



Zenas BioPharma

Enabling patients with autoimmune diseases to reimagine life

Corporate Presentation

October 2026



Disclaimer

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Forward-looking statements include, but are not limited to, statements regarding Zenas BioPharma, Inc.'s ("Zenas," the "Company," or "our") plans, objectives, expectations and intentions; our future financial or business performance; the timing and potential regulatory approval and commercialization of our product candidates, including the timing of and potential approval and commercial launch of obexelimab in IgG4-RD; the timing and results of ongoing and future clinical trials, including the timing of reporting the topline results from the SunStone trial and, if successful, the timing of a potential Phase 3 study in SLE; the timing of reporting Phase 1 clinical data and, if successful, the timing of initiation and reporting clinical data in the Phase 1 (POC) clinical trial of ZB021 in patients; the timing of regulatory submissions, including timing of our submission of a marketing application to the EMA for obexelimab in IgG4-RD; subject to IND clearance, the timing of initiation of Phase 1 clinical studies of ZB022 and ZB014 and reporting clinical data in 2027; the potential commercial opportunities for our product candidates, including the potential market size; the estimated disease prevalence and diagnosed patient population; the potential competition for our product candidates; the potential commercial attributes and opportunities for our product candidates; the potential for obexelimab to build a rheumatology franchise; the potential for obexelimab to be a front-line or preferred treatment option; the potential for obexelimab to be a differentiated treatment option; the potential for obexelimab to provide a safe and effective option for long-term maintenance treatment; the potential to pause obexelimab for vaccinations or management of illness; the ability of oral therapies to match the safety and efficacy of established biologics; our launch planning, including the size and timing for hiring of commercial field personnel; and the Company's cash guidance, including the ability to fund operations into 2029. 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Accomplished Executive Team

Extensive experience developing and commercializing biopharmaceuticals



Lonnie Moulder
Chief Executive
Officer &
Chairman



Joe Farmer
President &
Chief
Operating
Officer



**Lisa von Moltke,
M.D.**
Head of R&D &
Chief Medical
Officer



**Haley Laken,
Ph.D.**
Chief Scientific
Officer



Jerald Korn
Chief Legal and
Strategy Officer



**Heinrich
Schlieker**
Chief Technical
Officer



**Caroline
Chevalier**
Chief
Administrative
Officer

Deep experience across numerous biotech and pharmaceutical companies

70+ IND filings

30+ BLA/NDA filings

30+ Commercial product launches





Advancing a Portfolio of Potentially Best-in-Class I&I Product Candidates



Positioned to become a multi-franchise, fully-integrated, commercial-stage biopharmaceutical company

2026

- ✓ BLA accepted by FDA; May 2027 PDUFA date for obexelimab in IgG4-RD
- ✓ Two late-stage franchise programs for four I&I indications
- ✓ Early-stage programs with best-in-class potential
- ✓ Experienced team with strong track record of success
- ✓ Global development and commercialization capabilities
- ✓ Cash runway into 2029; capitalized to commercialize and advance pipeline



2031

- ✓ Potential approval of three¹ potentially best-in-class franchise molecules across five I&I indications
- ✓ Global commercial presence in indications representing markets of >\$30B²

Rheumatology and neuro-immune portfolio with recognized regulatory paths and significant commercial potential

Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Territory
Obexelimab (CD19 and FcγRIIb bifunctional mAb)	IgG4-RD	May 27 th PDUFA date; positive Phase 3 INDIGO trial ¹				Global excluding BMS territories ²
	RMS	Phase 2 MoonStone trial met primary endpoint				
	SLE	Phase 2 SunStone trial data expected in 4Q 2026				
Orelabrutinib (BTK inhibitor)	PPMS	Phase 3 Primrose trial ongoing				Global
	naSPMS	Phase 3 Monarch trial ongoing				
ZB021 (Oral IL-17AA/AF inhibitor)	I&I	Clinical data expected in 4Q 2026				Global excluding China & SE Asia ³
ZB022 (Brain-penetrant TYK2 inhibitor)	I&I	Clinical data expected 2027				Global
ZB014 (half-life extended CD19 and FcγRIIb mAb)	I&I	Clinical data expected 2027				Global

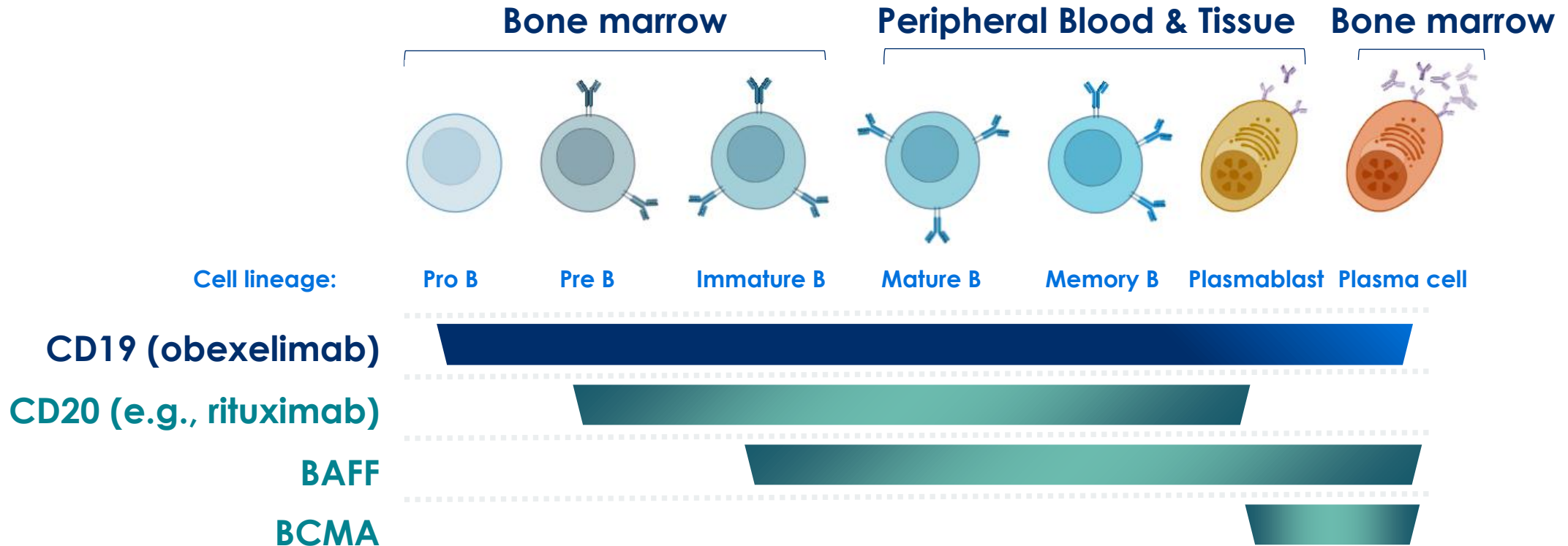
Multiple clinical and regulatory milestones throughout remainder of 2026 and in 2027



Obexelimab: a Potential I&I Franchise Molecule



Targeting CD19 and Fc γ RIIb provides broad coverage of B cell lineage

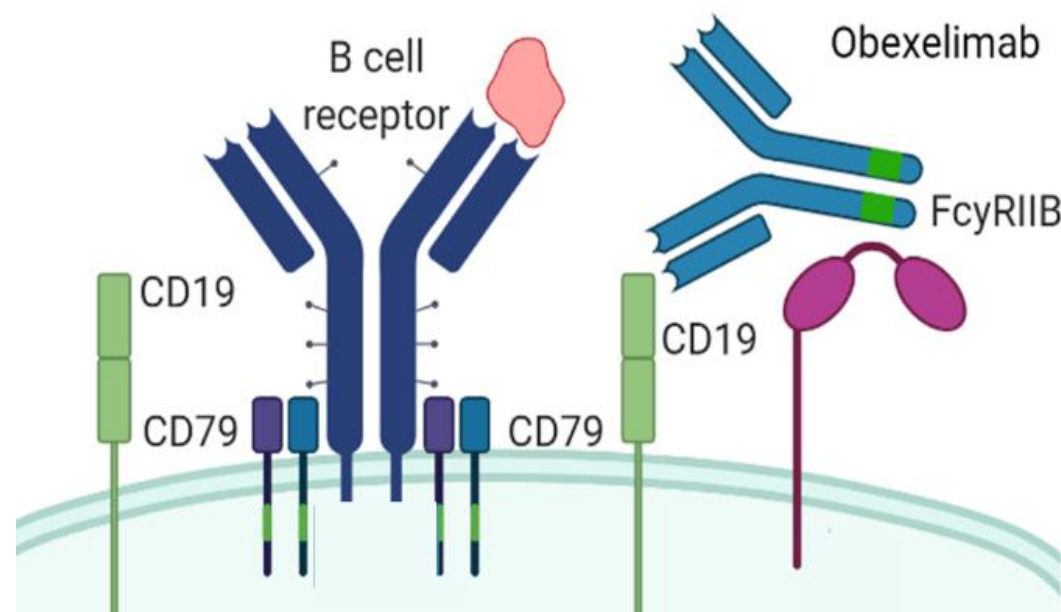


CD19 broadly **expressed across B cell lineage**, including **pro-B cells, pre-B cells, B cells, plasmablasts** and select **plasma cells**¹

Obexelimab is a differentiated B cell targeted therapy with a novel bifunctional MoA

Obexelimab's **co-engagement** of CD19 and FcγRIIb designed to result in an **inhibition of B cells**, rather than effector cell-dependent depletion¹⁻⁵

- FcγRIIb engagement **mimics the natural inhibitory signaling triggered by antigen-antibody** complexes
- Fc engineered to increase FcγRIIb affinity **~230-fold vs. native IgG1**¹
- **Avoids ADCC / CDC-mediated depletion** with activity independent of immune effector cell presence²
- **Potent inhibition of B cell** antibody production, proliferation, cytokine secretion, and antigen presentation to T cells¹⁻⁴
- **Persistent inhibitory activity** in blood and **within tissues**⁵
- Subcutaneous **dosing regimen selected for optimal pharmacokinetic and clinical activity**



Source: Zenas BioPharma

Targeting CD19 and Fc γ RIIb has the potential to build a rheumatology franchise

Compound	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Milestone	Partnerships ^{2,3}
Obexelimab ¹ (CD19 and Fc γ RIIb bifunctional mAb)	IgG4-RD	Phase 3 INDIGO trial primary endpoint and key secondary endpoints met				BLA decision by the FDA expected by May 2027 ⁴ MAA validation expected 4Q 2026	 ROYALTY PHARMA
	RMS	Phase 2 MoonStone 12-week primary endpoint met; 24-week data reported				Completion of open-label extension	
	SLE	Phase 2 SunStone trial enrollment complete				Topline results for overall & biomarker populations expected Q4 2026	
ZB014 (half-life extended CD19 and Fc γ RIIb mAb)	I&I	IND enabling ongoing				Phase 1 data expected in 2027	



IgG4-RD – Disease Overview & Current Treatment Landscape



IgG4-RD is a debilitating chronic fibro-inflammatory disease often affecting multiple organs potentially resulting in irreversible damage

Disease Overview:

- Patients present with **single or multi-organ involvement** and a progressive increase in new or worsening disease flares¹
- Early inflammatory disease progresses to a fibrotic stage, leading to **irreversible tissue damage and organ failure**¹

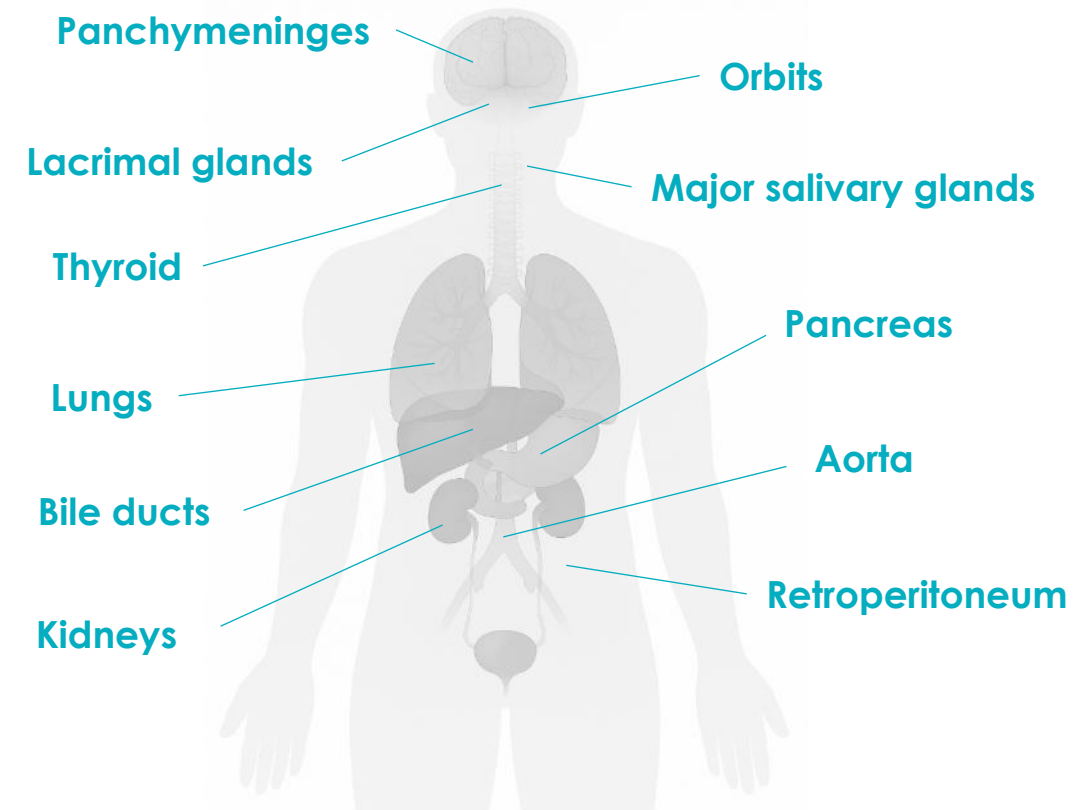
Pathophysiology:

