



Cenerimod (SLE)

Overview & Market
Opportunity

November 2024



Forward Looking Statements

This presentation contains “forward-looking statements”. These statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements may include, without limitation, statements about ongoing clinical trials and studies or the outcomes of clinical trials and studies; cenerimod is a first-in-class oral therapy with a novel mechanism of action and potential for highly differentiated benefit-risk profile in SLE; FDA fast-track designation; potential blockbuster based on the current epidemiology, the limitations of existing treatments and cenerimod’s unique value proposition; information on the slide labeled “Cenerimod US Market Opportunity”, including but not limited to, potential launch in 2028, potential loss of exclusivity in 2036, mid-single to low-double digit percentage royalty rate on annual net sales; product margins expected to be higher than Viatri’s average; the goals or outlooks with respect to the Company’s strategic initiatives, including but not limited to the Company’s two-phased strategic vision and potential, announced and completed divestitures, acquisitions or other transactions; the benefits and synergies of such divestitures, acquisitions, or other transactions, or restructuring programs; future opportunities for the Company and its products; and any other statements regarding the Company’s future operations, financial or operating results, capital allocation, dividend policy and payments, stock repurchases, debt ratio and covenants, anticipated business levels, future earnings, planned activities, anticipated growth, market opportunities, strategies, competitions, commitments, confidence in future results, efforts to create, enhance or otherwise unlock the value of our unique global platform, and other expectations and targets for future periods. 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For more detailed information on the risks and uncertainties associated with Viatri’s, see the risks described in Part I, Item 1A of the Company’s Annual Report on Form 10-K for the year ended December 31, 2023, as amended, and our other filings with the SEC. You can access Viatri’s’ filings with the SEC through the SEC website at www.sec.gov or through our website and Viatri’s strongly encourages you to do so. Viatri’s routinely posts information that may be important to investors on our website at investor.viatri.com, and we use this website address as a means of disclosing material information to the public in a broad, non-exclusionary manner for purposes of the SEC’s Regulation Fair Disclosure (Reg FD). The contents of our website are not incorporated into this presentation or our filings with the SEC. Viatri’s undertakes no obligation to update any statements herein for revisions or changes after the date of this presentation other than as required by law.



Outline

- Summary and market opportunity
- Background on epidemiology, current treatment paths and unmet need
- How our product works and why it is differentiated
- Clinical data
- Phase 3 design

Summary and market opportunity

Cenerimod (SLE) Summary

- Cenerimod is a first-in-class oral therapy with a novel mechanism of action and potential for highly differentiated benefit-risk profile in SLE
- During the Phase 2 CARE study with over 400 patients, Cenerimod 4mg met its primary endpoint, demonstrating statistically significant and clinically meaningful reduction in mSLEDAI-2K¹ with a differentiated safety profile vs. existing SLE treatments
- FDA fast track designation, two comprehensive phase 3 studies ongoing which reflect our learnings from phase 2, including higher enrollment of INF-1 High patients
- Currently in phase 3, on schedule for full enrollment in 2025 / study expected to readout in 2026
- Potential blockbuster based on the current epidemiology, the limitations of existing treatments and Cenerimod's unique value proposition

Cenerimod US Market Opportunity

		US Opportunity Notes
Epidemiology	Treated Patients	<ul style="list-style-type: none"> Estimated ~220-240k systemic lupus erythematosus (SLE) Treated Patients¹
	Disease Severity	<ul style="list-style-type: none"> ~34% of patients are moderate, ~17% of patients are severe²
Demand	Access	<ul style="list-style-type: none"> Agent choice dependent on specific manifestations and their severity impact Well-covered patient population, physicians comfortable with prior authorizations
	Adherence	<ul style="list-style-type: none"> High SLE reported treatment compliance Potential safety profile favorable for long-term maintenance therapy
Value Proposition	Value proposition	<ul style="list-style-type: none"> Attractive oral, once daily, potential to be positioned prior to biologics First in class S1P₁ therapy in SLE Potential for premium value proposition vs. existing SLE branded agents
Commercialization	Field Force	<ul style="list-style-type: none"> Target specialty coverage across ~5k HCPs – primarily rheumatologists
	Other SG&A	<ul style="list-style-type: none"> Incremental sales, medical & marketing to support US launch Leverage existing infrastructure across reimbursement & operations
Other Assumptions	Potential Launch & LOE*	<ul style="list-style-type: none"> Potential launch in 2028 Potential loss of exclusivity (LOE) in 2036
	Partnership & Profitability	<ul style="list-style-type: none"> Mid-single to low-double digit percentage royalty rate on annual net sales Product margins expected to be higher than VTRS average

*International opportunities: EU4 + UK: ~200k treated patients, potential launch year 2029, LOE 2039, China: potential launch year - 2030, LOE – 2036

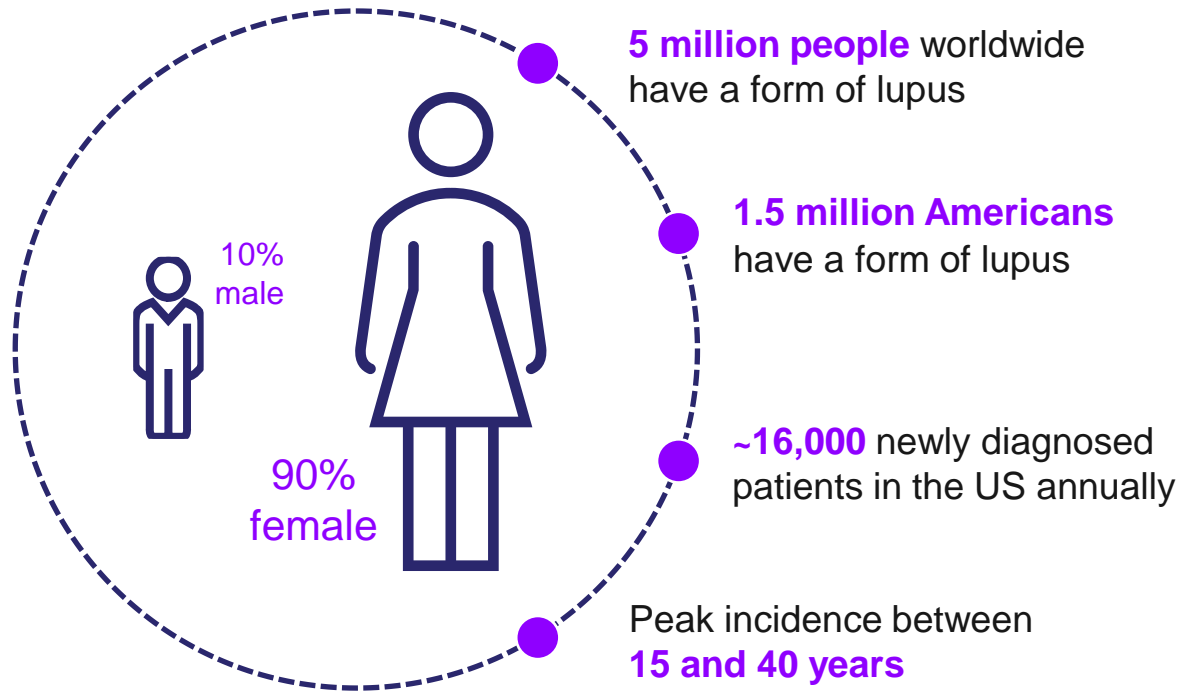
Notes: 1) Projected based on US Census, OECD, Evaluate Pharma and JRHEUM inputs and estimates 2) Per PubMed data

