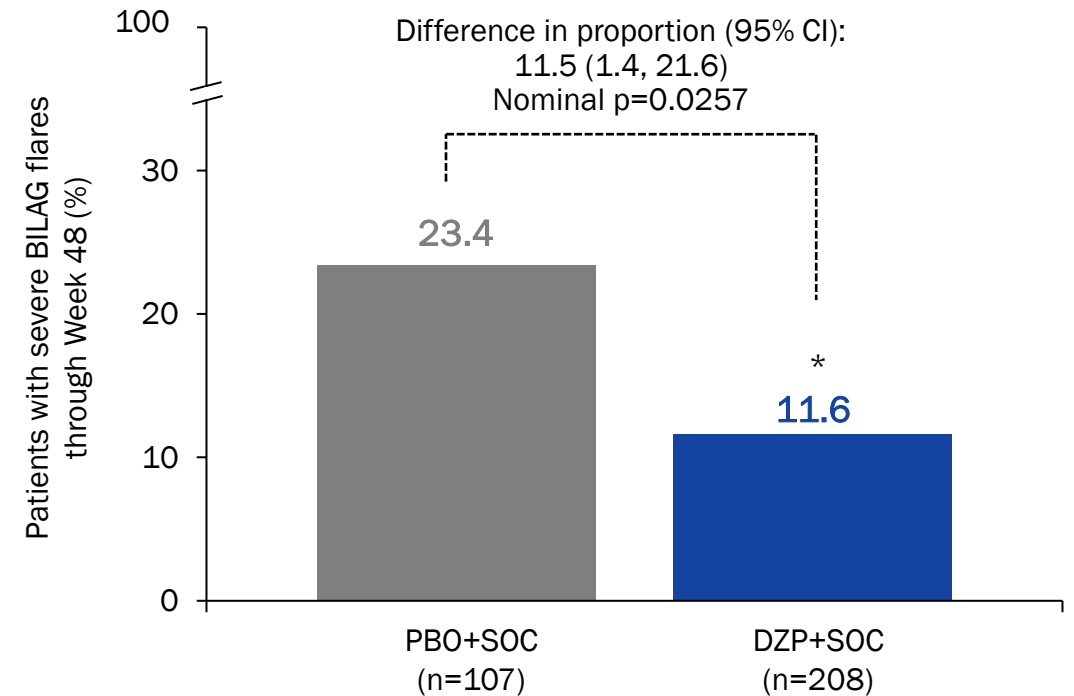


# DZP PATIENTS ACHIEVED A MEANINGFUL IMPROVEMENT IN STEROID USE AND REDUCTION IN FLARES

17% more patients on the DZP+SOC were able to reduce their steroids compared to PBO+SOC



50.4% reduction in proportion of patients receiving DZP+SOC with severe BILAG flares relative to patients receiving PBO+SOC



Note: Dapirolizumab pegol is being developed in collaboration with UCB

\*Nominal p<0.05

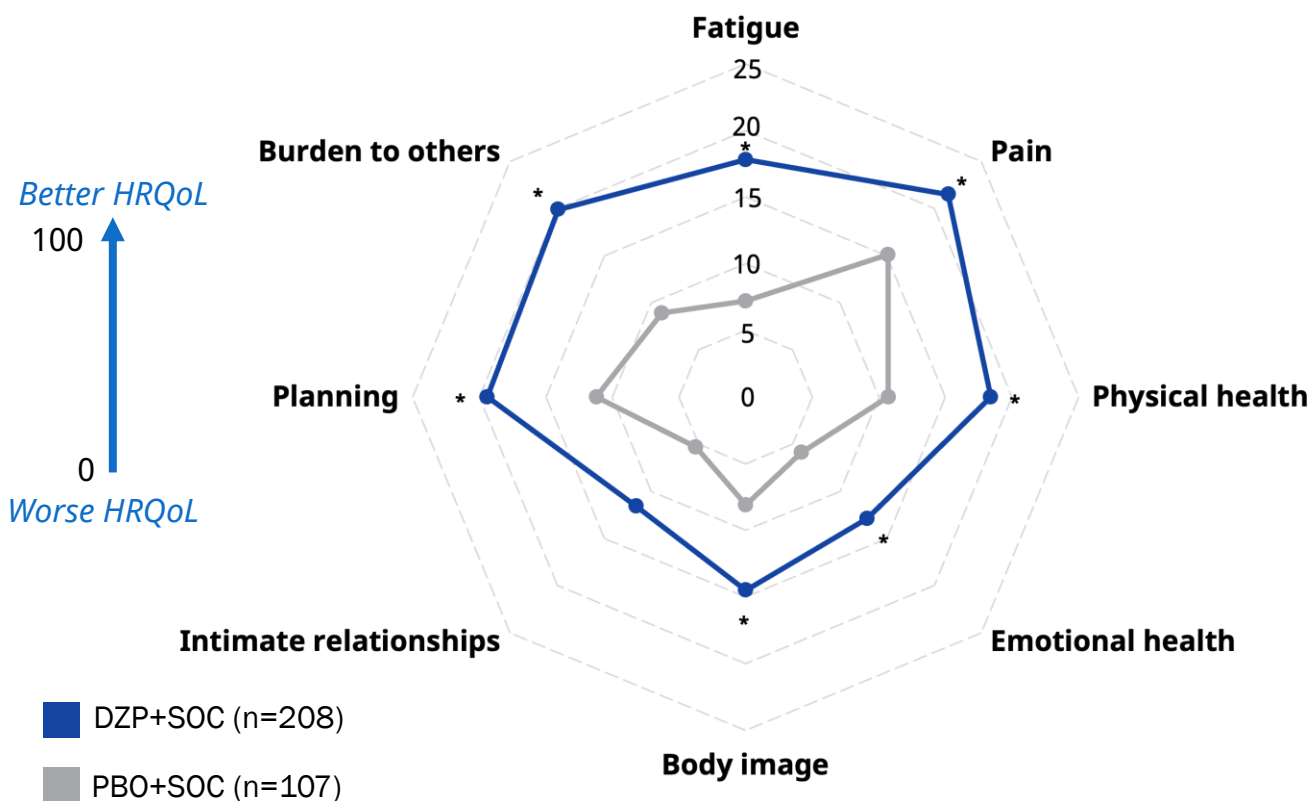
CI = confidence interval; DZP = dapirolizumab pegol; PBO = placebo; SOC = standard of care



# DATA HIGHLIGHTS THE POTENTIAL OF DAPIROLIZUMAB PEGOL TO ALLEVIATE FATIGUE, REDUCE DISEASE ACTIVITY AND IMPROVE QUALITY OF LIFE IN LUPUS

*Dapirolizumab pegol showed efficacy across multiple clinical endpoints in the positive PHOENYCS GO Phase 3 study, including fatigue, measures of disease activity and patient reported outcomes*

Change in LupusQoL scores from baseline to Week 48



PHOENYCS GO data at EULAR 2025 show that\* compared to SoC alone, DZP + SoC resulted in:

- Improvements from baseline to week 48 in LupusQoL scores across all domains<sup>1</sup>
- Improvements across multiple domains of fatigue measured by both FACIT and FATIGUE-PRO<sup>2</sup>
- Measures of disease activity and remission, improved over time through 48 weeks of treatment<sup>3</sup>

Note: Dapirolizumab pegol is being developed in collaboration with UCB; 1. Touma et al., Lupus, 2025; 2. Parodis et al., EULAR, 2025; 3. Morand et al., EULAR, 2025; \*Nominal p<0.05  
DZP = dapirolizumab pegol; FACIT = Functional Assessment of Chronic Illness Therapy; HRQoL = health-related quality of life; SoC = standard of care

# DAPIROLIZUMAB PEGOL WAS GENERALLY WELL TOLERATED IN THE PHASE 3 STUDY

n, (%)	DZP+SOC n=213	PBO+SOC n=108
<b>Any TEAE</b>	176 (82.6%)	81 (75.0%)
Serious TEAEs	21 (9.9%)	16 (14.8%)
Permanent discontinuation of drug or study discontinuation due to TEAEs	10 (4.7%)	4 (3.7%)
Hypersensitivity TEAEs starting on the day of or the day after an infusion	6 (2.8%)	0 (0.0%)
<b>Infections and infestations</b>	131 (61.5%)	56 (51.9%)
Mild	95 (44.6%)	35 (32.4%)
Moderate	66 (31.0%)	36 (33.3%)
Severe	3 (1.4%)	4 (3.7%)
Serious	8 (3.8%)	6 (5.6%)
<b>Herpes viral infections</b>	13 (6.1%)	14 (13.0%)
Herpes zoster	4 (1.9%)	7 (6.5%)
Ophthalmic herpes zoster	2 (0.9%) <sup>a</sup>	0 (0.0%)
Herpes ophthalmic	1 (0.5%) <sup>b</sup>	0 (0.0%)
<b>Thromboembolic TEAEs confirmed by an adjudication committee</b>	1 (0.5%)	0 (0.0%)
Acute myocardial infarction	1 (0.5%)	0 (0.0%)
<b>Deaths</b>	1 (0.5%)	0 (0.0%)
Gangrene-related sepsis	1 (0.5%)	0 (0.0%)

Note: Dapirolizumab pegol is being developed in collaboration with UCB; Safety set. MedDRA v24.0. [a] The two events were reported as “herpes zoster over left eyelid and forehead, V1” and “left herpes zoster ophthalmicus (dermatome V1/V2)”; [b] Reported as “herpetic queratitis”. DZP = dapirolizumab pegol; MedDRA = Medical Dictionary for Regulatory Activities; PBO = placebo; SLE = systemic lupus erythematosus; SOC = standard of care; TEAE = treatment-emergent adverse event.