- **Driven by expansion of CD19+ and IgG4+ B cells and plasmablasts** with significant tissue infiltration
 - Inflammatory cytokines and T cell activation through antigen presentation further exacerbate inflammation & fibrosis

Patient Population:

- IgG4-RD **affects approximately 30,000 to 40,000 people** in the U.S. with similar global prevalence²

IgG4-RD: Most common organs affected



Current IgG4-RD treatment landscape and unmet need

Current Treatments:

Glucocorticoids (GCs)	Toxicity with chronic use
B-Cell Depleters (Anti-CD19 or -20 mAbs)	Immune compromise with infection risk
Disease-Modifying Antirheumatic Drugs (DMARDs)	Only modest efficacy and toxicities



Unmet Need

Patients need a convenient, reversible, effective therapy for chronic use and safe and effective long-term disease management

94% of surveyed physicians agree that IgG4-RD is a disease that requires proactive maintenance treatment.¹

Current SOC have **limitations** that make chronic therapy difficult

IgG4-RD is a **chronic disease** that requires **chronic therapy**

Novel treatment strategies are needed for IgG4-RD

- As a chronic progressive and debilitating disease, **most patients require safe, effective, and convenient treatment options for long-term disease management**
- **Glucocorticoids**, while effective, **are associated with cumulative toxicity** and are unsuitable for long-term use
- **B cell-depletion** is effective but **has limitations** which become more pronounced with long-term use including:
 - ⚠ **Prolonged immunosuppression**
 - ⚠ **Hypogammaglobulinemia**
 - ⚠ **Increased risk of infections**
 - ⚠ **Impaired vaccine response**
 - ⚠ **Intravenous administration and infusion-related reactions**



Obexelimab for IgG4-RD



INDIGO: A Double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of obexelimab treatment for IgG4-RD

Indigo
study

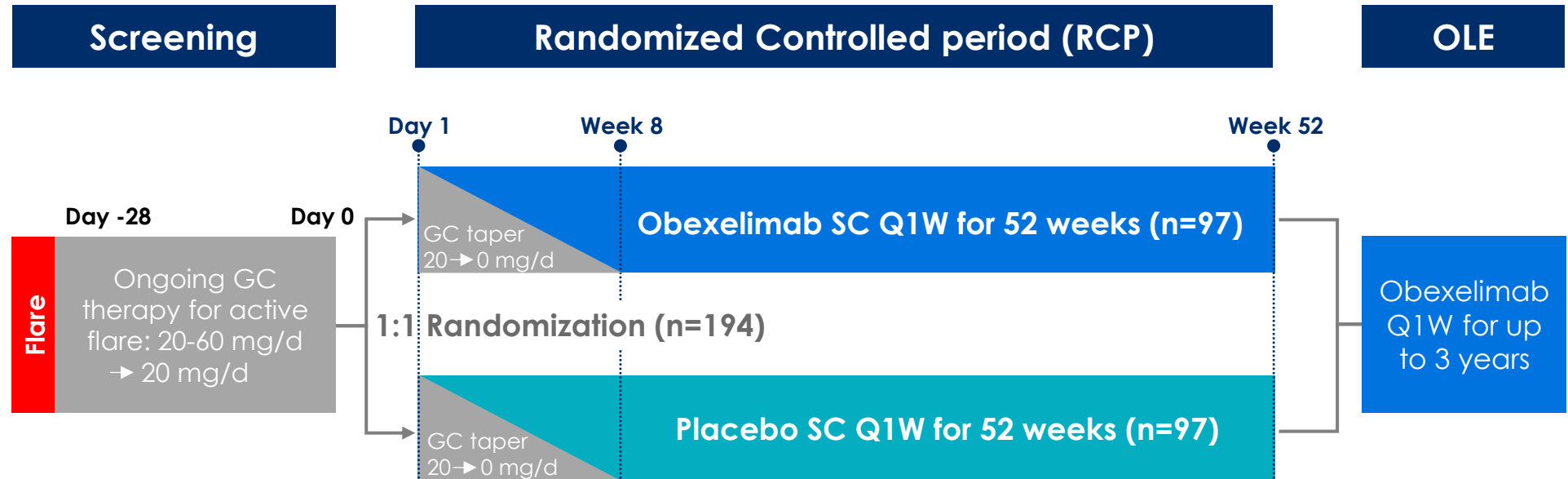


Inclusion

- Adults with IgG4-RD (ACR/EULAR-confirmed)
- Active disease **requiring** GC initiation/escalation

Exclusion

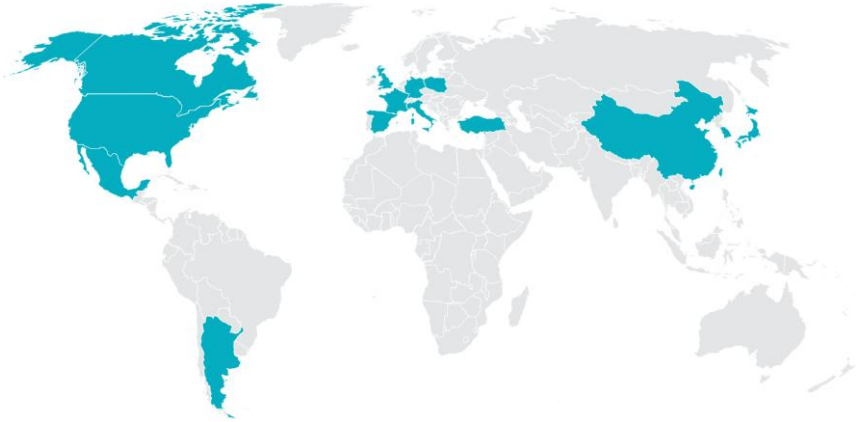
- Active infection
- Recent biologics or B-cell depletion
- High-dose steroids (>60 mg/day)



- **Primary endpoint: time to disease flare through week 52***
- Key secondary endpoints include time to investigator assessed flare, 52-week flare rate, complete remission rate, rescue medication use

INDIGO enrolled 194 patients at 114 sites across 15 countries representing a global IgG4-RD population