Sources: US Census, Evaluate Pharma, Healthcare Utilization and Costs of Systemic Lupus Erythematosus by Disease Severity in the United States (JRHEUM,) Initial disease severity, cardiovascular events and all-cause mortality among patients with systemic lupus erythematosus (PubMed), Medication decision-making and adherence in lupus: patient-physician discordance and the impact of previous 'adverse medical experiences' (PubMed)



Background on epidemiology, current treatment paths and unmet need

High Unmet Need for New Approaches in the Treatment of Systemic Lupus Erythematosus (SLE)



- ▶ Lupus can range from mild to severe depending on how it affects the body
- ▶ **Limited treatment options** with a high need for new approaches
- ▶ Despite the existence of several therapeutic agents in SLE, the disease keeps causing **significant morbidity**



Mild
joint and skin problems, tiredness



Moderate
inflammation of other parts of the skin and body, including the lungs, heart, and kidneys



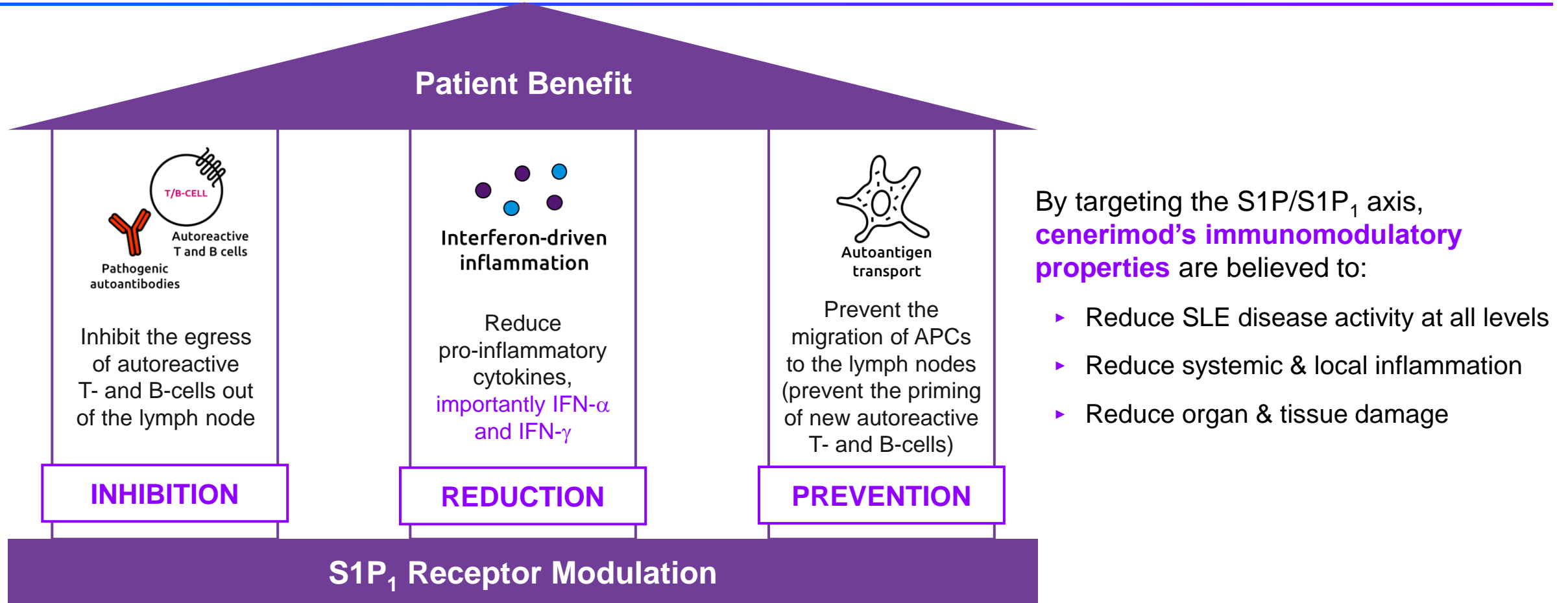
Severe
inflammation causing severe damage to the heart, lungs, brain, or kidneys, which can be life threatening

Limitations of Current SLE Treatments

Antimalarial Drugs	<ul style="list-style-type: none">▶ Hydroxychloroquine to manage skin and joint symptoms, and reduce flare frequency▶ Associated with retinal toxicity
Corticosteroids	<ul style="list-style-type: none">▶ Prednisone (among others) to control flares▶ Long-term use is associated with hypertension, hyperglycemia, Cushing syndrome, etc.
Immunosuppressants	<ul style="list-style-type: none">▶ Methotrexate, azathioprine, and mycophenolate mofetil to regulate / suppress the immune system▶ Infections and malignancy risk are the main limitations
Biologics	<ul style="list-style-type: none">▶ Belimumab (first FDA-approved biologic specifically for SLE in 2011), Rituximab (used off-label for certain cases with severe manifestations), and Anifrolumab (FDA-approved in 2021)▶ Premedication is needed for IV infusion, associated with lack / loss of efficacy and risk of anaphylaxis, increased risk of serious and fatal infections, increased malignancy risk