# PRECLINICAL FINDINGS IN PREGNANCY SUPPORT A POTENTIALLY DIFFERENTIATED PROFILE

*Based on current findings, DZP is not anticipated to cross the placenta to significant levels and supports further investigation in pregnant women*

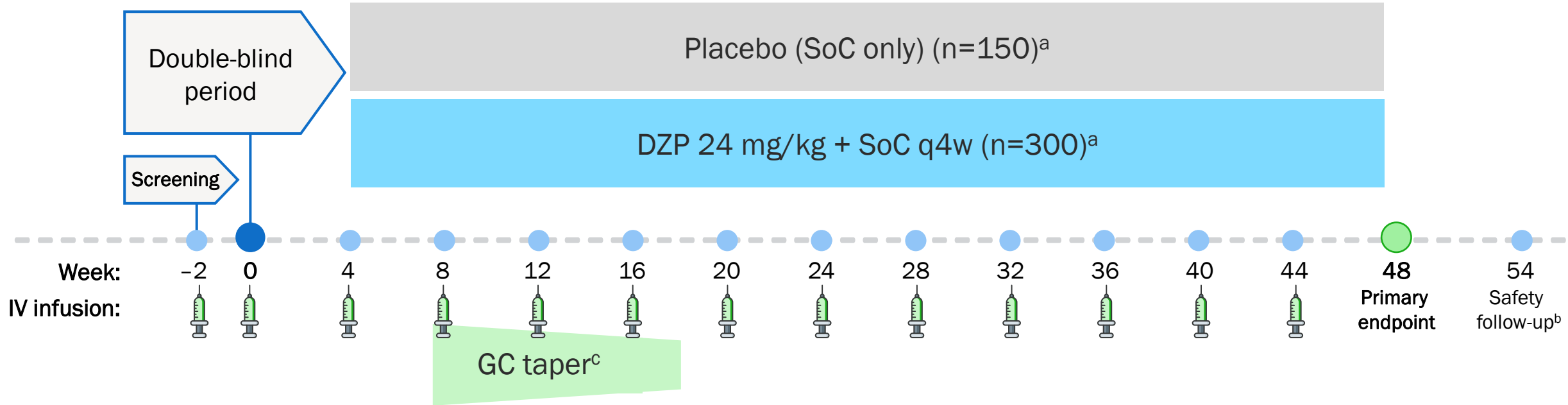
## ➤ In primates:

- DZP caused no adverse outcomes on pregnancy or infant development
- Placental transfer of DZP from mother to infant during pregnancy was very low, as was transfer of DZP into milk

## ➤ In the human ex vivo placental model:

- DZP transfer was below the level of detection in all but one experiment (21 out of 22 experiments )

# SECOND CONFIRMATORY PHOENYCS FLY PHASE 3 STUDY ONGOING



## Primary objective



BICLA response rate at Week 48

## Key objectives

Moderate-to-severe disease activity defined as:

- BILAG 2004 Grade B in  $\geq 2$  organ systems and/or a BILAG 2004 Grade A in  $\geq 1$  organ system at screening and baseline AND
- SLEDAI-2K  $\geq 6$  at screening

Dapirolizumab pegol is being developed in collaboration with UCB [a] Estimated enrollment; [b] For patients not entering open-label extension; [c] For patients receiving  $>7.5$  mg/day prednisone equivalent at baseline, tapering will be initiated no later than Week 8 to reach a target of 7.5 mg/day or below by Week 18. BICLA = BILAG-Based Composite Lupus Assessment; BILAG = British Isles Lupus Assessment Group; DZP = dapirolizumab pegol; GC = glucocorticoid steroids; IV = intravenous; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index - 2000; SoC = standard of care; q4w = every 4 weeks.

# DAPIROLIZUMAB PEGOL HAS THE POTENTIAL TO HAVE A MEANINGFULLY POSITIVE IMPACT ON PATIENTS



DZP is only the 3<sup>rd</sup> agent to show a positive global Phase 3 study in SLE



Data show a 50% reduction in flares, meaningful reduction in corticosteroid use, as well as a quality-of-life improvement, including fatigue



Preclinical findings in pregnancy support a potentially differentiated profile

Ongoing Phase 3 study designed to confirm the first successful Phase 3 with data expected in 2027-2028