Enrollment Countries



EAST ASIA

- China
- Japan
- Rep. of Korea
- Taiwan

N. AMERICA

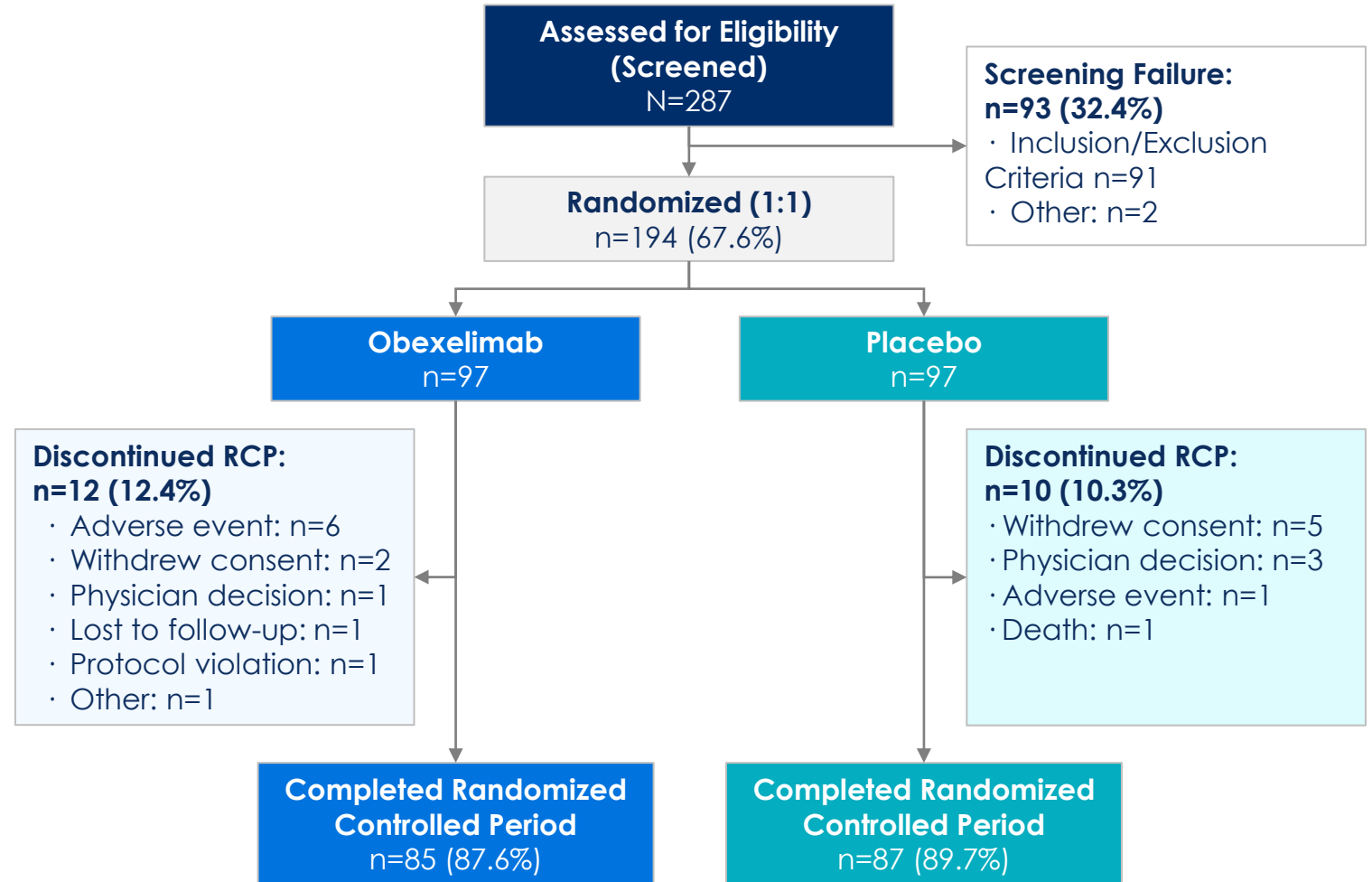
- Canada
- United States

LATIN AMERICA

- Argentina
- Mexico

EUROPE

- France
- Germany
- Italy
- Poland
- Spain
- Turkey
- United Kingdom



INDIGO is the largest clinical trial ever conducted for IgG4-RD

INDIGO baseline demographics were well balanced across both arms

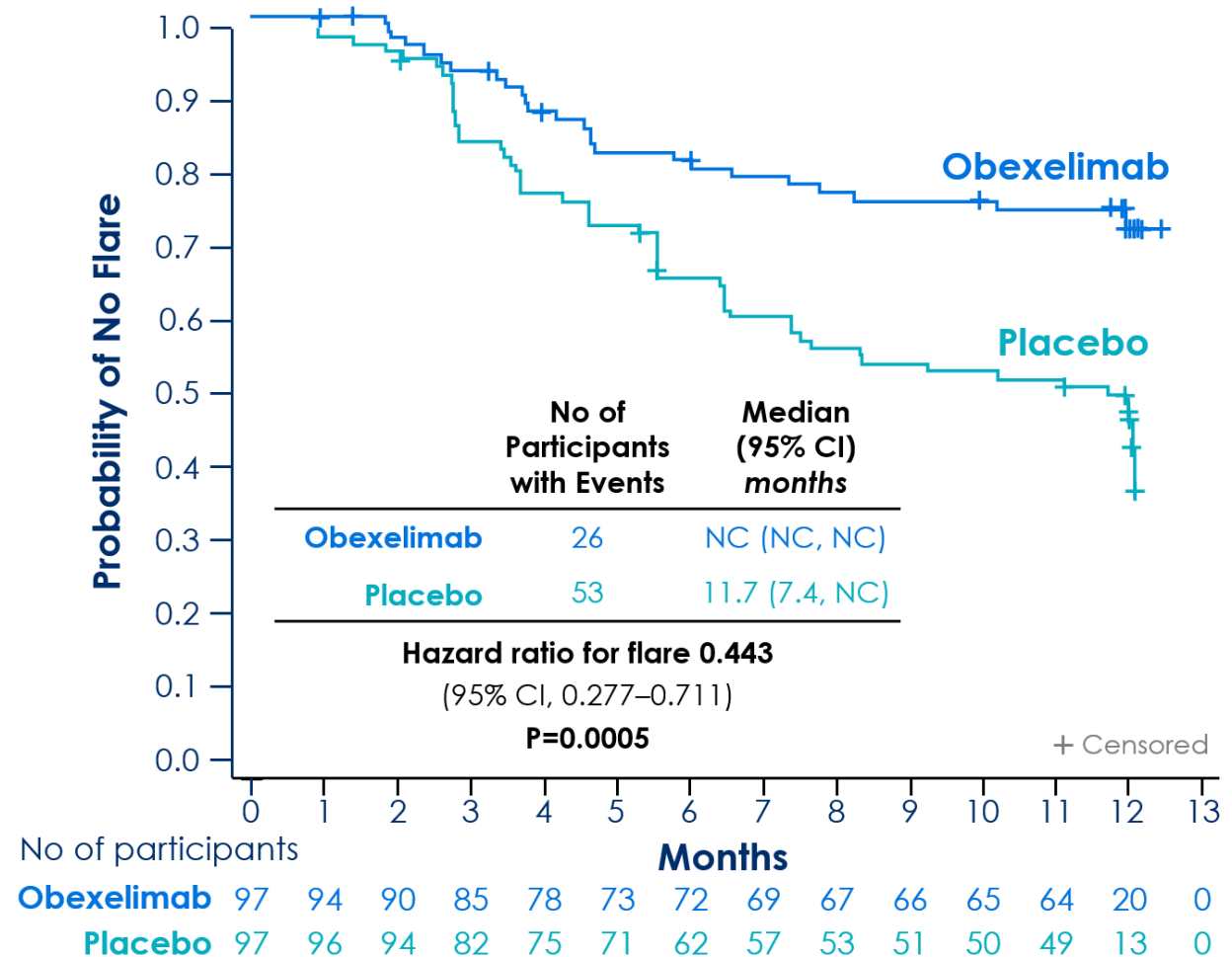
Characteristic	Obexelimab (N=97)	Placebo (N=97)
Age — yr	59.6 ± 13.4	58.7 ± 12.0
Male sex, n (%)	65 (67.0)	64 (66.0)
Race, n (%)		
Asian	59 (60.8)	51 (52.6)
White	27 (27.8)	39 (40.2)
Other	11 (11.3)	7 (7.2)
Region, n (%)		
Asia	51 (52.6)	48 (49.5)
US/Canada	24 (24.7)	16 (16.5)
Europe	19 (19.6)	28 (28.9)
Latin America	3 (3.1)	5 (5.2)

INDIGO clinical characteristics were well balanced across both arms

Characteristic	Obexelimab (N=97)	Placebo (N=97)
IgG4-related disease manifestation		
Recurrent — no. (%)	64 (66.0)	65 (67.0)
Newly diagnosed — no. (%)	33 (34.0)	32 (33.0)
Number of organs involved — no. (%)		
1	6 (6.2)	7 (7.2)
2–4	59 (60.8)	58 (59.8)
>4	32 (33.0)	32 (33.0)
Most commonly affected organs — no. (%)		
Salivary gland	60 (61.9)	66 (68.0)
Lacrimal gland	54 (55.7)	49 (50.5)
Pancreas	45 (46.4)	46 (47.4)
Lymph nodes	41 (42.3)	46 (47.4)
Disease duration — yr ¹	3.1 ± 4.2	2.5 ± 3.2
Median ACR–EULAR score (IQR) [¶]	38.0 (30.0–45.0)	38.0 (31.0–44.0)
Prior rituximab use — no. (%)	12 (12.4)	11 (11.3)

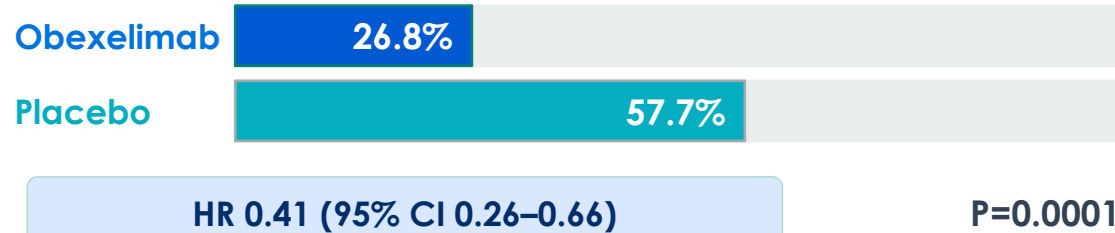
INDIGO primary endpoint, reduction in risk of disease flare, was met with high statistical significance

- **Obexelimab reduced the risk of IgG4-RD disease flare by 56% compared to placebo**
 - **73% of obexelimab patients were free of flares** (71 out of 97 patients)
 - Flares occurred in 26 patients (26.8%) on obexelimab and 53 (54.6%) on placebo

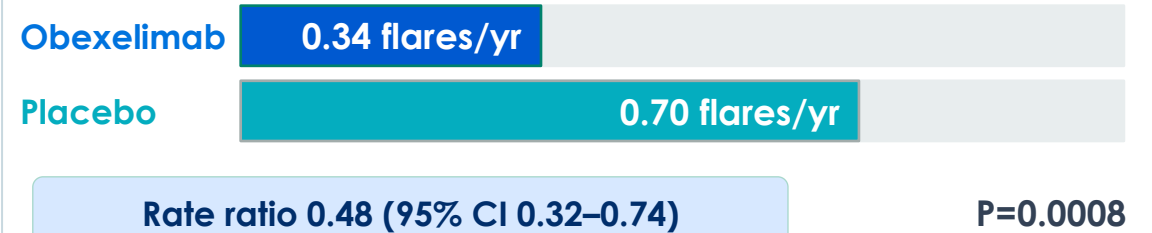


Obexelimab achieved all four key secondary endpoints with high statistical significance

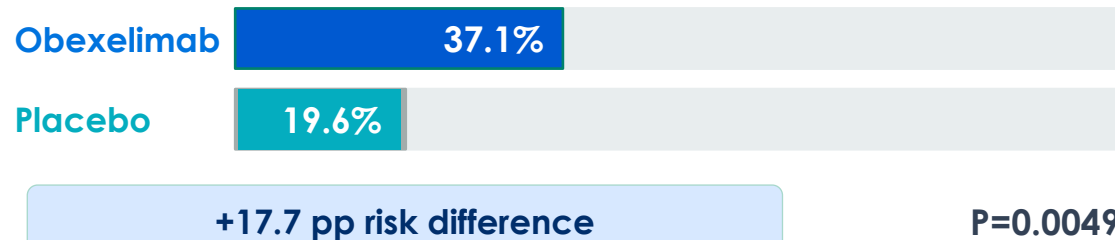
Time to first investigator-determined flare (patients with ≥ 1 flare)



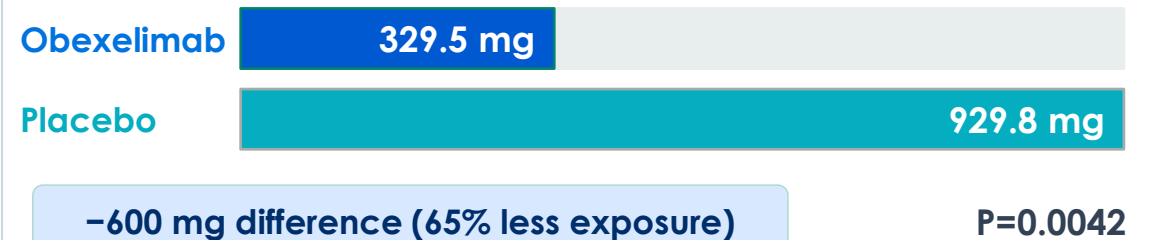
Annualized rate of adjudicated flares requiring rescue therapy



Patients achieving complete remission at Week 52



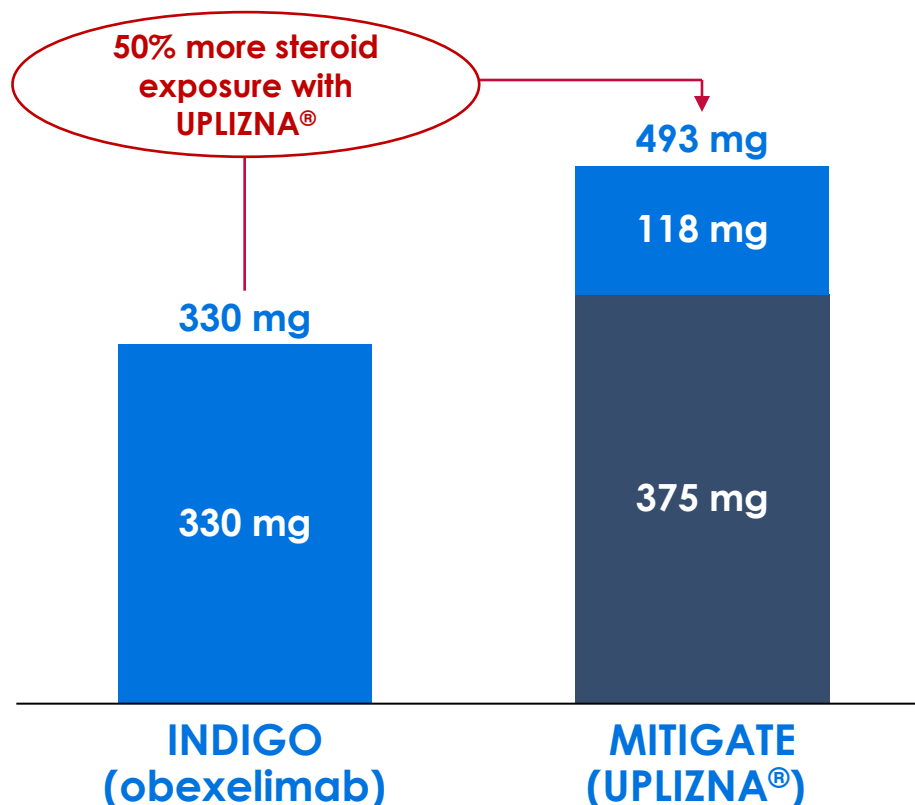
Cumulative glucocorticoid rescue dose through Week 52¹



INDIGO efficacy outcomes consistently demonstrated reductions in disease activity, flare burden, and glucocorticoid use with obexelimab across multiple endpoints

Average per-patient steroid exposure in INDIGO and MITIGATE

Total Prednisone or Equivalent use During RCP



- Rescue GC use²
- GC use as infusion premedication

- In MITIGATE, 100% of patients were exposed to at least 375 mg of steroids regardless of disease activity¹
- In INDIGO, only 23% of patients were exposed to steroids as rescue therapy²

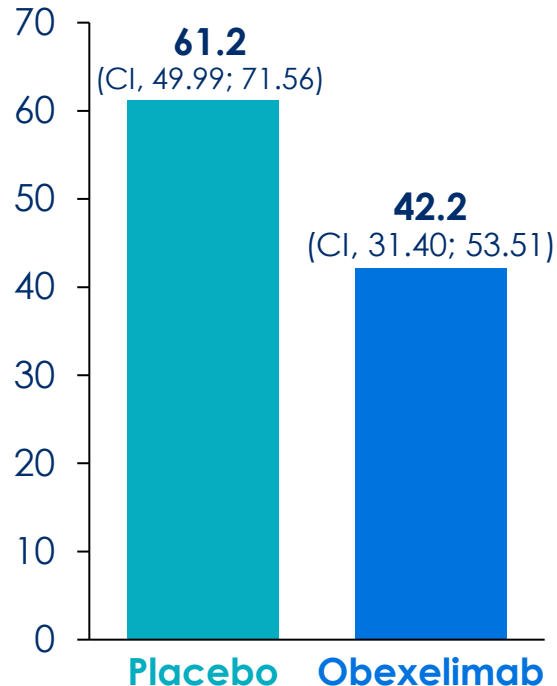
¹ Per protocol, MITIGATE required premedication with 100 mg IV methylprednisolone (or equivalent corticosteroid) prior to each infusion, patients received three infusions in the 52-week RCP. 1 mg methylprednisolone is equivalent to ~1.25 mg of prednisone or 375 mgs total across three doses

² For both trials, rescue therapy only includes GC use to treat active IgG4-RD (flare) and does not include use during the 8-week steroid taper period or to treat other conditions; obexelimab was not administered with routine GC prophylaxis for hypersensitivity prior to dosing