How our product works and why it is differentiated

Cenerimod Acts on the Three Main Pillars of SLE Pathogenesis



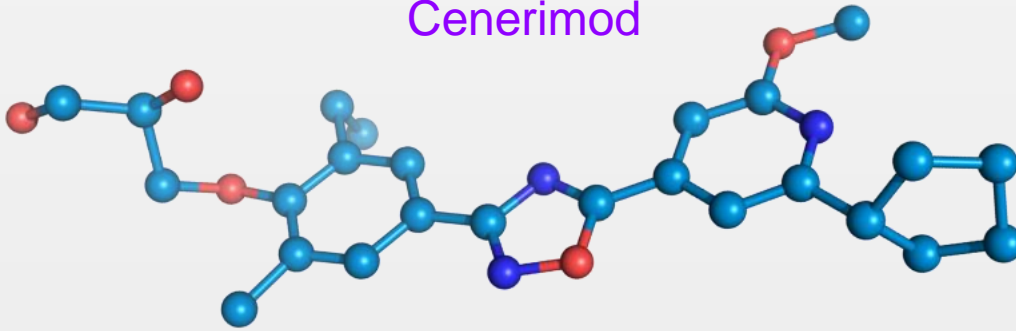
References: Strasser DS, RMD Open. 2020. PMID: 32917831; Gerossier E, Arthritis Res Ther. 2021. PMID: 34839819; Hermann V, Lupus Sci Med. 2019. PMID: 31798918; Askanase A, Arthritis Rheumatol. 2022;74(suppl 9):3293–7; Strasser DS, Arthritis Rheumatol. 2022;74(suppl 9):1981-2; Hoyler T, Lupus Science & Medicine. 2023. Abstract 2023-0588 Burg N et al. Nature Review Rheumatology 2022, 18

Cenerimod Targets More SLE Pathological Pathways than Any Other Recent Therapies

Compound	Mechanism of Action	Mechanism of Action Effects	Targets		
			T-cells	B-cells	Type I IFN
Cenerimod	S1P1 receptor modulator	Inhibits the egress of autoreactive T- and B-cells, reduces pro-inflammatory cytokines (incl. Type-1 IFN) and chemokines and prevents migration of antigen-presenting cells	✓	✓	✓
Benlysta® (belimumab)	B-Lymphocyte stimulator (BLyS) inhibitor	Reduces the survival of B cells, especially autoreactive B cells that produce antibodies		✓	
Saphnelo® (anifrolumab)	IFN receptor antagonist	Reduces Type-1 IFN signaling			✓
Rituximab	Anti-CD20 mAb	Causes B cell depletion		✓	

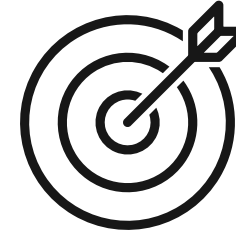
Cenerimod Unique in S1P Receptor Modulator Class

Cenerimod

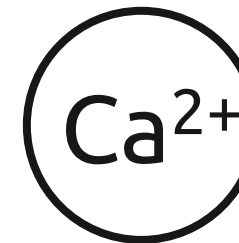


- ▶ Potent selective S1P1 modulator
- ▶ Oral, once-a-day
- ▶ Unique signaling properties (biased Ca⁺⁺ signaling) allowing:
 - ▶ Absence of vasoconstriction
 - ▶ Decreased bronchoconstriction
- ▶ Cenerimod progressive increase in exposure = gradual desensitization of the cardiac S1P receptors = mitigating cardiovascular manifestations
 - ▶ No need for up-titration to manage Heart Rate upon treatment initiation

S1P1 Selectivity



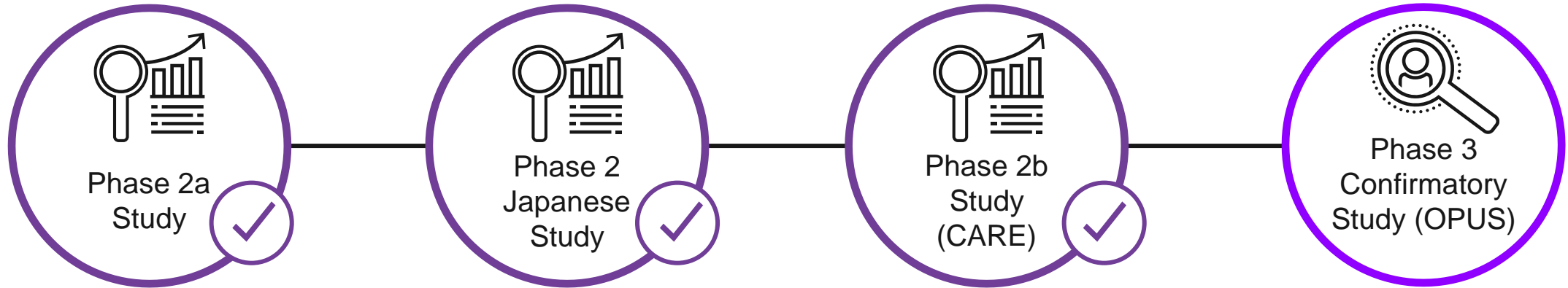
Attenuated
Calcium Response



References: Piali L, J Pharmacol Exp Ther 2011. PMID: 29226621; Rey M., PLoS One, 2013. PMID: 21345969