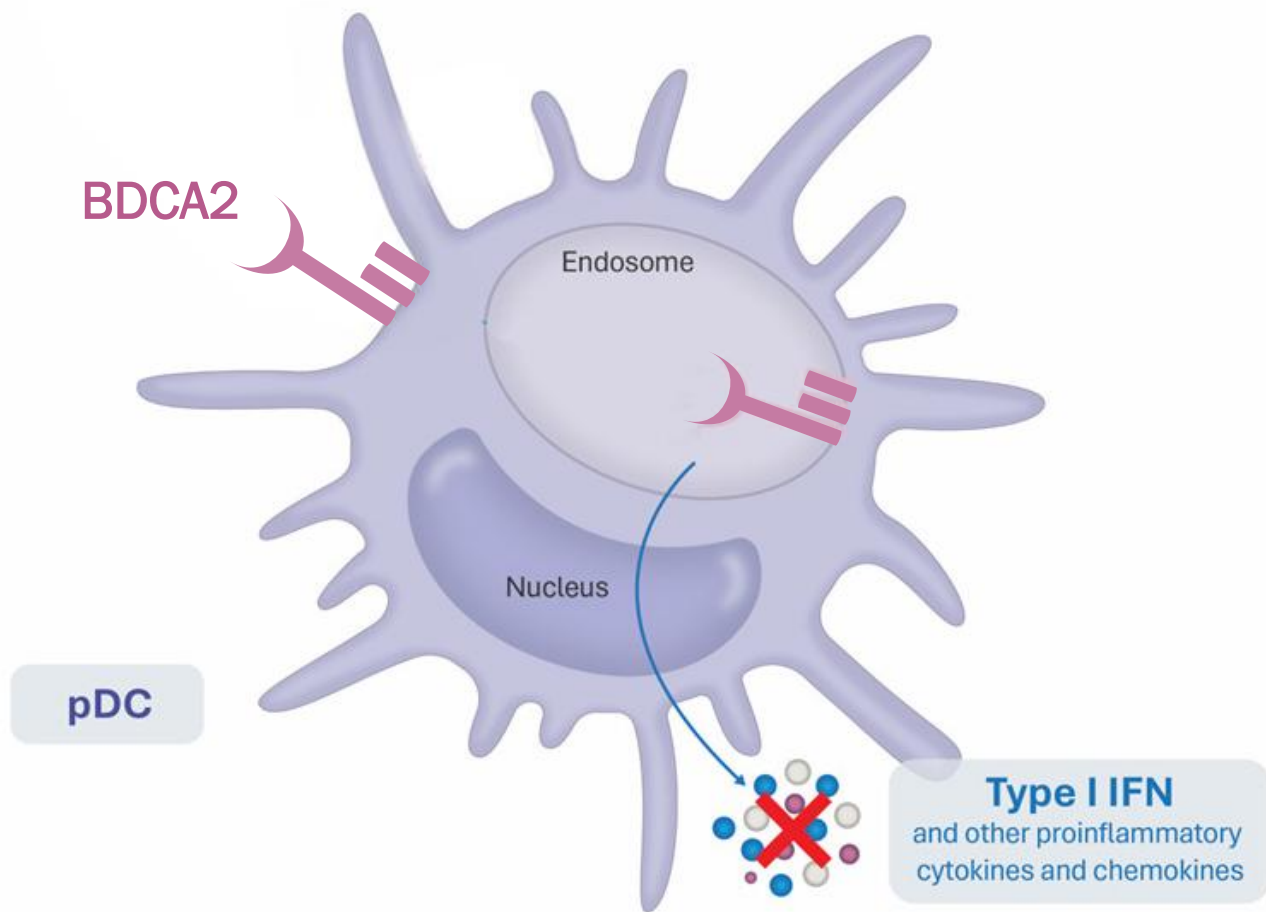
# QUESTION & ANSWERS

# LITIFILIMAB IN SLE

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**BDCA2 INHIBITOR**

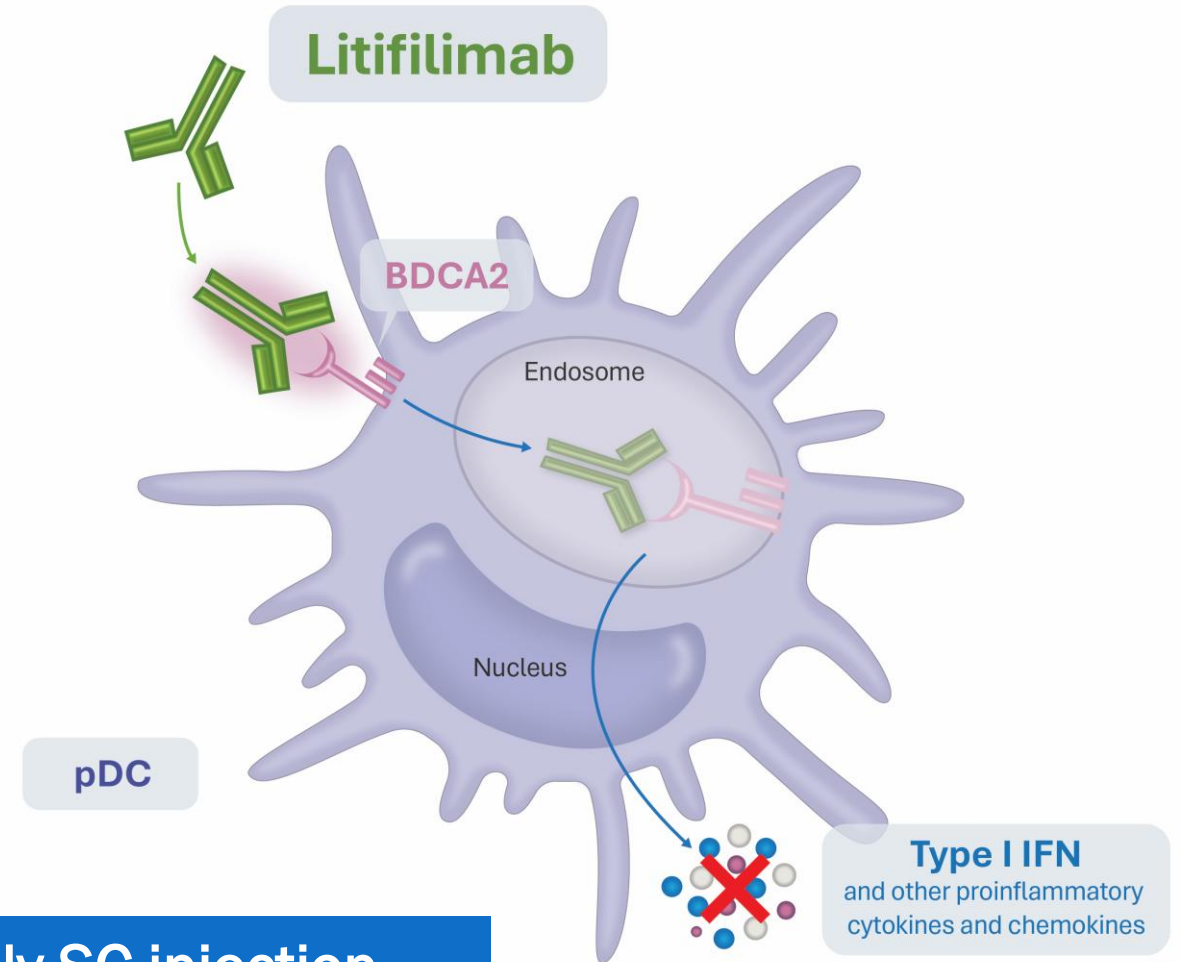
# ANTI-BDCA2 IS A POTENTIALLY ATTRACTIVE APPROACH FOR REDUCING PRODUCTION OF IFN-I, CYTOKINES AND CHEMOKINES IN LUPUS



- Production of IFN-I in pDC cells is inhibited by internalization of BDCA2 into the cell
- This makes BDCA2 an attractive target to inhibit the production of IFN-I and other cytokines and chemokines

# LITIFILIMAB IS DESIGNED TO BIND TO BDCA2 THEREBY INHIBITING THE PRODUCTION OF IFN-I

- Litifilimab is a monoclonal antibody that is designed to bind to BDCA2
- Binding of **litifilimab** to **BDCA2** leads to:
  - Rapid internalization of BDCA2 from the cell surface of pDCs
  - Thereby inhibiting the production of pDC-derived IFNs, IFN-I, cytokines, and chemokines<sup>1</sup>



Litifilimab is formulated as a once-monthly SC injection

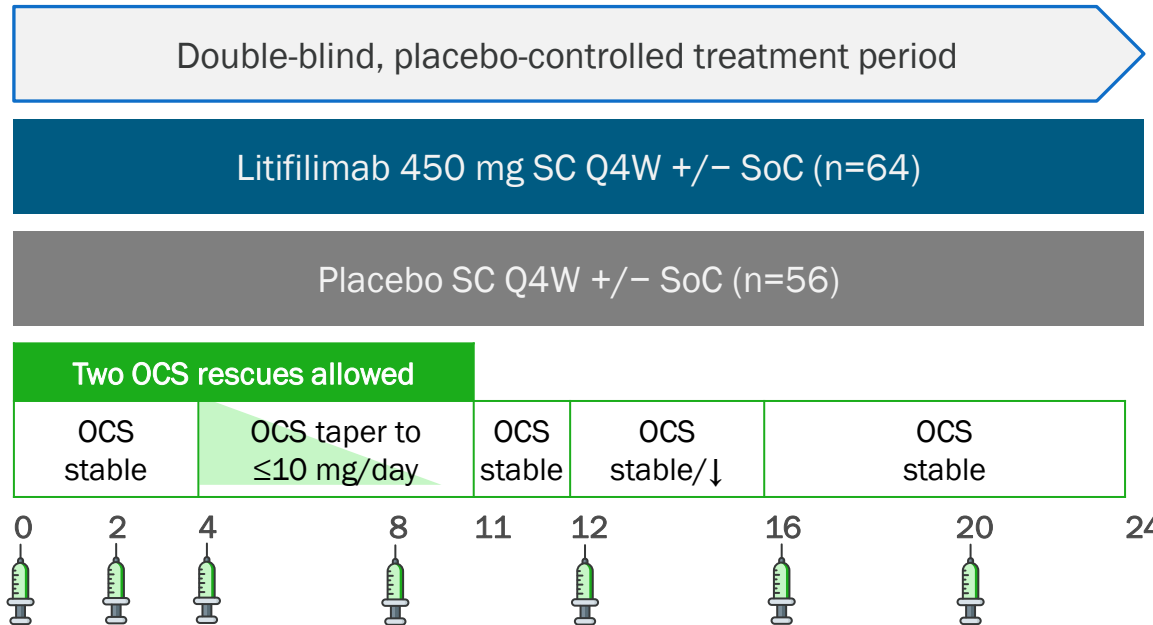
1. Pellerin A, et al. *EMBO Mol Med.* 2015;7(4):464-476. BDCA2 = blood dendritic cell antigen 2; IFN-I = interferon type I; pDC = plasmacytoid dendritic cell

# LILAC WAS A TWO-PART, PHASE 2, RANDOMIZED, DOUBLE-BLIND STUDY OF LITIFILIMAB

Part A study design in participants with SLE and active skin disease and joint involvement<sup>1</sup>

## 28-DAY SCREENING PERIOD

- ANA and/or anti-dsDNA antibody positive
- Stable lupus SoC
- Stable OCS ( $\leq 20$  mg/day)
- Joint count:
  - $\geq 4$  tender joints
  - $\geq 4$  swollen joints
- Active skin disease (SLEDAI-2K)



Randomization (1:1)

Efficacy and safety

## SELECT ENDPOINTS

- Primary efficacy**
  - Change from baseline in total active joint count at Week 24\*
- Secondary efficacy**
  - SRI-4
  - SLEDAI-2K
  - CLASI-50
- Safety**
  - AEs and SAEs