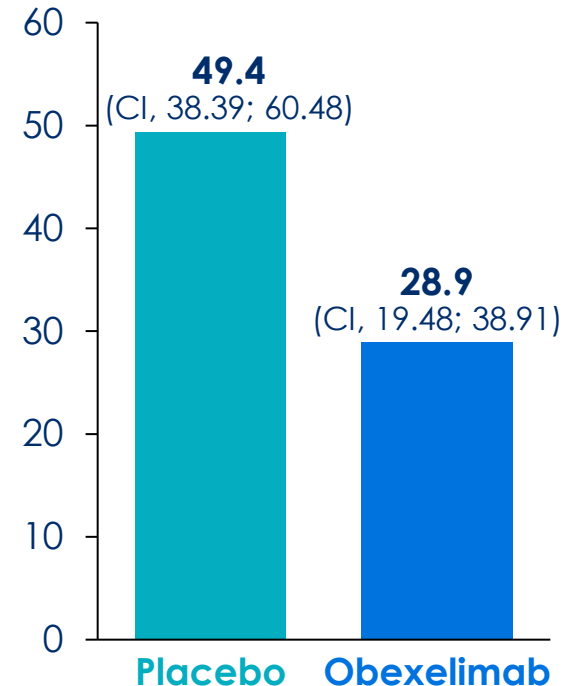
Obexelimab was associated with less accumulated glucocorticoid toxicity at week 52

Glucocorticoid Toxicity Index - Cumulative Worsening Score (GTI-CWS) measures domain-based cumulative worsening in glucocorticoid-related toxicity over time¹

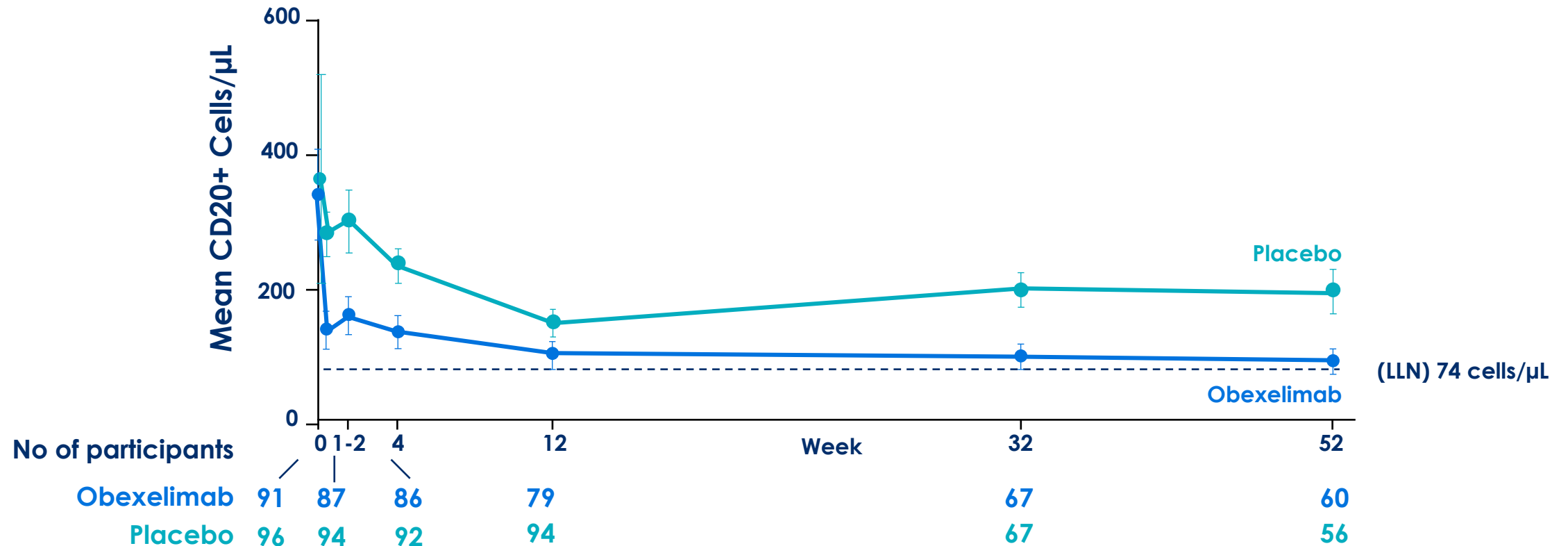
Percent of Patients With ≥ 20 Point GTI-CWS at Week 52



Percent of Patients With ≥ 30 Point GTI-CWS at Week 52



Circulating B cell levels remained above the lower limit of normal with obexelimab treatment



Maintenance of B cell levels above the lower limit of normal supports obexelimab's non-depleting inhibitory mechanism of action

The safety profile of obexelimab was consistent with placebo, with fewer serious and high-grade adverse events observed

Characteristic	Obexelimab (N=97)	Placebo (N=97)
Patients with ≥ 1 AE	95 (97.9%)	93 (95.9%)
Patients with ≥ 1 SAE	10 (10.3%)	18 (18.6%)
Patients with ≥ 1 Grade ≥ 3 AE	11 (11.3%)	23 (23.7%)
Patients with AE leading to discontinuation	9 (9.3%)	3 (3.1%)
Selected Treatment-emergent AEs (≥ 10 in either)		
Arthralgia	19 (19.6%)	11 (11.3%)
Nasopharyngitis	18 (18.6%)	14 (14.4%)
Upper respiratory infection	15 (15.6%)	22 (22.7%)
Insomnia	13 (13.4%)	10 (10.3%)
Back pain	11 (11.3%)	12 (12.4%)
Diarrhea	11 (11.3%)	6 (6.2%)
Adverse events of Special Interest		
Hypersensitivity ($\geq$ Grade 2)	16 (16.5%)	11 (11.3%)
Infections ($\geq$ Grade 3)	2 (2.1%)	4 (4.1%)
Malignancy	3 (3.1%) ¹	0
Injection site reaction ($\geq$ Grade 2)	2 (2.1%)	1 (1.0%)

INDIGO trial conclusions

- Obexelimab significantly **reduced the risk of IgG4-RD flare requiring rescue therapy** vs. placebo through Week 52
- Obexelimab **reduced cumulative glucocorticoid rescue use** and was associated with less glucocorticoid toxicity worsening versus placebo
- Obexelimab was **generally well tolerated**; no new safety signals were identified
- INDIGO demonstrated that B-cell inhibition through CD19 and FcγRIIb co-engagement may present a **novel inhibitory treatment approach** for IgG4-RD
- INDIGO supports obexelimab as **a differentiated subcutaneous therapeutic approach** for IgG4-RD

INDIGO establishes the efficacy of obexelimab as a B-cell-inhibiting agent with a distinct mechanism of action for the potential treatment of IgG4-RD

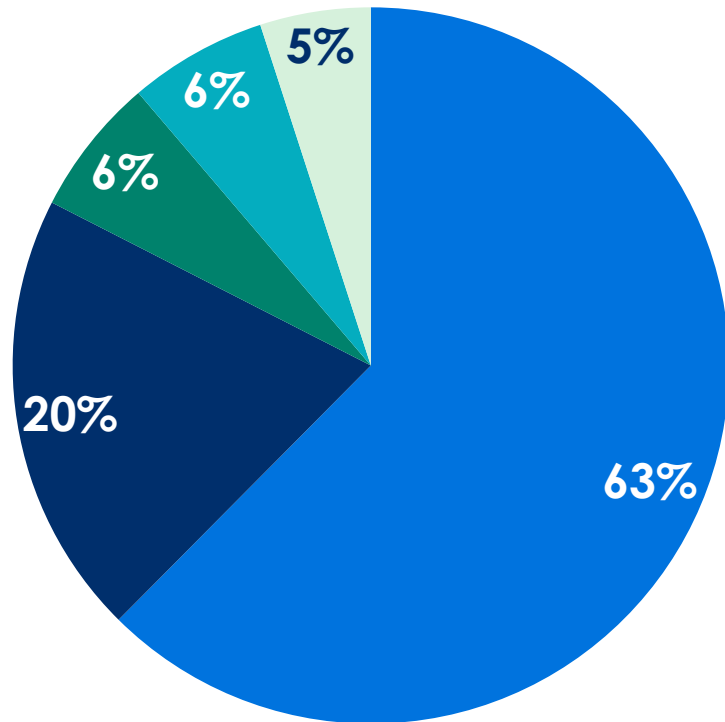


IgG4-RD Market Research



Survey of eighty U.S.-based IgG4-RD treating physicians assessed obexelimab based on INDIGO product profile

Specialty Representation



80 Survey Participants

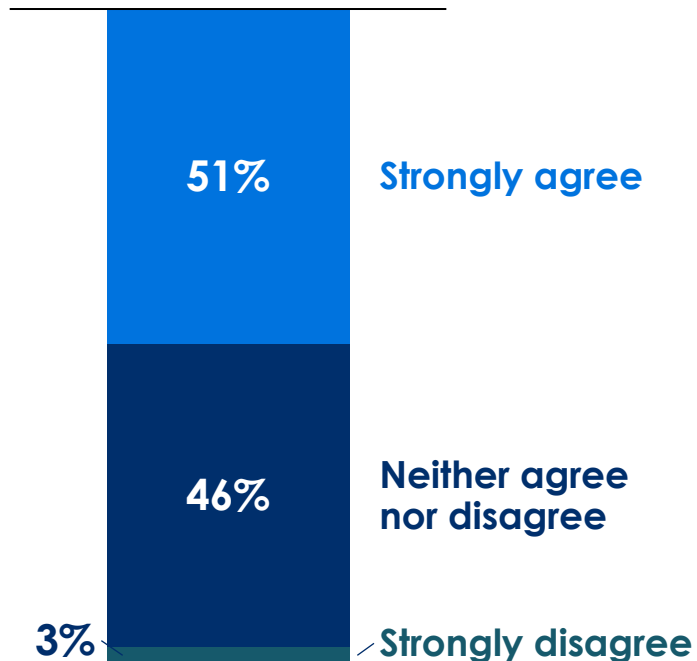
- 69% Community based; 31% Academic-based
- Participants managed ~18 IgG4-RD patients over the past year
- Greater than 80% are currently receiving drug therapy

Product Profile Key Components

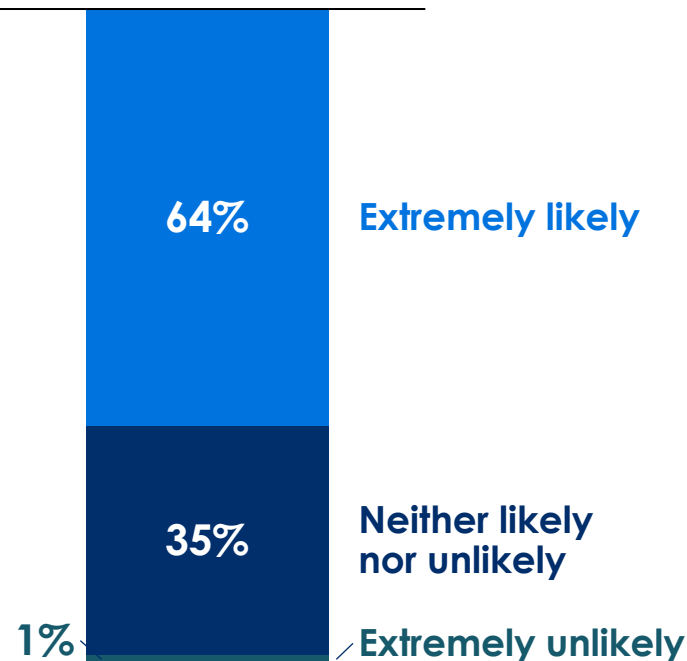
- Obexelimab deidentified as "Product X"
- Compared to placebo in randomized trial of 194 patients:
 - 56% reduction in risk of IgG4-RD flare (HR=0.443; p=0.0005), and 73% of patients flare-free through week 52
 - Superior complete remission rate (p=0.0049) and significant reduction in glucocorticoid use (p=0.0042)
 - Similar rates of SAEs, infections, and ISRs
 - Potential to pause treatment for vaccinations and treatment of intercurrent illness
- Self-administered, less than 10 second, weekly subcutaneous injection with an autoinjector pen

Majority of respondents see value in B cell inhibition over depletion and approximately two-thirds are extremely likely to prescribe obexelimab

See value in B cell inhibitor rather than a B cell depletor



Likelihood to Prescribe Obexelimab 3 Years From Now

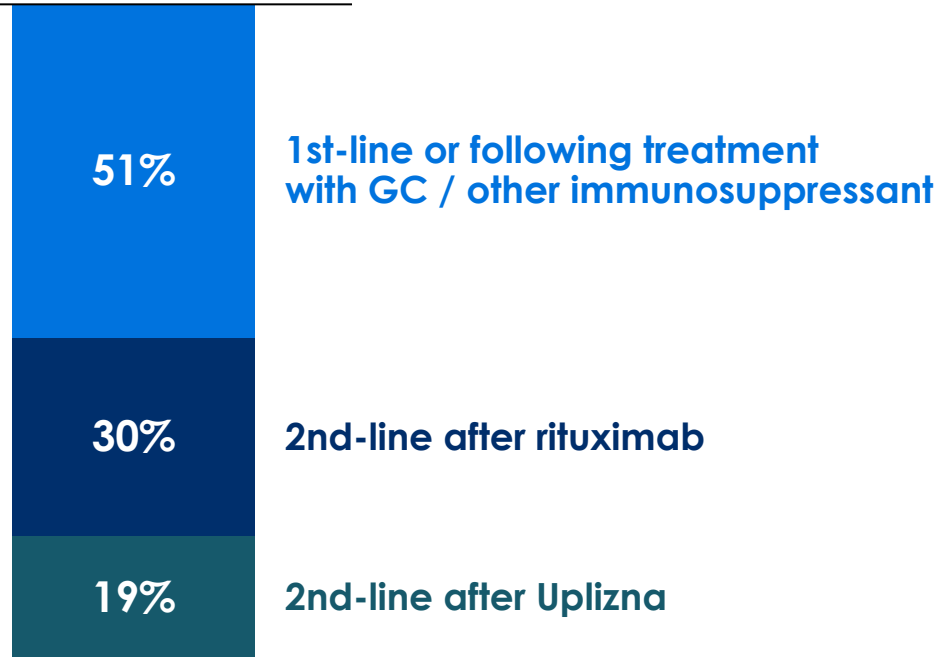


A 47% share of biologics would be allocated to Obexelimab; consistent with prior market research