Clinical data

Comprehensive Phase 2 Program Conducted in SLE

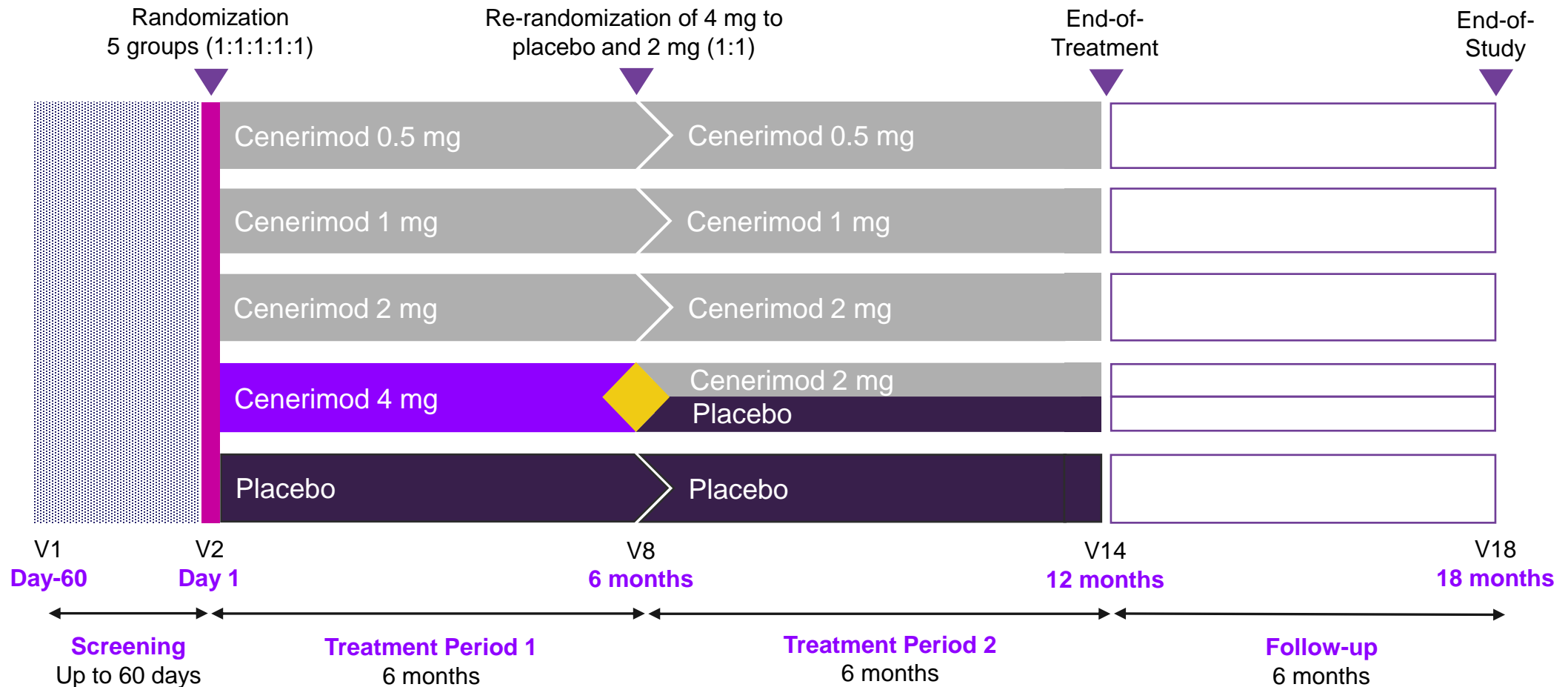


- ▶ Robust and consistent phase 2 data:
 - ▶ Efficacy results consistent across all three phase 2 studies
 - ▶ Higher response observed in expected phase 3 population (more severe patients)
 - ▶ Treatment effects continue to increase over time
 - ▶ Differentiated safety profile versus existing SLE treatments

Phase 2 CARE: Study Design

Primary Objective

Investigate Disease Activity Reduction with Cenerimod after 6 Months at 4 Different Doses (0.5, 1, 2, and 4 mg) in Subjects with Moderate to Severe SLE on Top of Standard of Care



Phase 2 CARE: Baseline Demographics & Disease Characteristics

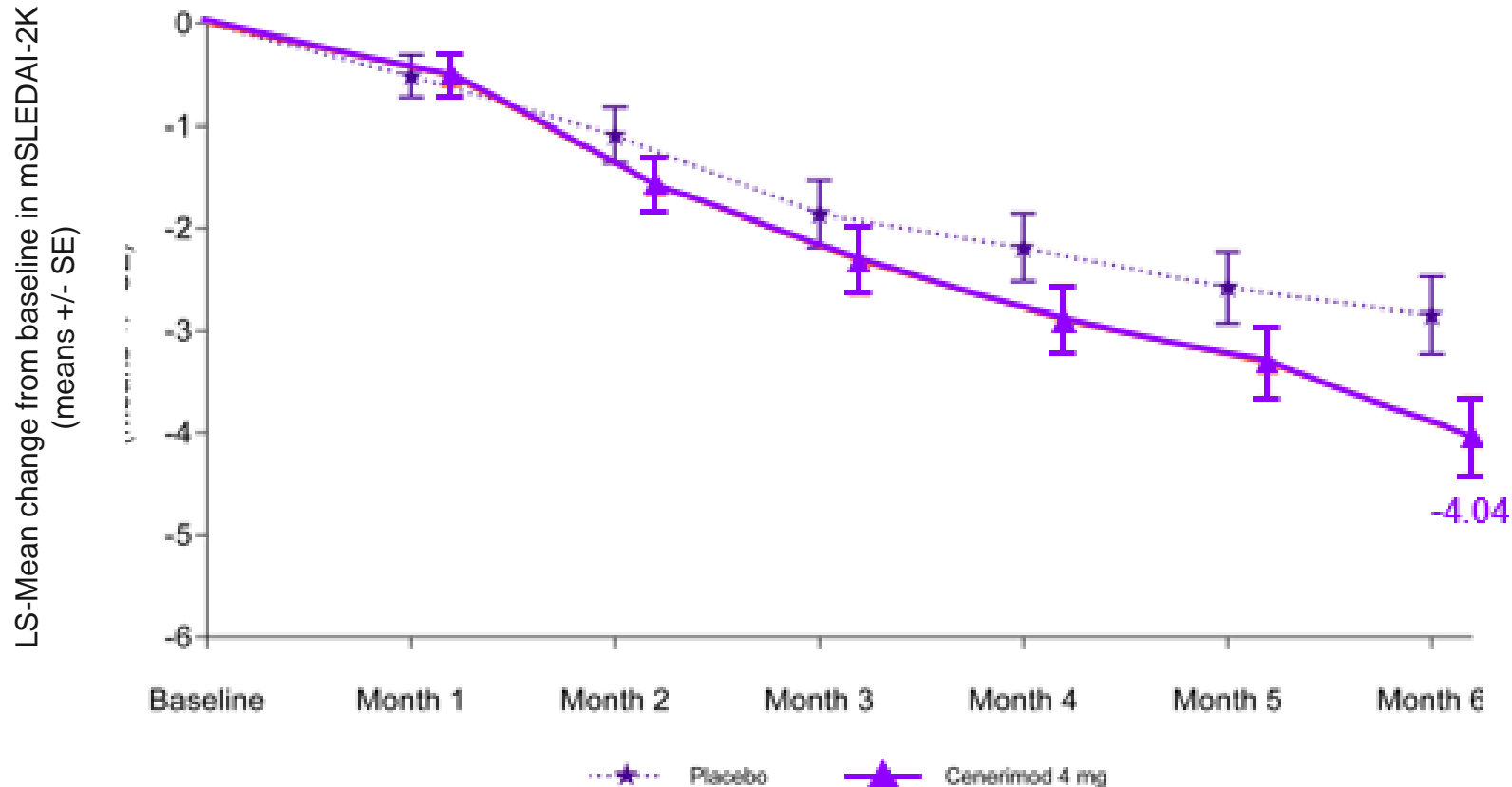
Baseline Demographics & Disease Characteristics Well-balanced across All Treatment Groups