\*Sum of swollen joints and tender joints as measured on a 28-joint assessment. A joint that was both swollen and tender was counted twice

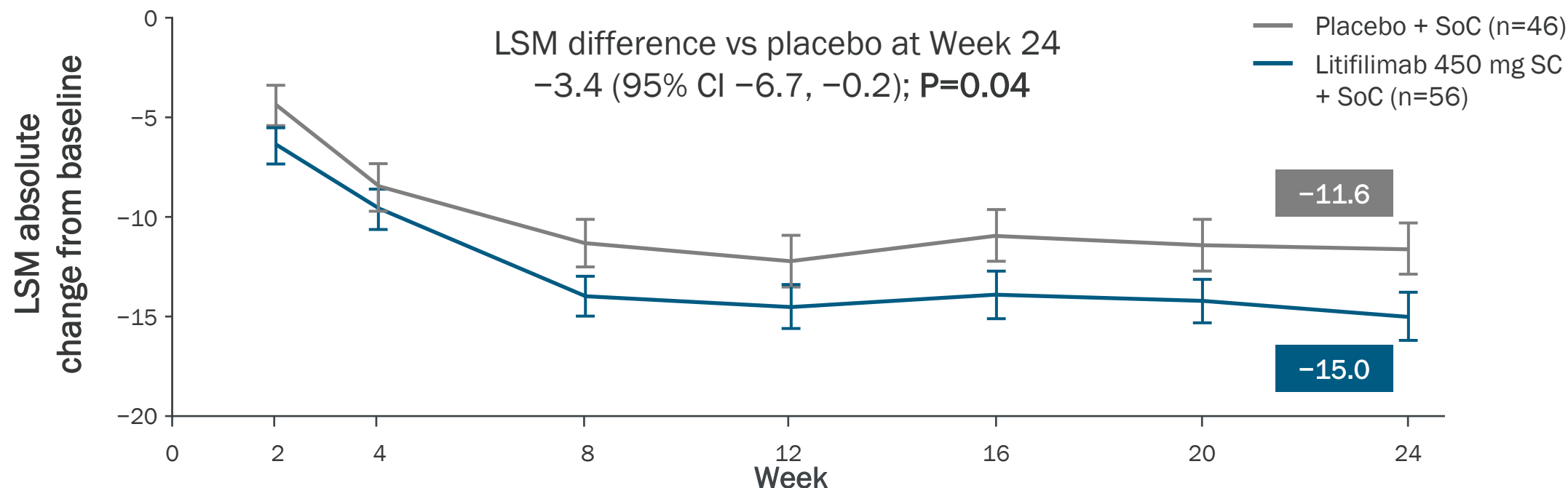
AE = adverse event; ANA = antinuclear antibody; CLASI-50 =  $\geq 50\%$  improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index - Activity Scale; dsDNA = double-stranded DNA; OCS = oral corticosteroids; Q4W = every 4 weeks; SAE = serious adverse event; SC = subcutaneous; SLE = systemic lupus erythematosus; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SoC = standard of care; SRI-4 = Systemic Lupus Erythematosus Responder Index-4

1. Furie RA, et al. N Engl J Med 2022;387:894-904

# PART A OF THE PHASE 2 LILAC STUDY MET ITS PRIMARY ENDPOINT

*Improved Joint Activity: Litifilimab significantly reduced the mean total number of active joints vs placebo*

Total active joint count\*† in patients with SLE and active skin disease and joint involvement (N=132‡) (primary endpoint at Week 24)<sup>1</sup>



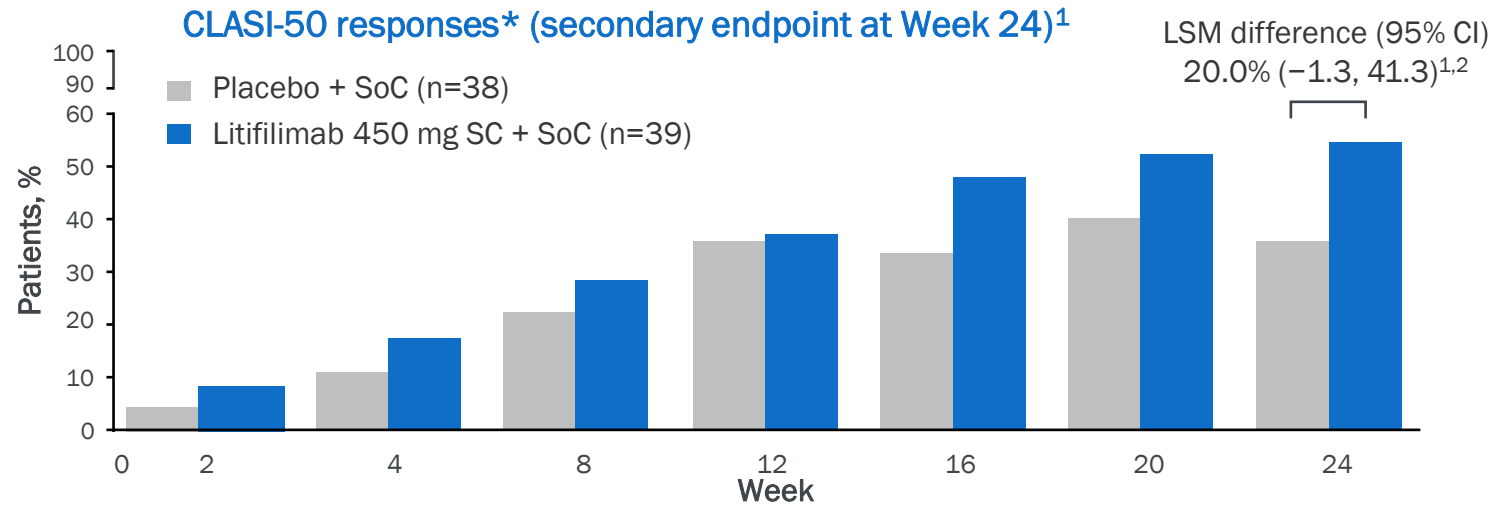
\*Sum of swollen and tender joints, as measured on a 28-joint assessment. A joint that was both swollen and tender was counted twice; †A post-hoc analysis to account for an imbalance in the sex of patients between the study groups provided results in the same direction as those of the primary analysis, but with smaller endpoint differences between groups. However, no formal inferences can be made. ‡Data from 12 patients who received litifilimab at doses of 50 and 150 mg were not reported

CI = confidence interval; LSM = least squares mean; SC = subcutaneous; SLE = systemic lupus erythematosus; SoC = standard of care