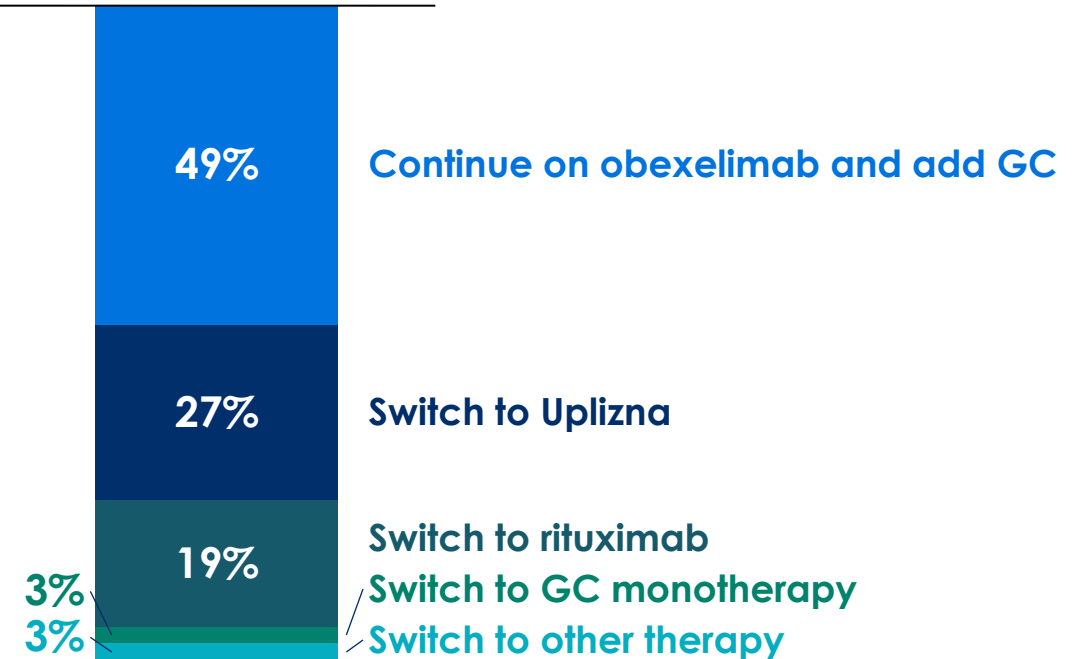
More respondents envision using obexelimab as a first-line therapy over other biologics for the overall IgG4-RD patient population

A majority of physicians would maintain patients on obexelimab after disease flare

Obexelimab Usage
by Line of Therapy

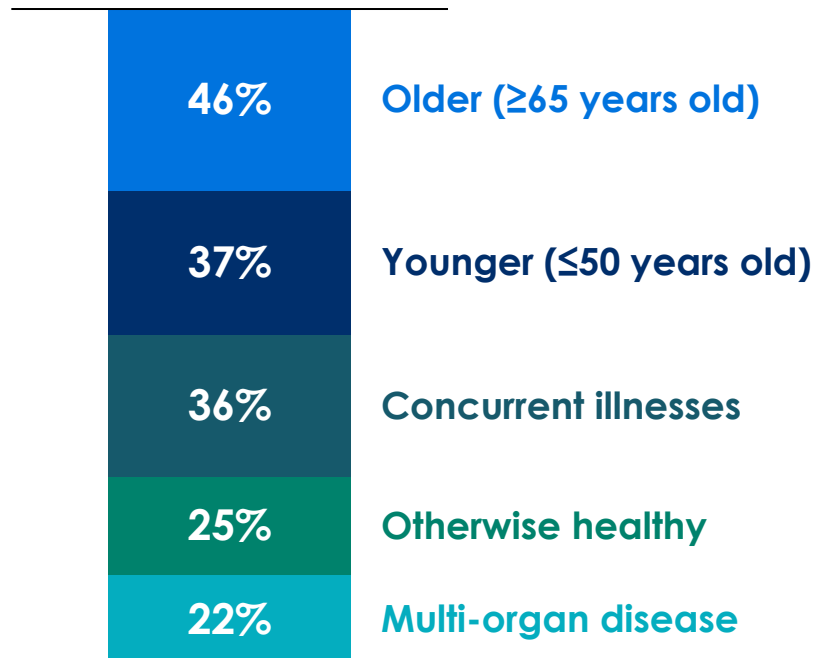


Next Steps if Flare
on Obexelimab



Obexelimab is the preferred therapy across all IgG4-RD patient segments

**IgG4-RD Patient Type
Classifications treated by survey
participants**

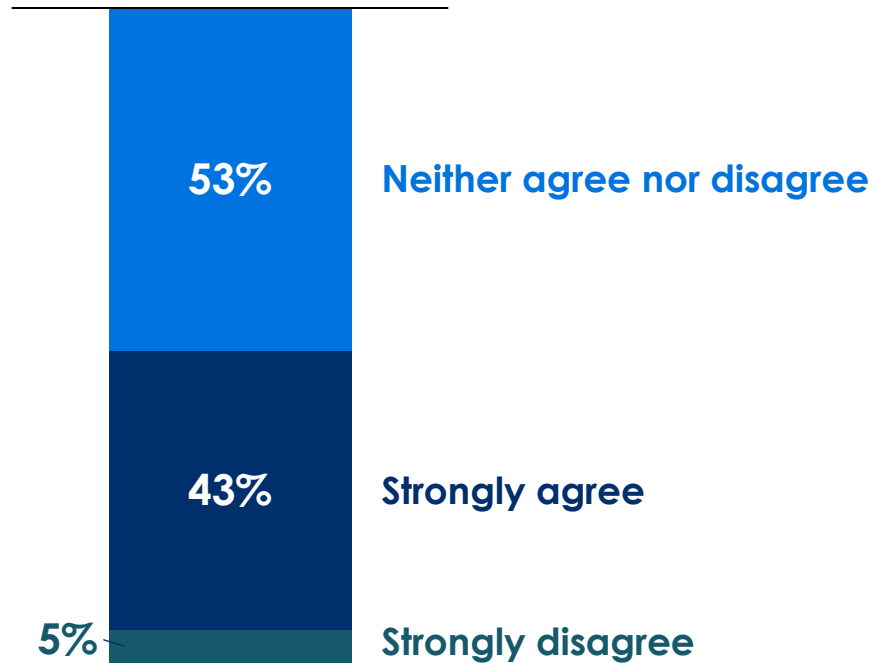


**Obexelimab share of
biologics ranged from
50%-55% across the
various patient types**

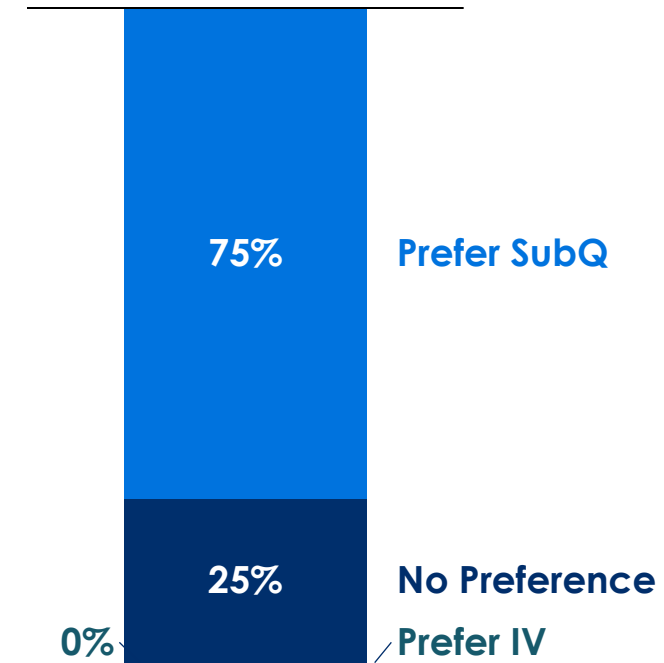
Weekly subcutaneous dosing positions obexelimab as a physician- and patient-preferred therapeutic option

Physicians and patients prefer subcutaneous administration over intravenous administration

Physician Preference
for Weekly SubQ Vs.
Q6M IV



IgG4-RD Patient RoA
Treatment Preference
(IV vs SubQ) (n=20)

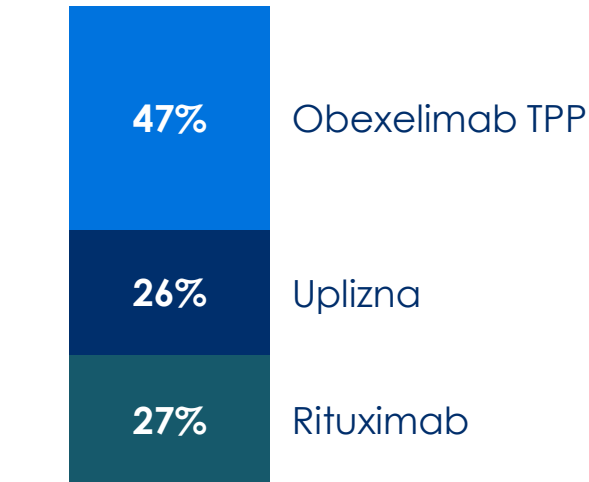


Obexelimab share preference consistent with previous market research and supports the attractiveness of key obexelimab product attributes

In a previous survey of 161 U.S. and EU3 Healthcare Professionals (HCPs), obexelimab would capture > 45% of the total biologics segment

Global market research survey

Percent share of biologics segment



Key reasons HCPs cited for choosing obexelimab:

- ✓ Self-administered SC weekly formulation with potential for robust and sustained disease control
- ✓ Inhibition versus long term B cell depletion is seen as advantageous for chronic treatment
- ✓ Potential to pause treatment for vaccination



IgG4-RD Commercial Approach



IgG4-RD, a substantial market opportunity

~30–40K

- estimated prevalent IgG4-RD cases in the U.S.¹

~25K

- Diagnosed and treated U.S. patients¹

~12.5K

- patients eligible for maintenance therapy²

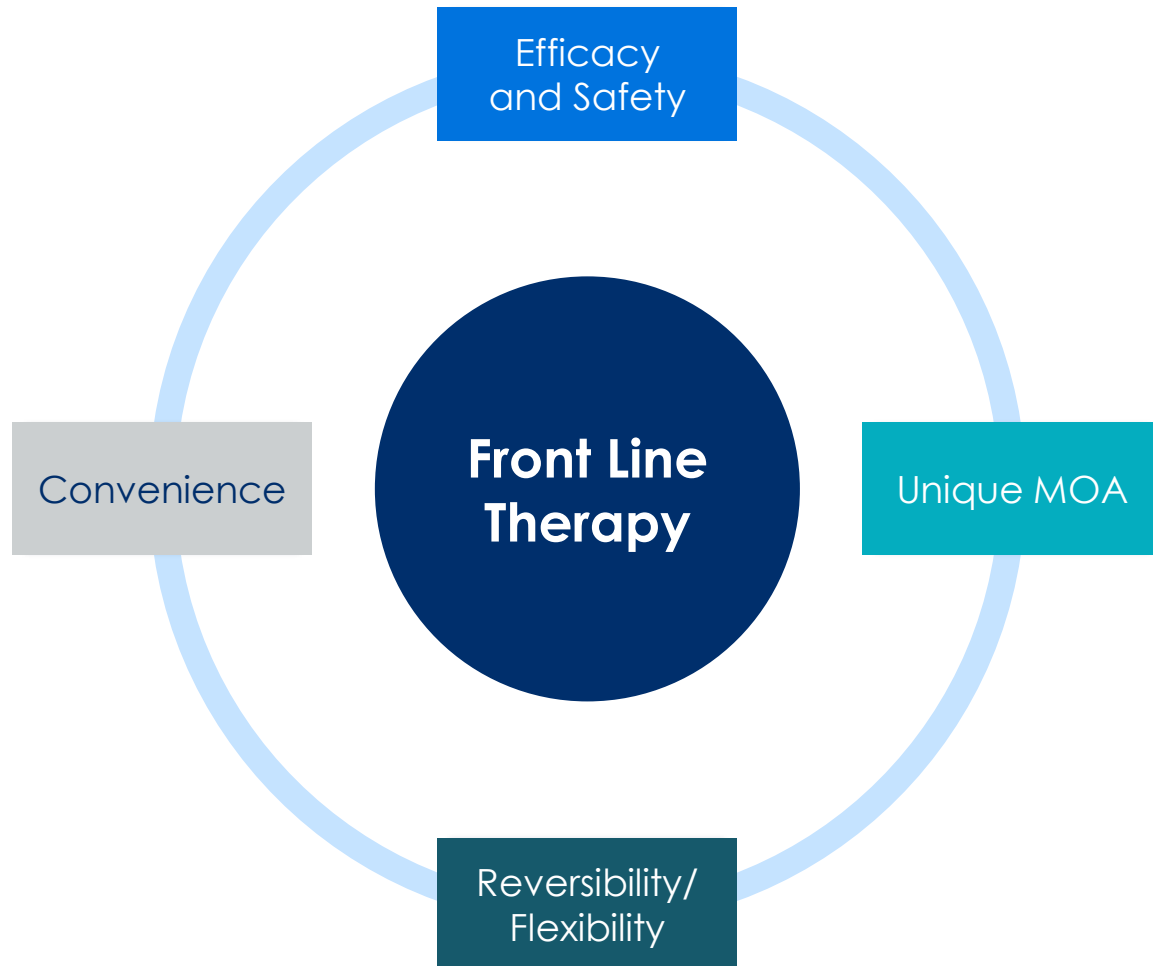
\$4 Billion

estimated U.S. commercial opportunity in IgG4-RD³

- Launch of first approved therapy supports the size of the opportunity
- Growth driven by increasing recognition, awareness, and the availability of effective therapies

Multiple precedents for rare diseases that evolved into large markets with the availability of effective therapies

Obexelimab would offer a new and differentiated approach to long-term disease management, if approved



Obexelimab will be positioned as the preferred **first line therapy** for the majority of patients

Opportunities for Obexelimab Initiation

Active Flares

1. Newly diagnosed patients experiencing a flare
2. Previously treated, not currently on therapy, experiencing a flare

Active Treatment

3. Patients currently treated with a biologic (UPLIZNA or rituximab) who see their physician prior to a 6 month infusion.