Moderate to severe SLE patients with multiple concomitant SLE treatments

Baseline characteristics	Overall population n=427
Age, mean \pm SD	41.6 \pm 11.9
Female, n (%)	406 (95.1)
Race – White, n (%)	337 (78.9)
Background SLE treatment, n (%)	
Corticosteroids	366 (85.7)
Antimalarials	314 (73.5)
Immunosuppressives	155 (36.3)
Biologics (belimumab)	13 (3.0)
mSLEDAI-2K, mean \pm SD	9.9 \pm 3.0
IFN-1 High %	51%

Cenerimod 4mg Demonstrated Statistically Significant(1) and Clinically Meaningful Response in Phase 2 Trial

Primary endpoint (reduction in mSLEDAI-2K⁽²⁾ at Month 6)



LSM change between
cenerimod 4 mg and
placebo at **Month 6**
(95% CI)

-1.19 (-2.25, -0.12),
P=0.0291

(Nominally statistically
significant)⁽¹⁾

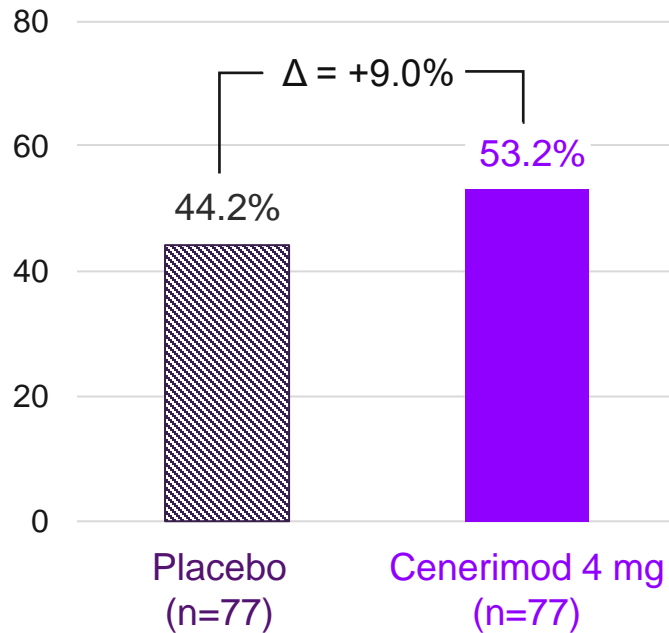
Full Analysis Set

(1) Nominally statistically significant due to the testing strategy (for adjusting for multiplicity of tests of the 4 doses against placebo)

(2) SLE disease activity index 2000 (SLEDAI-2K) modified to exclude leukopenia

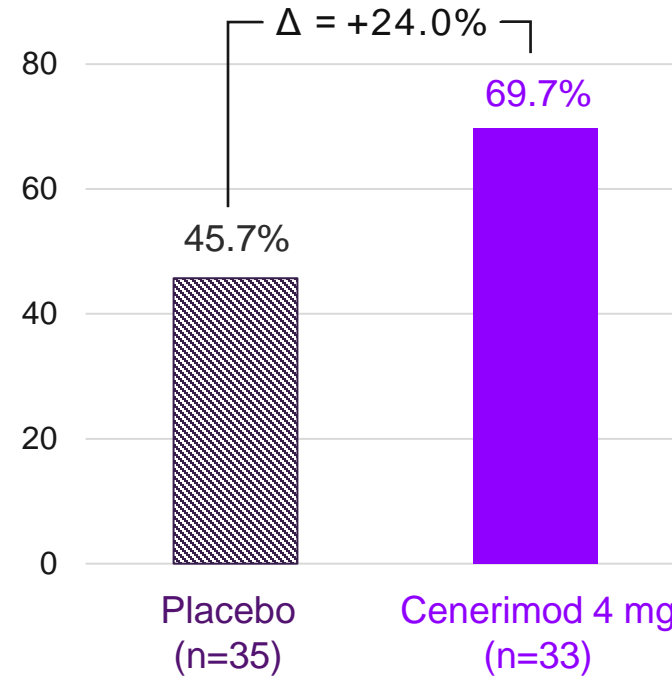
SRI-4 Response was Consistent with mSLEDAI-2K Secondary Endpoint

SRI-4 response⁽¹⁾ at 6 months (%)



Overall Population

SRI-4 response⁽¹⁾ at 6 months (%)



IFN-1 High Signature

Full Analysis Set

(1) SRI-4 response is defined as a response of all three components: mSLEDAI-2K (reduction from baseline ≥ 4), Physicians Global Assessment (increase from baseline ≤ 0.3), BILAG-2004 (no new BILAG A organ domain score and ≤ 1 new BILAG B organ domain score)

Phase 2 CARE Population Had an Under-Representation in % of IFN-1 High Patients Compared to Other Programs

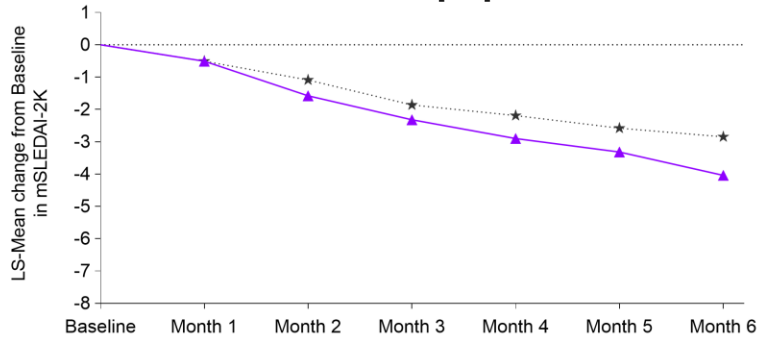
Drug	IFN-1 High (%)	Study	Source
Anifrolumab	83%	Phase 3 – Tulip-1/2	Furie / Morand 2019
Anifrolumab	75%	Phase 2 – MUSE	Furie 2017
Belimumab	83%	BLISS-52/76	Wilkinson 2020
Cenerimod	51% (4mg arm 45%)	Phase 2 – CARE	Idorsia