1. Furie RA, et al. N Engl J Med 2022;387:894-904

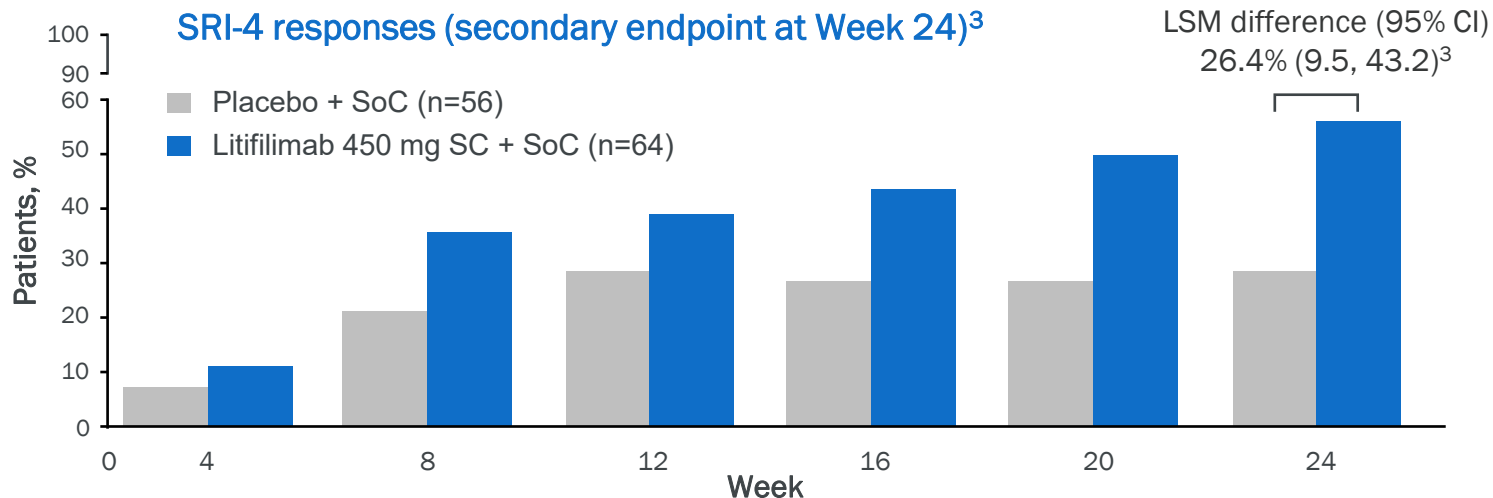


# SECONDARY ENDPOINTS IN LILAC ALSO SHOW IMPORTANT RESPONSE IN SKIN AND OVERALL SYMPTOMS



**Saw a meaningful improvement in skin manifestations**

- Majority of patients saw resolution in more than half of their affected skin



**Saw a meaningful improvement in systemic symptoms**

- Responses observed irrespective of baseline disease activity and steroid use

This study was not powered to detect statistical differences in secondary endpoints. CI = confidence interval; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity Index, CLASI-50 =  $\geq 50\%$  improvement from baseline in CLASI - Activity score; LSM = least squares mean; SC = subcutaneous; SoC = standard of care; SRI-4 = Systemic Lupus Erythematosus Responder Index-4  
 \*Assessed in patients with CLASI-A activity  $\geq 8$  at baseline  
 1. Furie RA, et al. Arthritis Rheumatol 2022;74(Suppl. 9):0364 (Abstract); 2. Furie RA, et al. N Eng J Med 2022;387:894-904; 3. Furie RA, et al. N Engl J Med 2022;387:894-904 (Suppl)

# LITIFILIMAB HAD AN ACCEPTABLE SAFETY PROFILE WITH NO INCREASED RISK OF INFECTION IN LILAC PART A

## Phase 2 LILAC Part A<sup>1,2</sup>

Event, n (%)	Placebo (n=56)	Pooled litifilimab SC (n=76)*
Patients with any AE	38 (68)	45 (59)
Mild AE	14 (25)	27 (36)
Moderate AE	18 (32)	15 (20)
Severe AE	6 (11)	3 (4)
Serious events	6 (11)	4 (5)
Events leading to drug withdrawal	3 (5)	2 (3)
Events leading to study withdrawal	3 (5)	0
Death	3 (5)	0
Infections and infestations	22 (39)	27 (36)

\*The pooled litifilimab population included patients who received litifilimab at doses of 50 mg (6 patients), 150 mg (6 patients) and 450 mg (64 patients); The most common AEs were diarrhea, nasopharyngitis, UTI, fall, and headache<sup>1</sup>  
 AE = adverse event; SC = subcutaneous

1. Furie RA, et al. N Engl J Med 2022;387:894-904; 2. Furie RA, et al. N Engl J Med 2022;387:894-904 (Suppl)

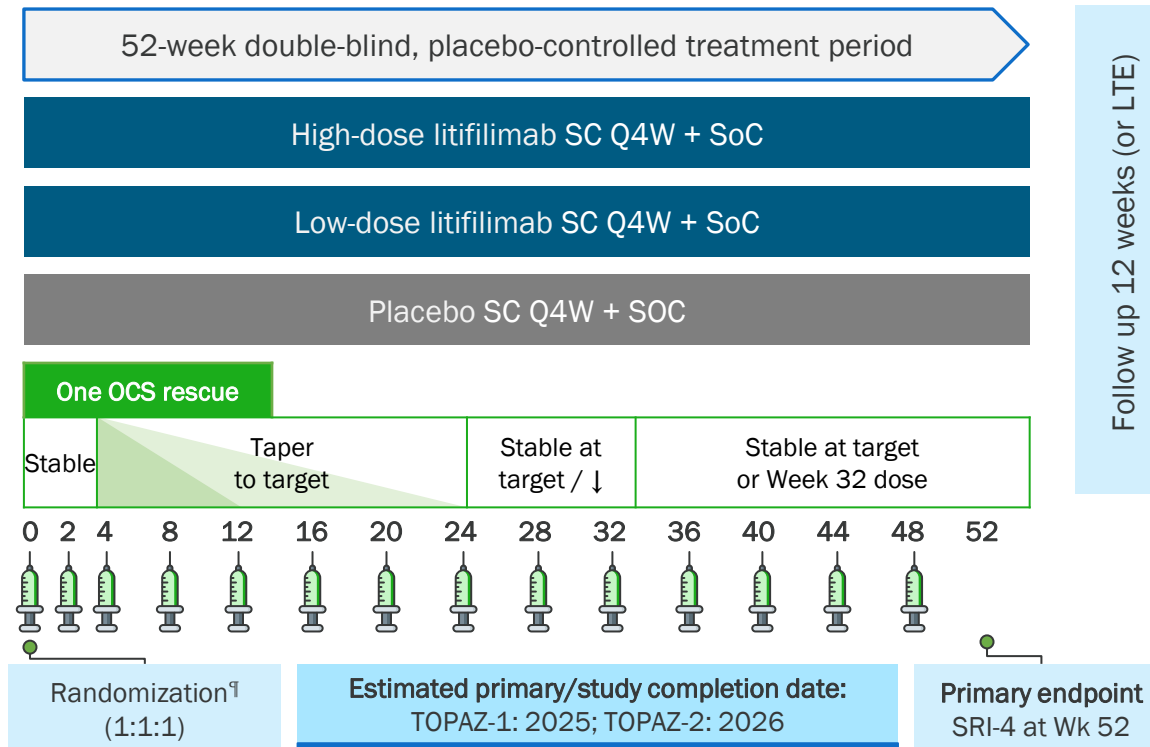
# TWO PHASE 3 STUDIES ONGOING IN SLE WITH FIRST DATA EXPECTED IN 2026

TOPAZ-1 and TOPAZ-2 are two identically designed multicenter, randomized, double-blind, placebo-controlled Phase 3 studies to evaluate the efficacy and safety of litifilimab in patients with SLE receiving non-biologic SoC that are actively recruiting participants<sup>1-3\*</sup>

## KEY INCLUSION CRITERIA

- Aged ≥18 years
- SLE diagnosis<sup>†</sup> ≥24 weeks prior to screening
- Modified SLEDAI-2K ≥6<sup>‡</sup>
- Modified cSLEDAI-2K ≥4<sup>§</sup>
- BILAG A in ≥1 organ system or BILAG B in ≥2 organ systems
- Stable (≥4 weeks) non-biologic SoC for ≥12 weeks
- ≤20 mg/day prednisolone equivalent

**N≈540**  
Currently recruiting



## SELECT ENDPOINTS

### Key secondary efficacy

- SRI-4 (Week 24)
- Joint-50 response
- Steroid-sparing effects
- CLASI-50 response
- Annualized flare rate

### Exploratory endpoints

#### PROs

- LupusQoL, SF-36, FACIT-Fatigue, PHQ-9, WPAI:Lupus

#### Safety

- AEs and SAEs

\*TOPAZ-1 and -2 have different geographical recruitment sites; <sup>†</sup>EULAR/ACR criteria; <sup>‡</sup>excluding alopecia, fever, lupus-related headache, and organic brain syndrome; <sup>§</sup>excluding anti-dsDNA, low complement C3 and/or C4, alopecia, fever, lupus-related headache, and organic brain syndrome; <sup>¶</sup>stratified based on OCS use, CLASI-A score, and geographic region. ACR, American College of Rheumatology; AE = adverse event; BILAG = British Isles Lupus Assessment Group; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-50 = ≥50% improvement from baseline in CLASI - Activity score; CLASI-A = CLASI - Activity; cSLEDAI-2K = clinical SLEDAI-2K; dsDNA = double-stranded DNA; EULAR = European Alliance of Associations for Rheumatology; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy - Fatigue Scale; LTE = long-term extension; LupusQoL = Lupus Quality of Life; OCS = oral corticosteroids; PHQ-9 = Patient Health Questionnaire 9; PRO = patient-reported outcome; Q4W = every 4 weeks; SAE = serious adverse event; SC = subcutaneous; SF-36 = Short Form 36; SLE = systemic lupus erythematosus;

1. NCT04895241. Updated. January 17, 2024. Available from: <https://clinicaltrials.gov/ct2/show/NCT04895241> (Accessed June 28, 2023); 2. NCT04961567. Updated. January 17, 2024. Available from: <https://clinicaltrials.gov/ct2/show/NCT04961567> (Accessed June 28, 2023); 3. van Vollenhoven RF, et al. Lupus Sci Med 2023;10:LP-184 (Abstract)