Three strategic imperatives define our launch plan

Shape the market

- Make proactive and chronic disease management the standard

Differentiate clearly

- B cell inhibition provides a unique MOA

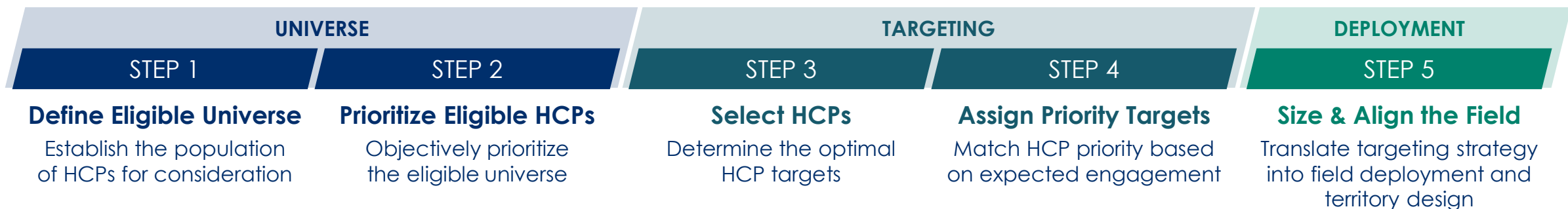
Activate with discipline

- Build the conditions for fast, focused uptake

Focused and Launch-Ready Patient Engagement Strategy:

- Build the right engagement model
- Define the right patient moments
- Prioritize the right customers

Targeting strategy: ~7,100 target HCPs



Patient volume is the primary segmentation driver; biologic use and specialty refine prioritization.

Tier	HCPs	% of Patients	Defining criteria
Tier 1	~7,100	72% ¹	Highest volume treating HCPs, or highest biologic users
Tier 2			Next highest volume HCPs, or high/moderate biologic users
Tier 3			Moderate-volume treaters
Tier 4			Rheum/GE treaters with less volume, or single-patient biologic users

Total Tier 1–4 (field-facing targets): ~7,100 HCPs
 GE - Gastroenterologists

Reach 72% of patients thru diagnosis, testing or treatment

Precision targeting to reach IgG4-RD prescribers

HCP Prioritization

~7,100

priority HCPs identified
across key specialties

*Rheumatologists represent
highest priority targets*

Account-Level Focus

91%¹

of patient opportunity
affiliated with **target
accounts²**

*Top 100 accounts
concentrate 65%¹ of
treated patient opportunity*

Optimal Field Size

45

field reps required for
full coverage

*Deployed across five
balanced regions to
ensure consistent
HCP coverage*

Field sales force of 45 will cover >90% of patient opportunity at target accounts

Planning for comprehensive surround support for HCPs

A coordinated, cross-functional model that delivers consistent education and support at every HCP touchpoint



Strategic Engagement (6)

Aligns Commercial KOL strategy and builds trusted relationships that inform commercial strategy.



Field Sales Professionals (45)

Delivers approved clinical and product resources to increase understanding and appropriate utilization.



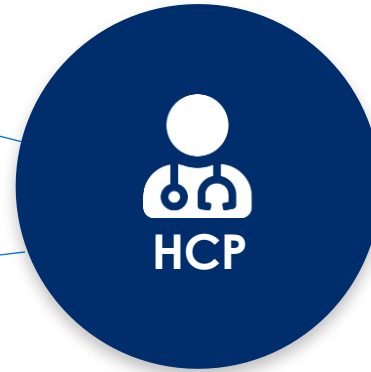
Nurse Educators (6)

In-depth, peer-to-peer disease-state and treatment education to advance understanding of IgG4-RD.



Market Access (14)

Supporting HCPs and patients as they navigate access & reimbursement.



One coordinated Zenas experience



PATIENT + PROVIDER OFFICE

OFFICE ACCESS SUPPORT

Zenas Field Reimbursement Managers*

Ensure smooth and quick reimbursement education and support for patients and providers

CASE COORDINATION

HUB + selected Specialty Pharmacy

Patients enter HUB or Specialty Pharmacy for initial benefits verification and support / drug dispensed

PATIENT SUPPORT

HUB/Specialty Pharmacy nurse support

Provide patient onboarding and education / ongoing patient communication, including refill support

Zenas is prepared to launch

Experienced Team ready to execute a **proven launch Playbook**

Launch ready ahead of **May PDUFA**

Well positioned and **well funded** to capitalize on the **substantial opportunity in IgG4-RD**



Enabling patients with
autoimmune diseases
to reimagine life



Obexelimab for Systemic Lupus Erythematosus



System Lupus Erythematosus (SLE): A debilitating chronic autoimmune disease that attacks healthy tissue

Disease Overview:

- A **chronic autoimmune disease** with unpredictable flares in joints, skin, kidneys and other vital organs that **cause progressive organ damage**

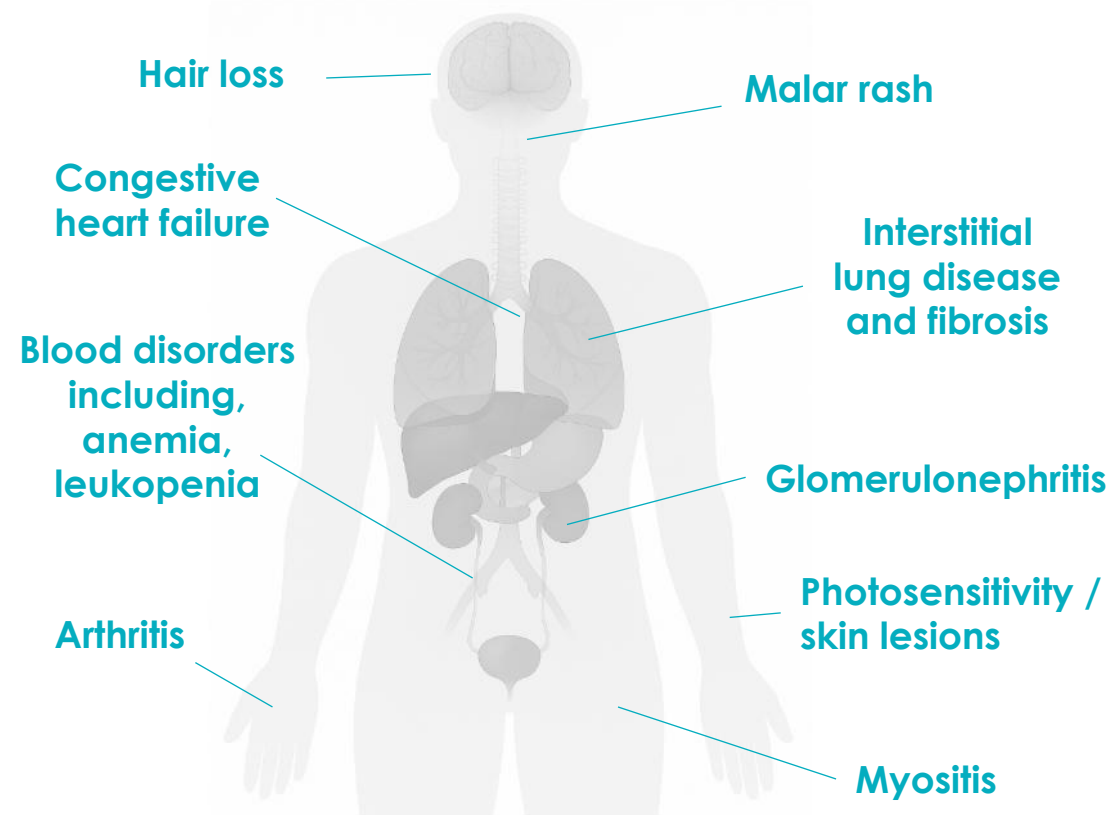
Pathophysiology:

- **B cell dysfunction** results in the production of autoantibodies toward cellular and nuclear components

Therapeutic Opportunity:

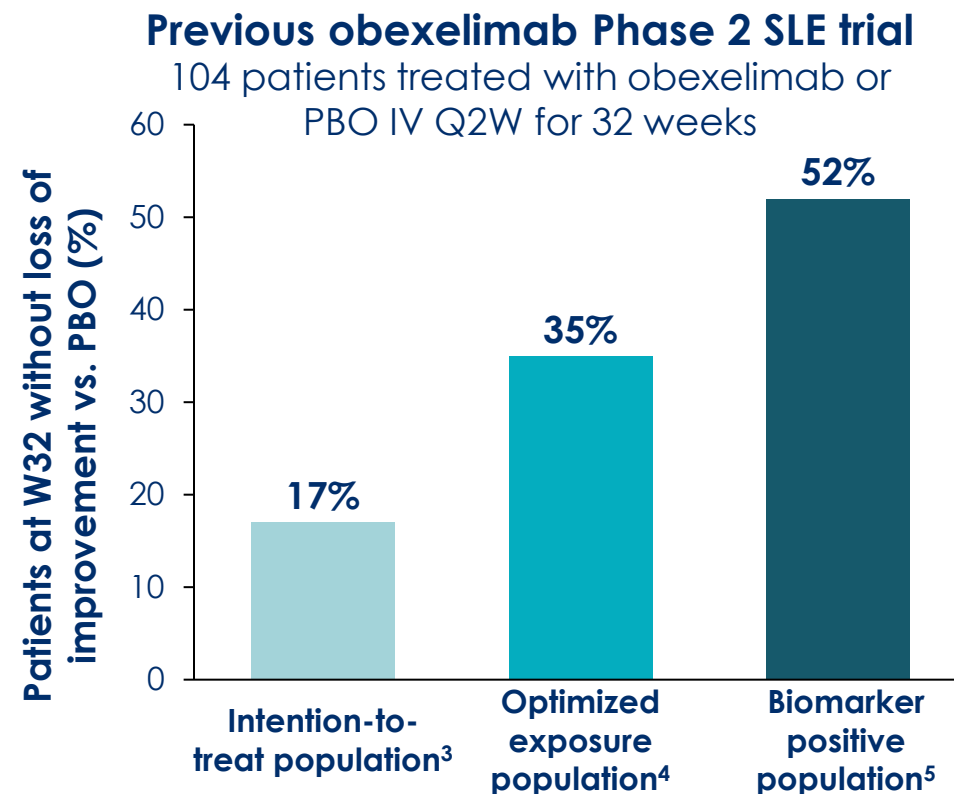
- **B-cell therapies proven effective** in clinical trials
- **Significant opportunity** remains for safe and effective therapies **for long-term disease management**
 - >80% of SLE patients are women diagnosed in their 30s and facing decades of treatment

SLE: common disease manifestations



Clinical evidence supports obexelimab's differentiated mechanism of action in SLE

- **Two approved therapies** have modest effect sizes of 12–17% over placebo¹
- **Direct B-cell inhibition** has the potential for **better outcomes than indirect modulation** (Benlysta®)²
- **Obexelimab proof of concept established** in previous Phase 2 SLE trial with IV dosing
- **Obexelimab's optimized subcutaneous dosing** confirmed in IgG4-RD and RMS clinical trials

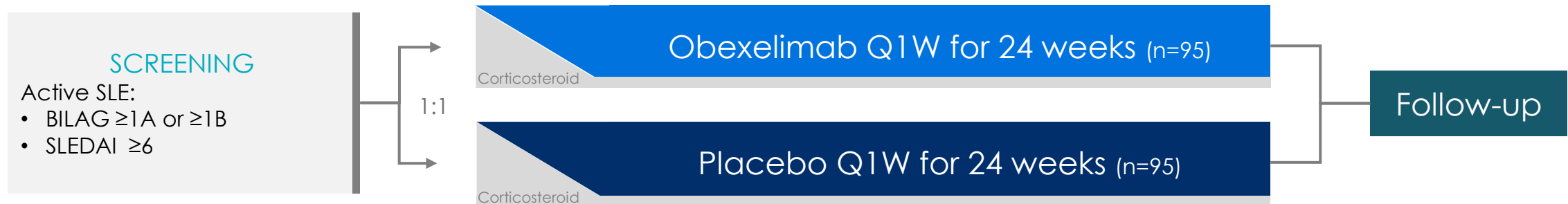


Direct CD19-based broad B-cell inhibition offers the potential for a safe and effective therapy for the long-term management of SLE patients

¹ BENLYSTA® and SAPHNELO® SRI-4/BICLA assessments; ² This conclusion is derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted; ³ Defined as all randomized patients receiving at least one dose of study medication; ⁴ C_{trough} Quartiles 3 & 4 in efficacy evaluable analysis; ⁵ Biomarker positive defined as patients in predefined lupus phenotypic gene expression clusters 3 & 6 (~30% of evaluated population). Post-hoc analysis; Source: Merrill et al.