- ▶ IFN-1 high typically believed to represent ~70-80% of moderately to severe SLE patients⁽¹⁾
- ▶ IFN-1 high status is associated with indicators of more active and severe disease:
 - ▶ Higher levels of anti-dsDNA, and lower levels of C3 & C4
 - ▶ Arthritis & skin disease
 - ▶ Proteinuria and increased risk of progression to lupus nephritis

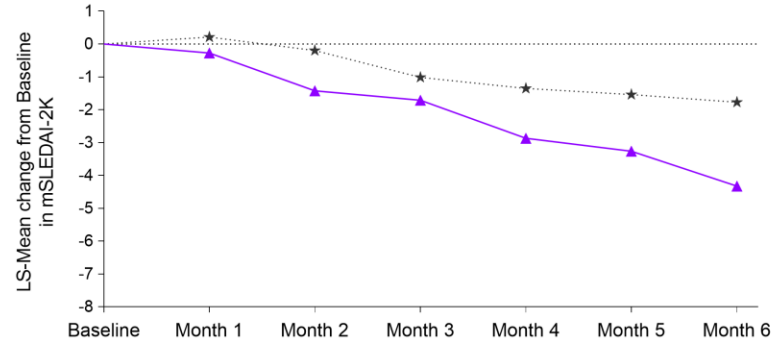
(1) CARE manuscript submitted and under review

Phase 2 CARE: Cenerimod Treatment Effect Consistently Increased in More Severe Patients vs. the Overall Population

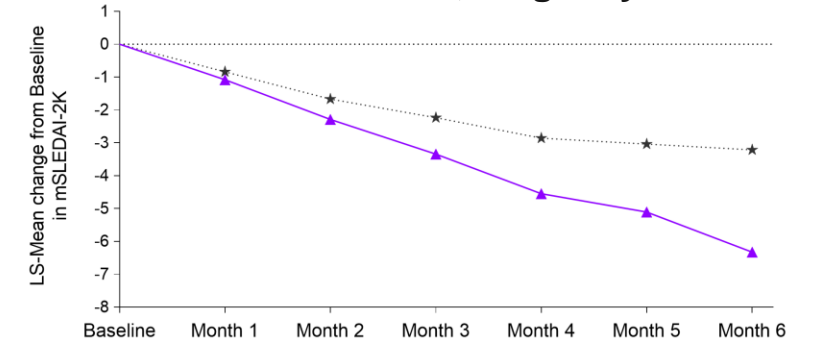
Overall population



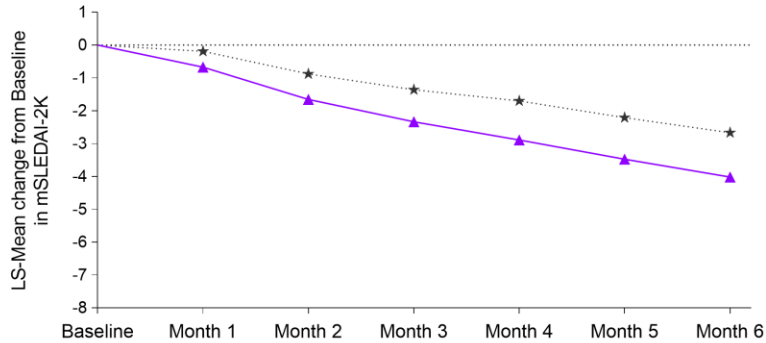
Anti-dsDNA ≥ 30 IU/ml



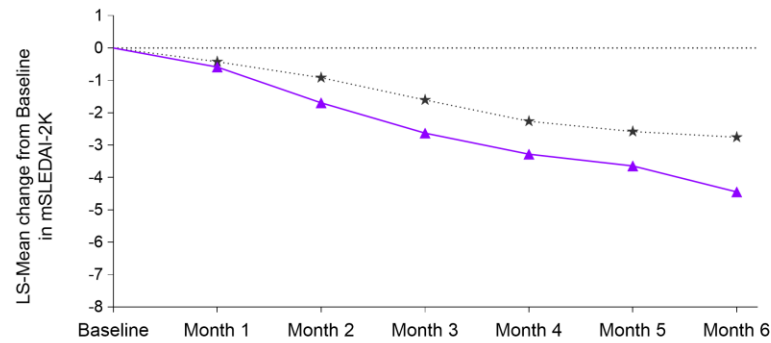
C4 < LLNR, 4mg only



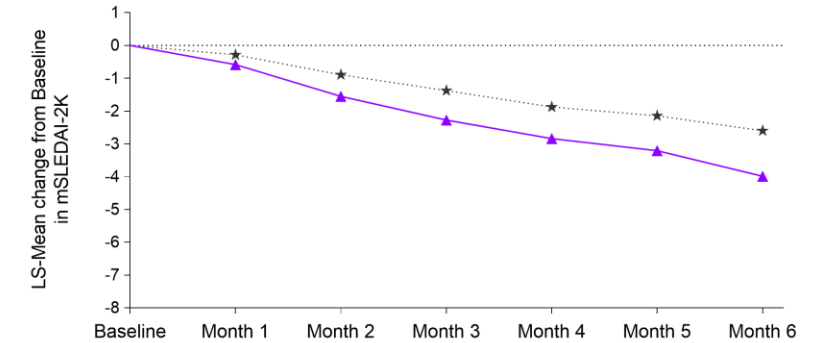
≥ 10 SLEDAI-2K



≥ 7.5 mg OCS



BILAG 1A and/or 2B



...★... Placebo
 —▲— Cenerimod 4 mg

Phase 2 CARE: Low Rates of AEs and SAEs, Generally Similar Across Treatment Groups