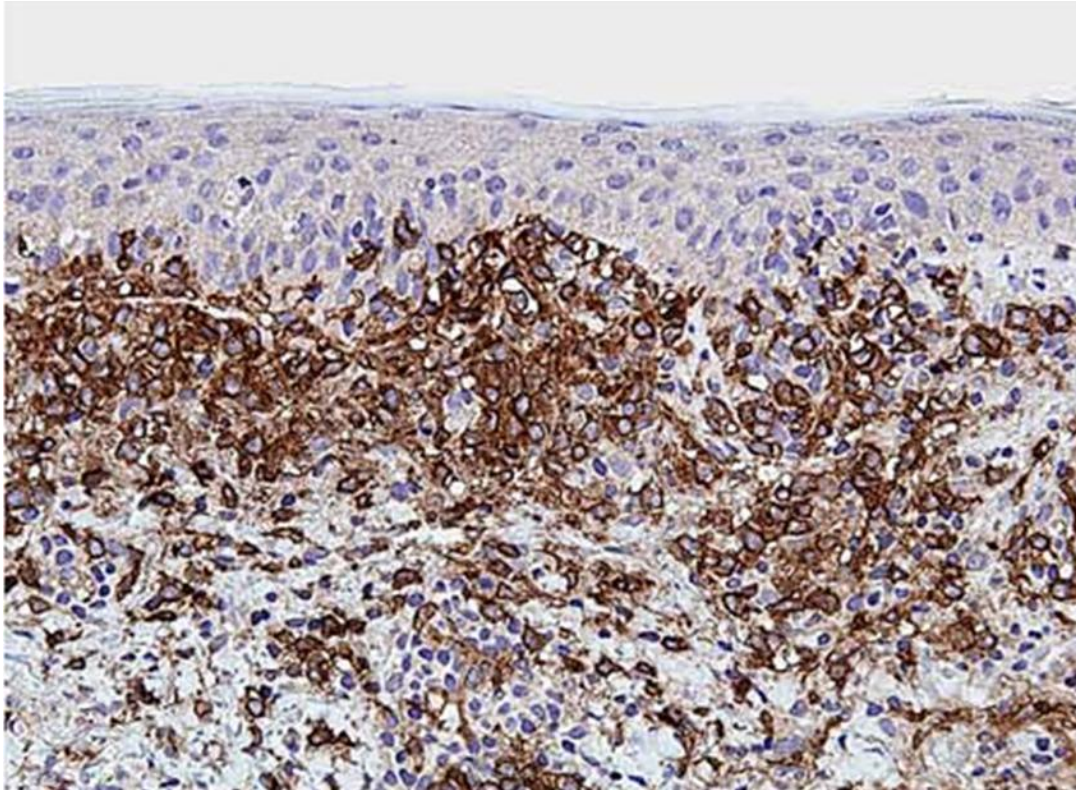
# LITIFILIMAB IN CLE

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**BDCA2 INHIBITOR**

# BIOPSIES SHOW PLASMACYTOID DENDRITIC CELLS ACCUMULATE IN SKIN LESIONS HIGHLIGHTING THE POTENTIAL FOR BDCA2 IN TREATING CLE

pDC infiltration (measured by CD123 expression)



Cutaneous distribution of pDC in LE. Skin serial sections are obtained from a pDC-rich LE case (pDC content score = 3 [ $> 50\%$  of positive cells in total mononuclear infiltrate]) and immunostained for CD123

- In CLE, pDCs migrate to the skin<sup>1</sup> and frequently comprise 20–30% of dermal infiltrates<sup>2-4</sup>
- Therefore, anti-BDCA2 has the potential to reduce IFN-I in the skin of CLE patients

LE = lupus erythematosus

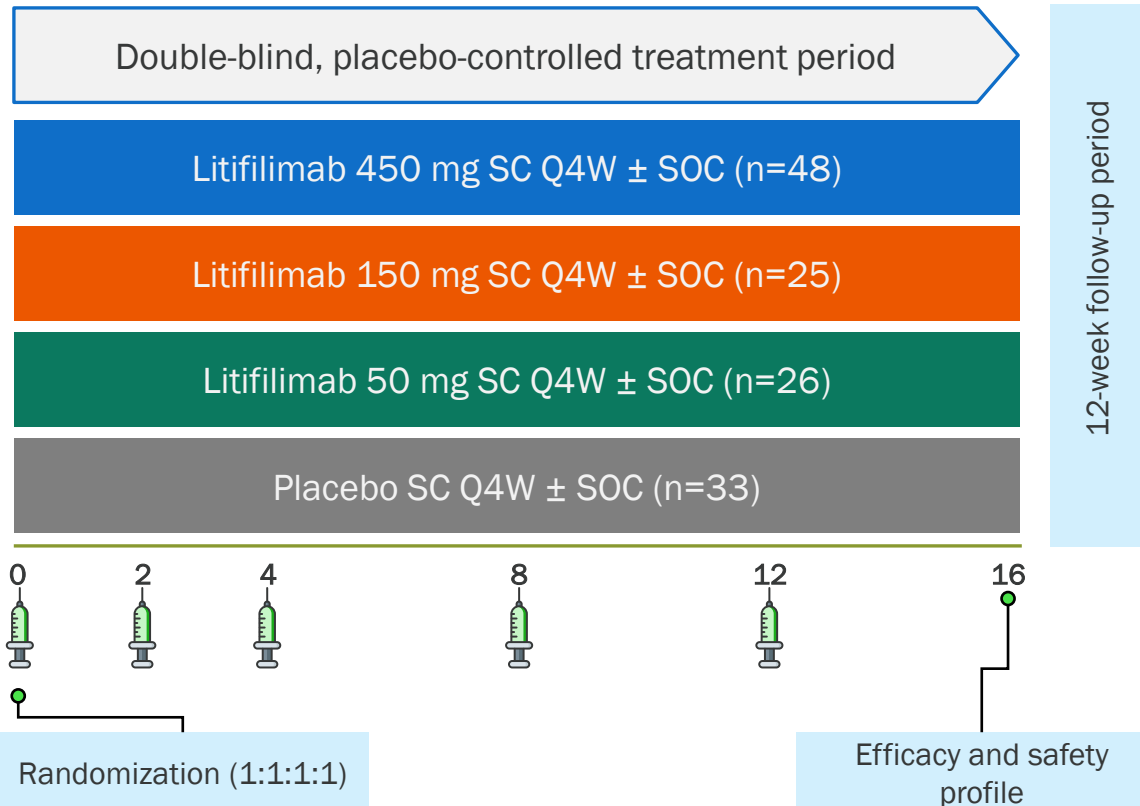
1. Sozzani S, et al. *Trends Immunol.* 2010;31(7):270-277; 2. McNiff JM, Kaplan DH. *J Cutan Pathol.* 2008;35(5):452-456; 3. Vermi W, et al. *Immunobiology.* 2009;214(9-10):877-886; 4. Rakhshan A, et al. *An Bras Dermatol.* 2020;95(3):307-313

# LILAC WAS A TWO-PART, PHASE 2, RANDOMIZED, DOUBLE-BLIND STUDY OF LITIFILIMAB

Part B study design in participants with CLE, with or without systemic manifestations<sup>1</sup>

## 28-DAY SCREENING PERIOD

- Histologically confirmed CLE diagnosis
- Active CLE: CLASI-A  $\geq 8$ 
  - Subacute CLE: CLASI-A  $\geq 2$  and/or
  - Chronic CLE: CLASI-A  $\geq 2$  and CLASI-D  $\geq 1$
- Stable OCS ( $\leq 15$  mg/day)



## SELECT ENDPOINTS

### Primary efficacy

- Percent change in CLASI-A from baseline to Week 16

### Secondary efficacy

- CLASI-50 response rate at Weeks 12 and 16
- CLASI-A percent change from baseline at Week 12
- $\geq 7$ -point reduction in CLASI-A score from baseline at Weeks 12 and 16