Enrollment in Phase 2 SunStone SLE trial completed with topline data expected Q4 2026

- Designed to **confirm obexelimab activity** in overall and biomarker populations
- Incorporates **learnings** from previous Phase 2 trial **to increase probability of success**
 - Larger size with higher powering and optimized subcutaneous dosing to improve PK
 - Adjudication committee to assess eligibility and outcomes; strict corticosteroid tapering rules



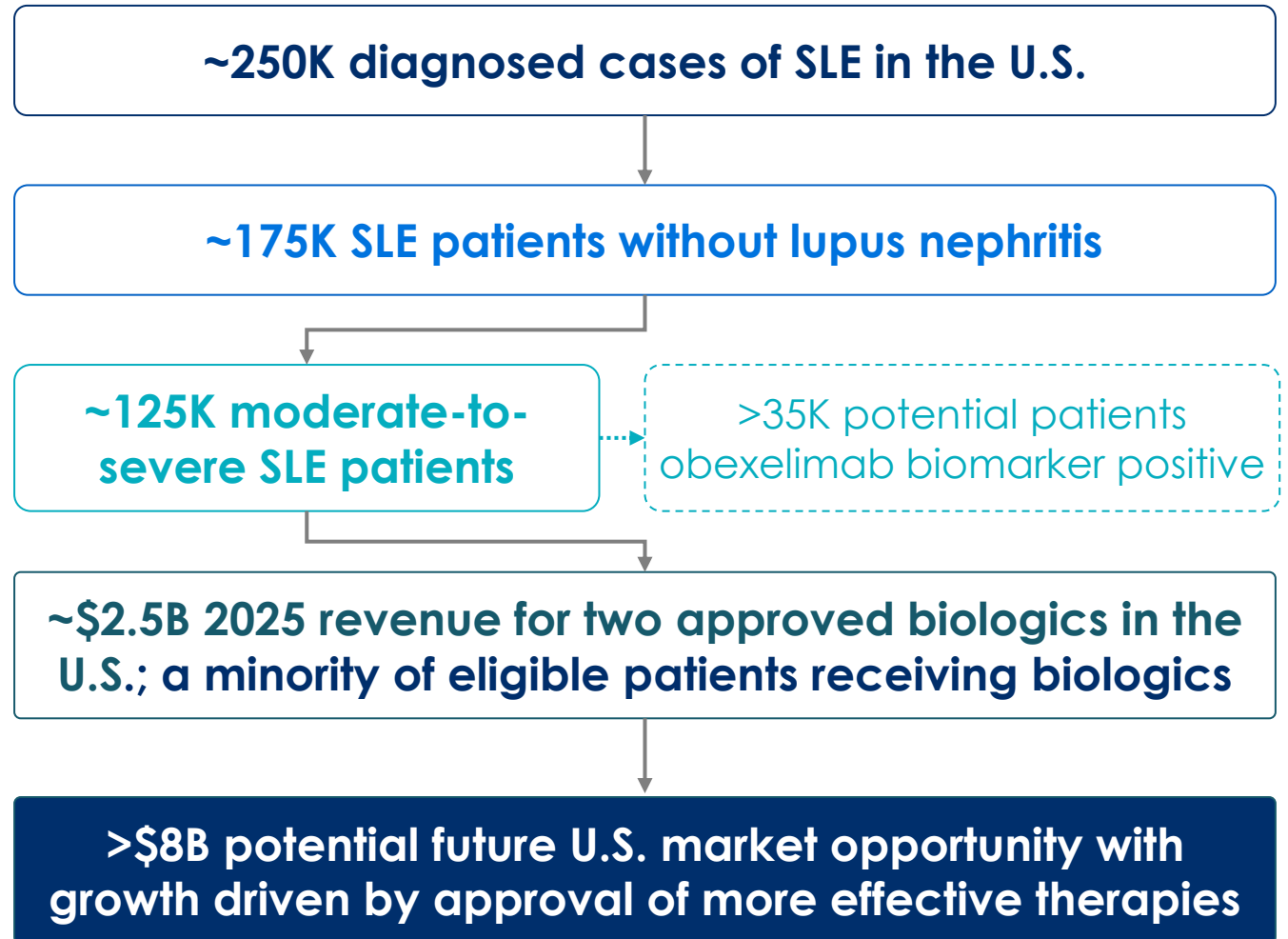
- Design: randomized, double-blind, placebo-controlled
- **Primary Endpoint: reduction of SLE disease activity at week 24 by BICLA assessment**
 - Powered to detect ~20% difference between obexelimab and placebo
 - Primary endpoint to be assessed in overall and biomarker positive populations

SLE represents a significant and growing commercial opportunity in the U.S. alone

**~125K
Addressable
SLE Patients**

In U.S. alone representing a
commercial market of

\$8B+





BTK: A Compelling Target for Progressive Multiple Sclerosis



naSPMS and PPMS have the highest unmet need across MS subtypes and limited therapeutic options

Subtype	naSPMS (~90K diagnosed patients in U.S.) ^{1,2}	PPMS (~60-100K diagnosed patients in U.S.) ^{1,3}
Clinical characteristics	Initially RRMS followed by steady increase in disability without relapses	Steady increase in disability without relapses / disease flares
FDA approved therapies	None ⁴	One
Preferred treatments	RRMS treatments used off-label	Ocrevus approved but higher efficacy agents are desired
Unmet medical need	Therapies that prevent disability progression	More effective therapies that prevent disability progression

Different subtypes of SPMS exist and patients with non-active disease have highest unmet medical needs

Secondary Progressive Multiple Sclerosis is an advanced manifestation of RMS where relapses become less frequent or stop but gradual worsening of disability occurs

Three subtypes of Secondary Progressive Multiple Sclerosis exist:

➤ Active SPMS:

- Still shows occasional relapses or MRI activity
- Most drugs approved for RMS including anti-CD20s are also approved for active SPMS

➤ Non-relapsing SPMS:

- No clinical relapses but MRI may still show activity or new lesions
- Patients have residual relapses/MRI activity – drugs approved for RMS may be somewhat effective

➤ **Non-active SPMS:**

FDA identified population with highest unmet needs

- No new relapses and no MRI activity
- Significantly stricter “progressive” classification than nrSPMS – naSPMS is a truly progressive disease
- No drugs approved and drugs approved for RMS unlikely to be impactful given their peripheral-acting mechanism and lack of impact on compartmentalized inflammation

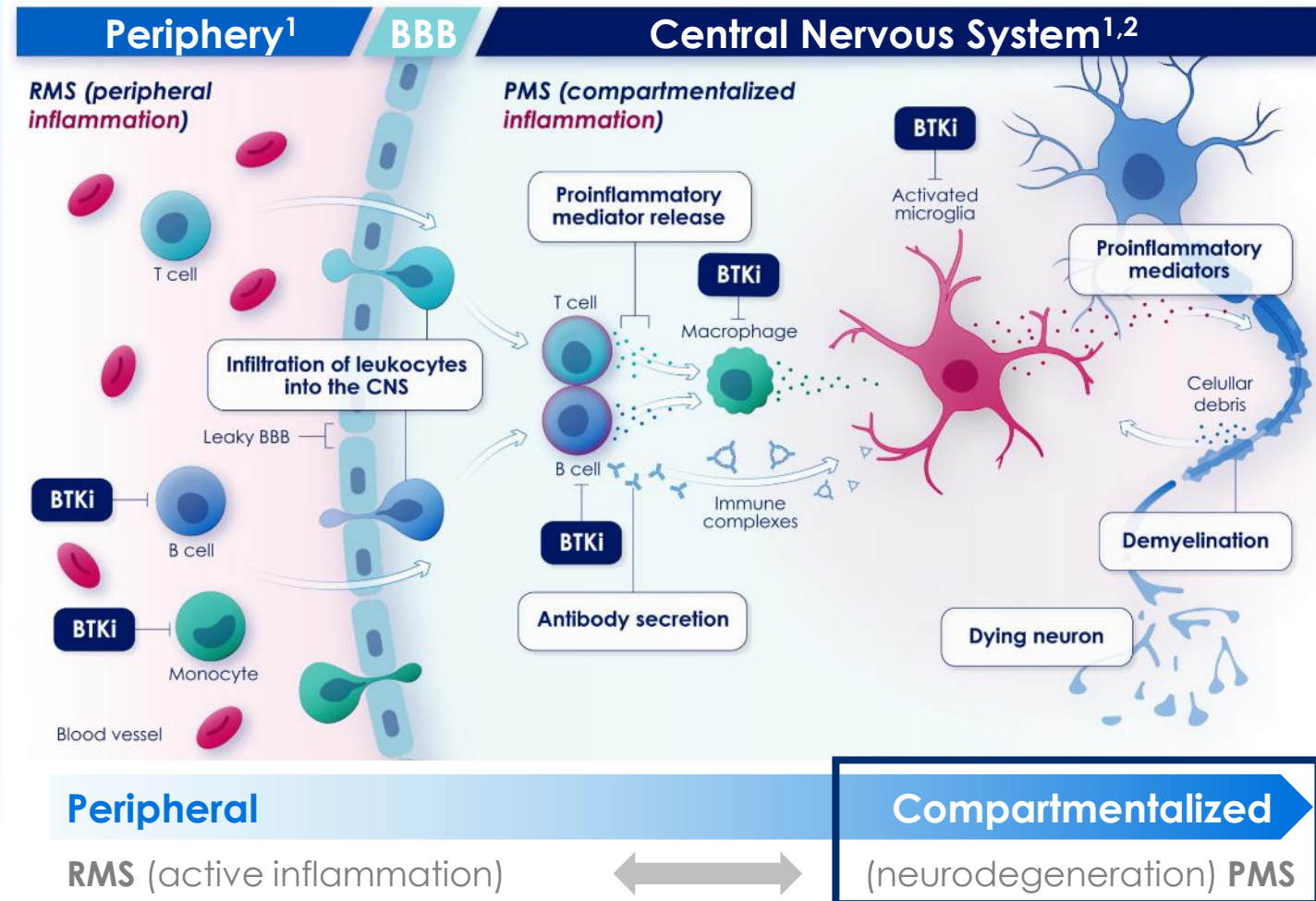
BTK is a validated target in MS with unique potential to address compartmentalized inflammation and disease progression

Significant unmet need in MS for:

- CNS-penetrant mechanisms that address **compartmentalized local inflammation** and directly impact the biology of progressive disease and **neurodegeneration**³

BTKi addresses underlying **biology of progressive disease**

- Impacts **peripherally and centrally** located pathogenic B cells and macrophages, and directly inhibits **microglia**
- **Peer BTKi program achieved primary endpoint in Phase 3 PPMS trial – a clearly defined progressive population**⁴



Orelabrutinib is a potential best-in-class therapy for progressive MS, a disease with a significant commercial opportunity and only one approved therapy

- No other BTKi programs advancing in both naSPMS and PPMS
- Orelabrutinib and remibrutinib are the only BTKi programs being developed for SPMS and are on similar timeline
- Orelabrutinib only B cell-directed therapy being developed specifically for naSPMS
- Successful Phase 3 fenebrutinib PPMS study validates BTKi central mechanism and differentiation within the BTKi class

Late-stage Progressive MS Pipeline					
Owner	Program	MoA	RoA	Indication(s)	
	Orelabrutinib	BTKi	Oral QD	PPMS (ongoing)	naSPMS (ongoing)
	Fenebrutinib	BTKi	Oral BID	PPMS (NDA under review)	N/A
	Remibrutinib	BTKi	Oral BID	N/A	SPMS ¹ (Initiated 4Q25)
	Frexalimab	CD40L	IV Q4W SC Q4W	N/A	nrSPMS (Initiated 4Q23)

CRL = Complete Response Letter; Tolebrutinib not included: failed to meet primary endpoint in PPMS and received CRL for non-relapsing SPMS (nrSPMS) NDA by FDA but approved for nrSPMS in Europe.