Onset During 6-Month Treatment

Subjects with at least one	Cenerimod 0.5 mg N=85 n (%)	Cenerimod 1 mg N=85 n (%)	Cenerimod 2 mg N=86 n (%)	Cenerimod 4 mg N=84 n (%)	Placebo N=86 n (%)
Adverse Event (AE)	42 (49.4)	55 (64.7)	51 (59.3)	49 (58.3)	47 (54.7)
AE leading to study drug discontinuation	1 (1.2)	3 (3.5)	9 (10.5)	8 (9.5)	4 (4.7)
Serious adverse event	0	3 (3.5)	2 (2.3)	2 (2.4)	3 (3.5)
Fatal AE	0	1 (1.2)	0	0	0
Adverse Events >5%⁽¹⁾					
Lymphopenia	1 (1.2)	4 (4.7)	9 (10.5)	12 (14.3)	1 (1.2)
Hypertension⁽²⁾	2 (2.4)	4 (4.7)	1 (1.2)	5 (6.0)	2 (2.3)
Headache	9 (10.6)	5 (5.9)	7 (8.1)	7 (8.3)	3 (3.5)
Abdominal pain	1 (1.2)	5 (5.9)	0	2 (2.4)	0
COVID-19	5 (5.9)	0	5 (5.8)	2 (2.4)	2 (2.3)

(1) >5% in any group and higher than placebo.

(2) Hypertension: Most subjects with AEs denoting hypertension had a medical history of hypertension and/or were receiving corticosteroids; monthly BP measurements showed no increases in mean systolic or diastolic blood pressure; hypertension did not lead to discontinuation or temporary interruption of study drug in any subjects.

Adverse Events of Special Interest: Overall Mild and Transient

Onset During 6-Month Treatment

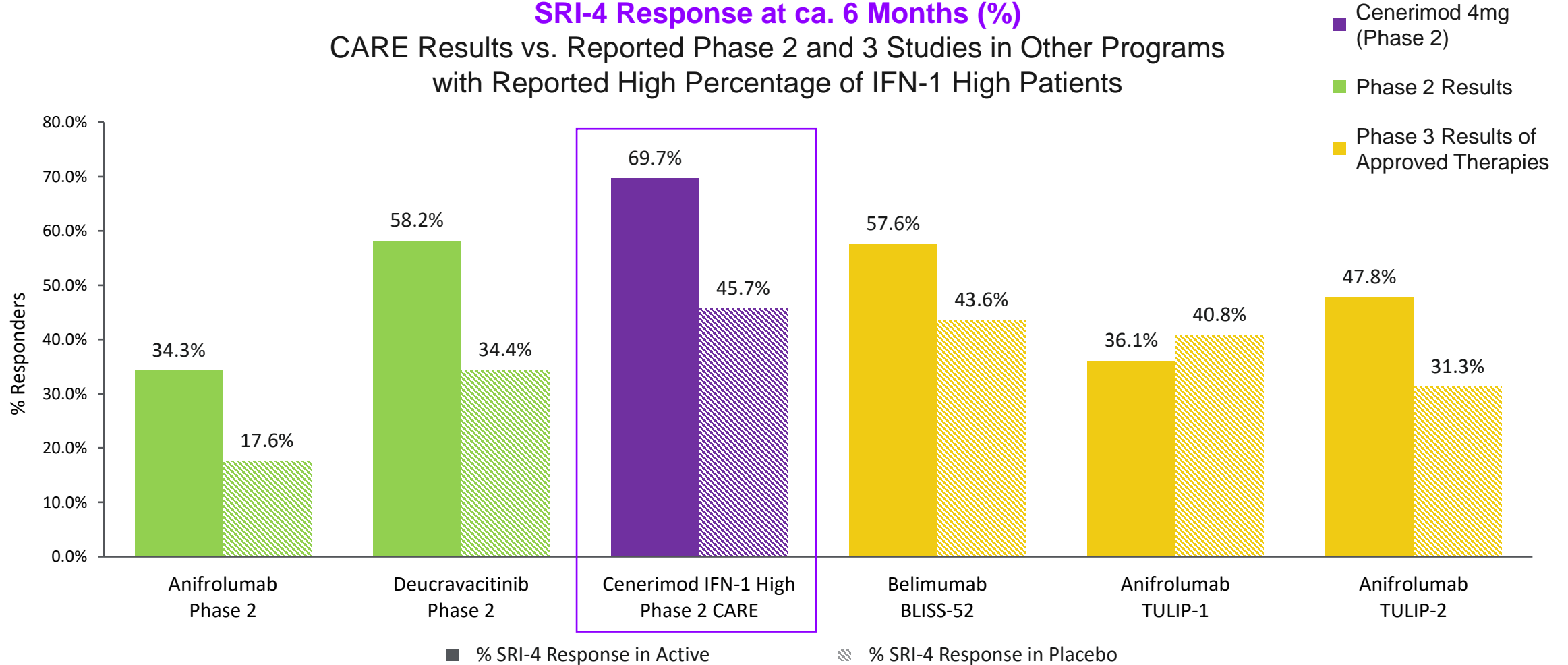
Category / Preferred Term	Cenerimod 0.5 mg N=85 n (%)	Cenerimod 1 mg N=85 n (%)	Cenerimod 2 mg N=86 n (%)	Cenerimod 4 mg N=84 n (%)	Placebo N=86 n (%)
Effect on HR and rhythm-related AEs	2 (2.4)	1 (1.2)	4 (4.7)	4 (4.8)	1 (1.2)
Infection-related AEs	8 (9.4)	3 (3.5)	7 (8.1)	3 (3.6)	8 (9.3)
Pulmonary-related AEs	1 (1.2)	3 (3.5)	2 (2.3)	3 (3.6)	2 (2.3)
Hepatobiliary disorders / liver enzyme abnormality-related AEs	2 (2.4)	4 (4.7)	2 (2.3)	1 (1.2)	0
Malignancy (non-skin) related AEs	0	0	0	0	1 (1.2)
Malignancy (skin) related AEs	0	0	0	0	0

- ▶ **Heart Rate and rhythm:** Day 1 cardiovascular monitoring revealed no unexpected finding or concern at any dose
 - ▶ No second-degree or higher AV blocks were observed
 - ▶ No increased incidence of medically relevant bradycardia or rhythm-related AEs over 6-months
- ▶ **Macular Edema:** one subject in the 1mg group was reported with macular edema adjudicated by the Ophthalmology Safety Board as not related to cenerimod as the event was already present at screening