### Safety profile

- AEs and SAEs

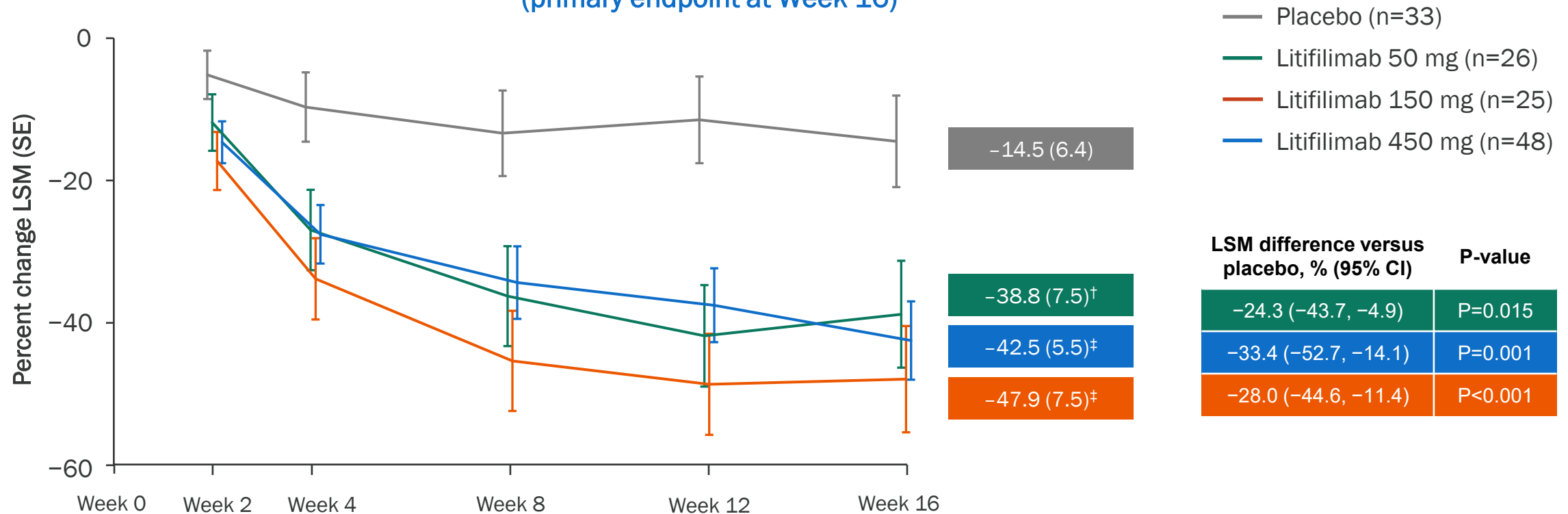
AE = adverse event; CLASI-50 =  $\geq 50\%$  improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-D = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Damage; CLE = cutaneous lupus erythematosus; OCS = oral corticosteroid(s); Q4W = every 4 weeks; SAE = serious adverse event; SC = subcutaneous; SCLE = subacute cutaneous lupus erythematosus; SOC = standard of care; SRI-4 = Systemic Lupus Erythematosus Responder Index-4

1. Werth VP, et al. N Engl J Med 2022;387:321-331

# PART B OF THE PHASE 2 LILAC STUDY MET ITS PRIMARY ENDPOINT IN CLE PATIENTS WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

*Litifilimab significantly reduced skin disease activity vs placebo, on top of standard of care*

Percentage change in CLASI-A score from baseline over time (primary endpoint at Week 16)\*



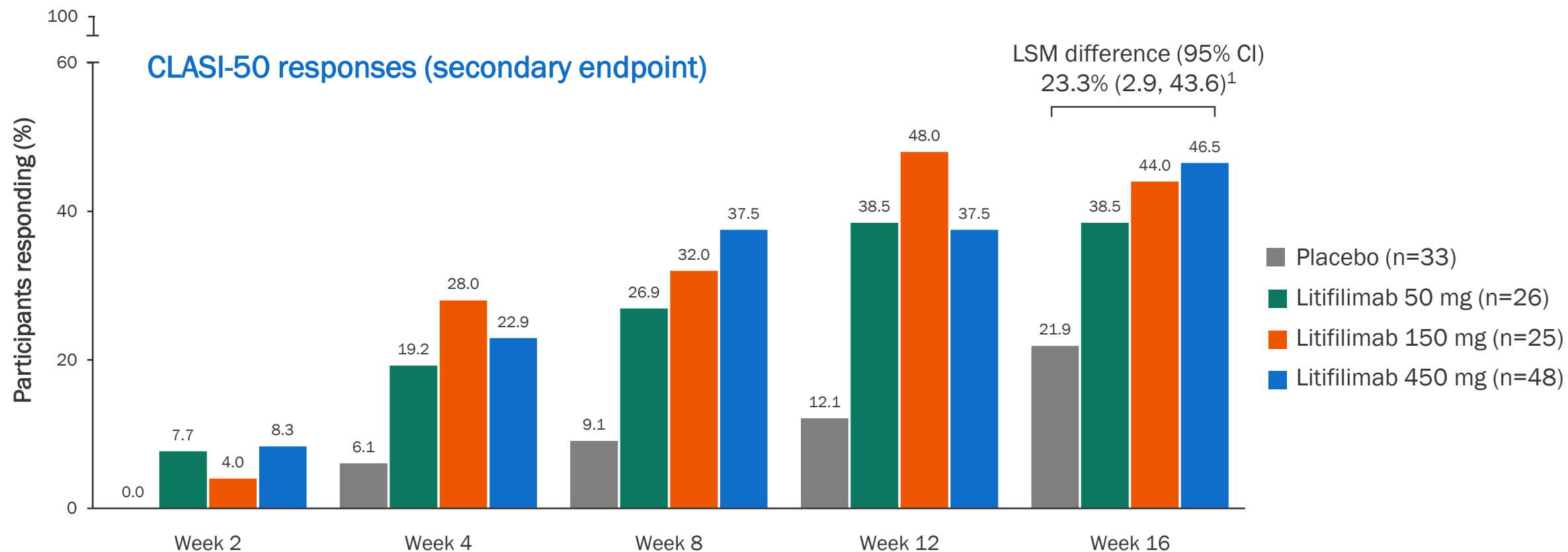
Observed consistent safety profile with no new safety signals

\*Mixed-effects model for repeated measurements; <sup>†</sup>P<0.05 versus placebo; <sup>‡</sup>P≤0.001 versus placebo

CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLE = cutaneous lupus erythematosus; CI = confidence interval; LSM = least squares mean; SE = standard error

1. Werth VP, et al. N Engl J Med 2022;387:321-331

# LITIFILIMAB ALSO SHOWED SIGNIFICANT DEPTH OF RESPONSE IN CLE



Almost half of all patients at the two highest doses showed greater than 50% improvement in skin manifestation at 16 weeks

The study was not powered to assess the secondary endpoints, and no definitive conclusions can be drawn from these results.

CI = confidence interval; CLASI-50 =  $\geq 50\%$  improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLE = cutaneous lupus erythematosus; LSM = least squares mean

1. Werth VP, et al. N Engl J Med 2022;387:321-331; 2. Werth VP, et al. Oral presentation at ACR 2020 (Abstract 0986)

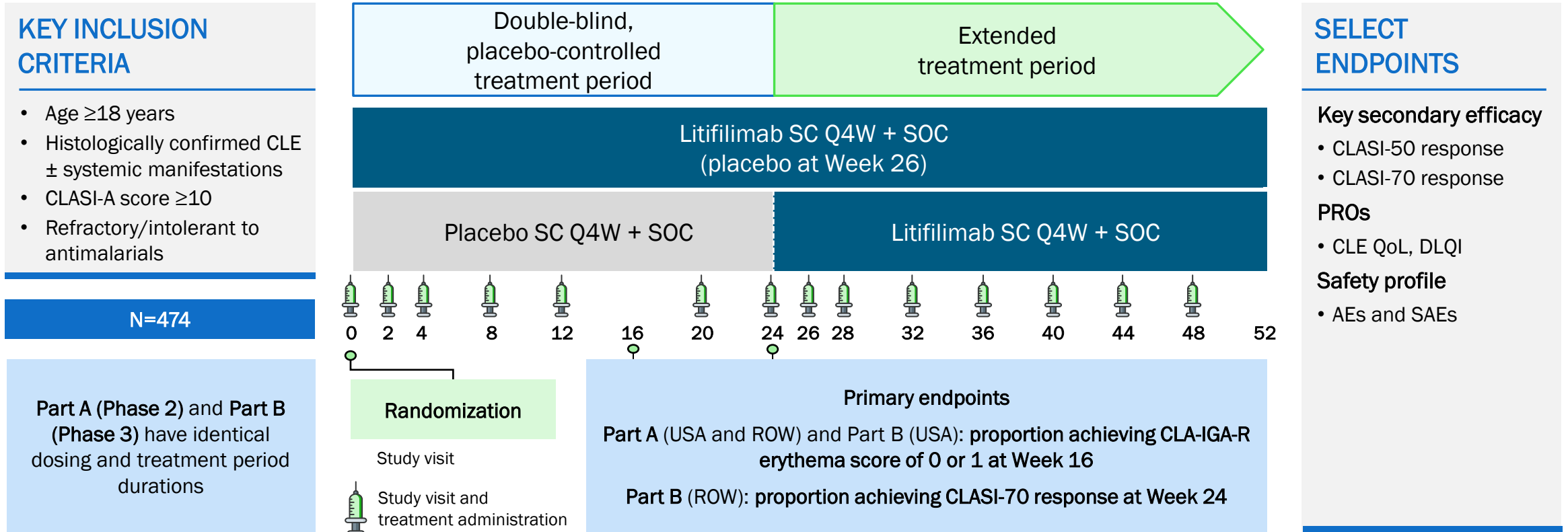
# PATIENT EXHIBITED REDUCED ERYTHEMA, SCALES, AND SWELLING ON THE FACE



After 24 weeks of litifilimab SC Q4W treatment:  
Patient with SLE and DLE exhibited reduced erythema, scales, and swelling on the face