Cenerimod Has Highly Competitive Efficacy Profile vs Other Phase 2 or Approved Treatments

SRI-4 Response at ca. 6 Months (%)




CARE Results vs. Reported Phase 2 and 3 Studies in Other Programs with Reported High Percentage of IFN-1 High Patients



Cenerimod Has an Optimized S1P Safety Profile that Compares Favorably vs Approved SLE Treatments

- ✓ First dose effect: HR reduction comparable to other S1P modulators but no need for up-titration; no unexpected finding or concern at any dose in phase 1 MAD and phase 2 studies
- ✓ Echocardiography and Holter: no clinically meaningful effect observed
- ✓ No increased risk of infections and opportunistic infections, malignancy, macular edema, liver enzyme elevations (compared to placebo)
- ✓ No clinically meaningful effect on pulmonary function and blood pressure

Treatment with Cenerimod was **not associated with an increased risk of Serious Adverse Events and infection**, a major concern to physicians and patients

	Cenerimod  CARE Phase 2		Sotyktu  (Deucravacitinib) Phase 2		Saphnelo  (Anifrolumab) Phase 2	
	4 mg (N=84)	Placebo (N=86)	3 mg bid (N=91)	Placebo (N=90)	300 mg (N=99)	Placebo (N=101)
Overall AEs (%)	78.6	70.9	93.4	87.8	84.8	77.2
Infections (%)	33.3	36.0	65.9	53.3	69.7*	55.4*
Serious AEs (%)	3.6	7.0	7.7	12.2	18.8	16.2

*Pooled safety DB (ph2 + ph3), 52-weeks



Current status: Phase 3

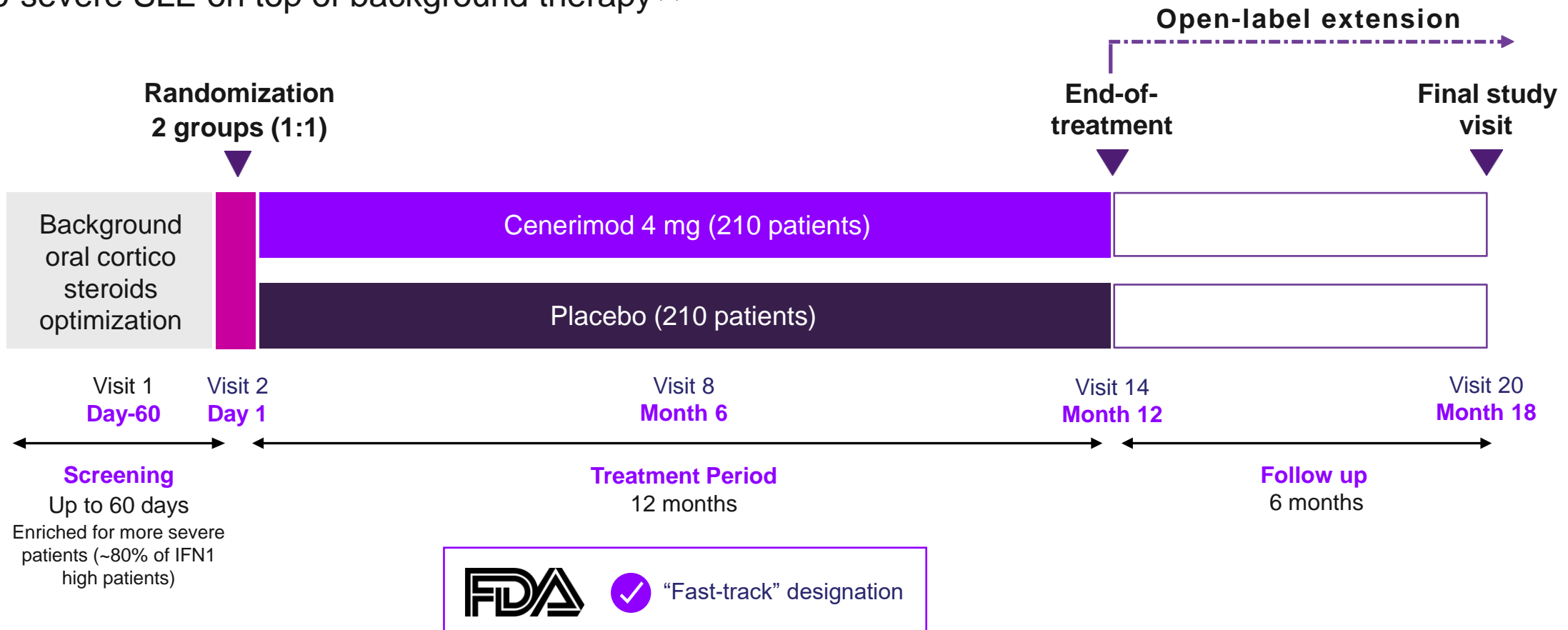


Current status: Approved

Phase 3 design

Phase 3 Study Design

Two Phase 3 multicenter, randomized, double-blind, placebo-controlled, parallel-group studies to evaluate the **efficacy**, **safety**, and **tolerability** of cenerimod in adult patients with moderate-to-severe SLE on top of background therapy⁽¹⁾



Phase 3 Study Design – Learnings from Phase 2



	Difference in study design between CARE and OPUS	Rationale based on CARE findings and HAS feedback
Design	Two adequate and well controlled studies with 840 patients (420 per study)	Study powered for type I error of 5% (p <0.05) study powered for key secondary endpoints
Population	<ul style="list-style-type: none"> • IFN-1 high (75 to 85%) • BILAG 1A and/or 2B • PGA ≥ 1.0 on a 0 to 3 VAS • EGFR: include severely impaired patients • Anti-Smith (anti-Sm) antibody elevated to above normal 	Enriched responder population vs CARE to maximize treatment effect
Primary Endpoint	SRI-4 response	<ul style="list-style-type: none"> • 24% more SRI-4 responders with cenerimod 4 mg than placebo in IFN-1 High population • Regulatory precedent and supported by both FDA and EMA at EOP2 meeting
Timing of Primary Endpoint	12 months	Cenerimod maximum treatment effect (delta vs placebo) expected by 12 months
Oral Corticosteroids	Forced tapering	Allow detection of OCS sparing – maximize treatment effect (if tapering not achieved patients are considered non-responder)