# AMETHYST IS INTENDED AS A REGISTRATIONAL STUDY TO EVALUATE LITIFILIMAB IN CLE

## AMETHYST study design<sup>1,2</sup>



AE = adverse event; CLA-IGA-R = Cutaneous Lupus Activity of Physician's Global Assessment-Revised; CLASI-50/70 =  $\geq 50/70\%$  improvement from baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-D = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Damage; CLE = cutaneous lupus erythematosus; CLEQoL = Cutaneous Lupus Erythematosus Quality of Life; DLQI = Dermatology Life Quality Index; PRO = patient-reported outcome; Q4W = every 4 weeks; ROW = rest of the world; SAE = serious adverse event; SC = subcutaneous; SCLE = subacute cutaneous lupus erythematosus; SELENA = Safety of Estrogens in Lupus Erythematosus National Assessment; SFI = Systemic Lupus Erythematosus Disease Activity flare index; SOC = standard of care

1. Werth V, et al. J Invest Dermatol. 2023;143(5 Supp):S100 (Abstract 583). 2. NCT05531565. Updated: July 8, 2024. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT05531565> (Accessed September 20, 2024)

# THE LILAC STUDIES SUPPORT COMPELLING PROOF OF CONCEPT FOR LITIFILIMAB IN BOTH SLE AND CLE

## SLE (Lilac A)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

**Trial of Anti-BDCA2 Antibody Litifilimab for Systemic Lupus Erythematosus**

Richard A. Furie, M.D., Ronald F. van Vollenhoven, M.D., Kenneth Kalunian, M.D., Sandra Navarra, M.D., Juanita Romero-Diaz, M.D., Victoria P. Werth, M.D., Xiaobi Huang, Ph.D., George Clark, B.S., Hua Carroll, M.D., Adam Meyers, M.S., Cristina Musselli, M.D., Catherine Barbey, Ph.D., and Nathalie Franchimont, M.D., Ph.D., for the LILAC Trial Investigators\*

Published September 7, 2022 N Engl J Med 2022;387:894-904 DOI: 10.1056/NEJMoa2118025

## CLE (Lilac B)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

**Trial of Anti-BDCA2 Antibody Litifilimab for Cutaneous Lupus Erythematosus**

V.P. Werth, R.A. Furie, J. Romero-Diaz, S. Navarra, K. Kalunian, R.F. van Vollenhoven, F. Nyberg, B.H. Kaffenberger, S.Z. Sheikh, G. Radunovic, X. Huang, G. Clark, H. Carroll, H. Naik, F. Gaudreault, A. Meyers, C. Barbey, C. Musselli, and N. Franchimont, for the LILAC Trial Investigators\*

Published July 27, 2022 N Engl J Med 2022;387:321-331 DOI: 10.1056/NEJMoa2118024

Further supported by investment partnership with Royalty Pharma

# LITIFILIMAB HAS THE POTENTIAL TO TREAT PATIENTS IN BOTH SLE AND CLE

- Litifilimab targets BDCA2 as a once-monthly subcutaneous injection focused on modulating expression of IFN-1 as well as other pro-inflammatory cytokines
- Delivered successful Phase 2 Proof of Concept trials in both SLE and CLE; both published in the New England Journal of Medicine
- Meaningful data across joint, skin and overall symptoms
- Investment partnership for Phase 3 studies with Royalty Pharma in 2025
- Running two Phase 3 studies in SLE and a third in CLE

*First SLE data expected in 2026 with CLE data expected in 2027*

# CONCLUDING REMARKS



Priya Singhal, M.D., M.P.H.

Head of Development

# LUPUS IS A KEY COMPONENT OF A STRENGTHENING PIPELINE TO SUPPORT OUR LONG-TERM GROWTH OBJECTIVE

Phase 1	Phase 2	Phase 3		Regulatory Review in Certain Markets
BIIB142 (IRAK4 degrader)* – Autoimmune disease <i>Phase 1 planned</i>	BIIB080 (tau ASO)^ Early AD	Lecanemab (Aβ mAb)* SC-AI Initiation Early AD	Felzartamab (anti-CD38 mAb) – AMR	Lecanemab (Aβ mAb)* SC-AI Maintenance Early AD <i>Now FDA approved</i>
Felzartamab (anti-CD38 mAb) – LN	BIIB122 (LRRK2 inhibitor)* – PD	Lecanemab (Aβ mAb)* Preclinical AD	Felzartamab (anti-CD38 mAb) – IgAN	HD Nusinersen (SMN2 splice modulator) SMA <i>PDUFA Sept 22</i>
	BIIB091 (peripheral BTK Inhibitor) – MS	Dapirolizumab pegol (anti-CD40L)* – SLE	Felzartamab (anti-CD38 mAb) – PMN	Zuranolone (GABA <sub>A</sub> PAM)* – PPD <i>Now approved in U.K. Positive CHMP opinion in E.U.</i>
	Felzartamab (anti-CD38 mAb) DSA- MVI <i>Phase 2 planned</i>	Litifilimab (BDCA2 mAb) – SLE	SKYCLARYS (Nrf2 activator) – Pediatric FA	
		Litifilimab (BDCA2 mAb) – CLE	Zorevunersen (SCN1A ASO)* – Dravet syndrome	
		Salanersen (BIIB115) (SMN ASO)^ – SMA <i>Phase 3 planned by early 2026</i>		

■ AD and Dementia  
 ■ Immunology  
 ■ MS  
 ■ Nephrology  
 ■ Neurodevelopmental  
 ■ Neuromuscular disorders  
 ■ Neuropsych  
 ■ Parkinson's disease

Pipeline Updates: Added = BIIB142 in autoimmune disease \*Collaboration program; ^ Licensed from Ionis Pharmaceuticals, Inc.; AD = Alzheimer's disease; AMR = antibody mediated rejection; ASO = antisense oligonucleotide; CLE = cutaneous lupus erythematosus; FA = Friedreich ataxia; GABA = γ-Aminobutyric acid; HD = higher dose; IgAN = IgA nephropathy; LN = lupus nephritis; LRRK2 = leucine rich repeat kinase 2; MS = multiple sclerosis; DSA- MVI = donor specific antibody negative microvascular inflammation; PAM = positive allosteric modulator; PD = Parkinson's disease; PMN = primary membranous nephropathy; PPD = postpartum depression; SC-AI = subcutaneous autoinjector; SLE = systemic lupus erythematosus; SMA = spinal muscular atrophy



# OUR DISCIPLINED SCIENTIFIC APPROACH IS POISED TO DELIVER KEY EXPECTED MILESTONES OVER THE NEXT 18 MONTHS

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## Study Starts

- ✓ *Felzartamab Phase 3 in IgAN*
- ✓ *Felzartamab Phase 3 in PMN*
- ✓ *SKYCLARYS Phase 3 in pediatric FA*
- ✓ *Zorevunersen Phase 3 in DS*
- Salanersen Phase 3 in SMA
- Felzartamab registrational Phase 2 in DSA negative MVI
- BIIB142 Phase 1 in autoimmune disease

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## Clinical Trial Readouts

- ✓ *Salanersen Phase 1b interim in SMA*
- Litifilimab Phase 3 in SLE  
*First Phase 3 by end of 2026*
- Litifilimab Phase 3 in CLE  
*Late 2026 to early 2027*
- BIIB080 Phase 2 in Early AD  
*By mid-year 2026*
- Felzartamab Phase 1 in LN  
*2026*

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## Regulatory Decisions

- ✓ *Zuranolone in PPD*  
*Now approved in U.K. & Positive CHMP opinion in E.U.*
- ✓ *LEQEMBI SC-AI maintenance in Early AD*  
*Now FDA approved*
- LEQEMBI SC-AI initiation in Early AD  
*FDA Rolling Submission initiated*
- Nusinersen (SPINRAZA) higher dose in SMA  
*FDA PDUFA: September 22, 2025*



# QUESTION & ANSWERS