¹ Positive Phase 3 results in relapsing-remitting multiple sclerosis (RRMS)

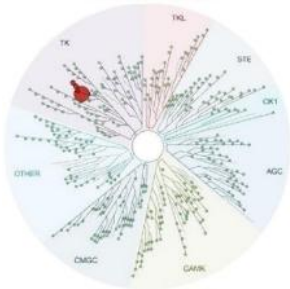
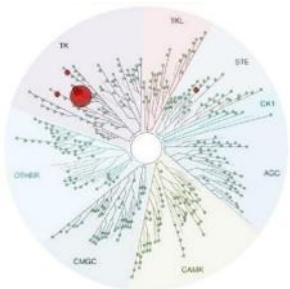
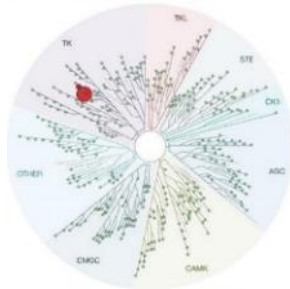
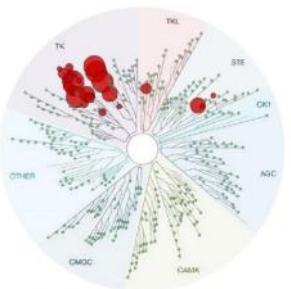


Orelabrutinib: a Potentially Best- in-Class BTKi



Orelabrutinib's pharmacologic attributes impart best-in-class potential combining high selectivity and CNS penetrant activity

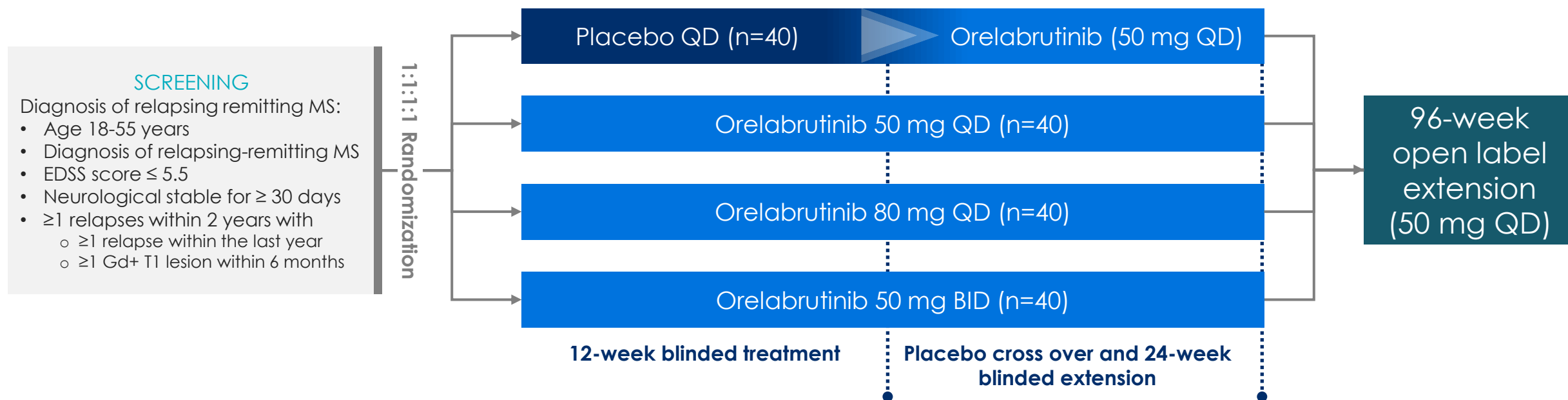
- ✓ High selectivity
- ✓ High CNS penetration
- ✓ Low IC₉₀
- ✓ Highest CNS conc. to IC₉₀ ratio

	<u>Orelabrutinib</u>	<u>Fenebrutinib</u>	<u>Remibrutinib</u>	<u>Tolebrutinib</u>
Binding / dosing ¹	Covalent / 80mg QD	Non-covalent / 200mg BID	Covalent / 100mg BID (Approved dose of 25mg BID for CSU)	Covalent / 60mg QD (Highly Variable PK; CV ~60%)
Selectivity ² (scanMAX (Eurofins) kinome scan at 1μM)				
CNS concentration ³	16.7	43.1	0.783	~ 0.3 to1
Potency ⁴ (IC ₉₀)	3.5	41.3	5.9	3.1
CNS concentration to IC₉₀ ratio	~5	~1	~0.2	~0.3

¹ InnoCare Pharma, Sanofi, and Roche published reports; ² Darragh et al. 2025; ³ Orelabrutinib: Data on file; Tolebrutinib: calculated from Cabanis et al. 2024; Fenebrutinib: American Academy of Neurology Annual Meeting 2024. Remibrutinib: Lefevre et al ECTRIMS 2024; ⁴ Orelabrutinib: Data on file; Tolebrutinib and fenebrutinib: Turner et al. 2024. Remibrutinib: Angst et al. 2020 (IC₉₀ estimated from IC₅₀); Notes: Orelabrutinib 80 mg data inferred from 150 mg dosing; Potency based on kinase activity; Based on comparisons of published data for tolebrutinib, fenebrutinib and remibrutinib, no head-to-head comparison studies were conducted

Orelabrutinib Phase 2 RRMS trial

Standard design with MRI measurements and highly predictive of successful outcome in large randomized trials

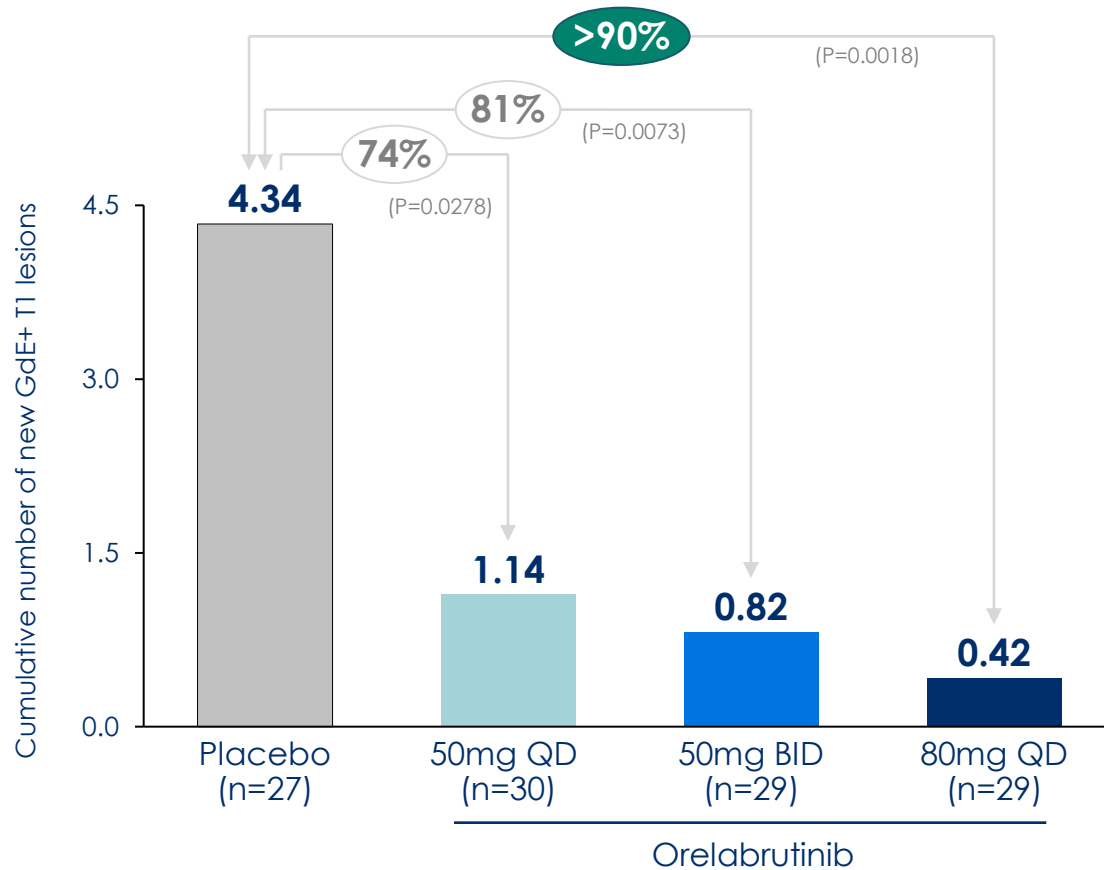


Phase 2 RRMS Trial Summary:

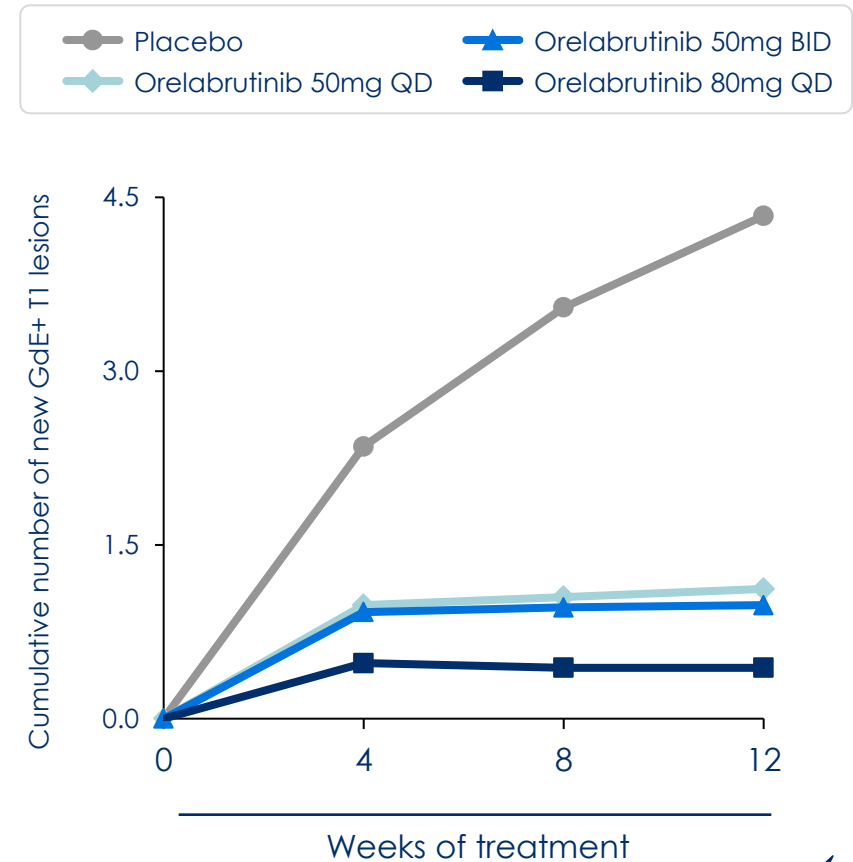
- Design: double-blind, randomized, placebo-controlled with placebo crossover at week 12
- Treatment: Three different doses of orelabrutinib vs. placebo control through week 12
- **Primary endpoint:** MRI endpoint assessing number of new T1 Gd-enhancing lesions at week 12
- **Secondary endpoints:** through 24-week blinded extension included T1 Gd-enhancing lesions and new or enlarging T2 lesions at weeks 12, 16, 20, and 24 and safety

Orelabrutinib treatment resulted in a rapid and deep reduction in new GdE+ T1 lesions across all evaluated doses

Significant reduction in new GdE+ T1 lesions observed for all orelabrutinib doses at week 12 (primary endpoint)

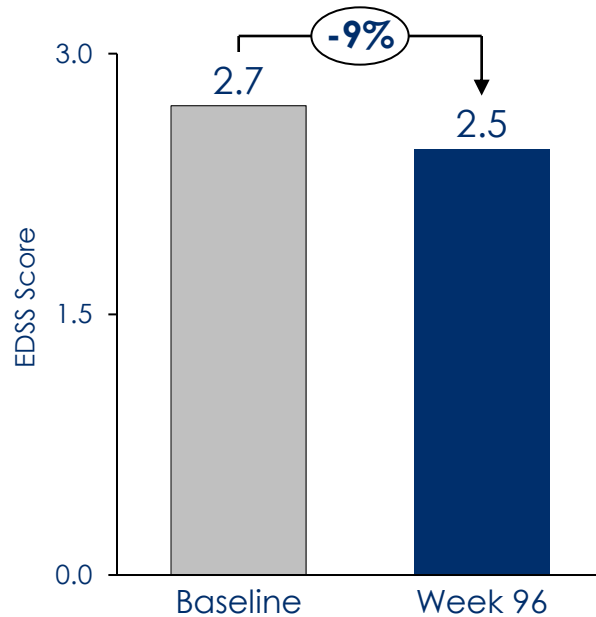


Meaningful and sustained reduction in new GdE+ T1 lesions observed as early as week 4

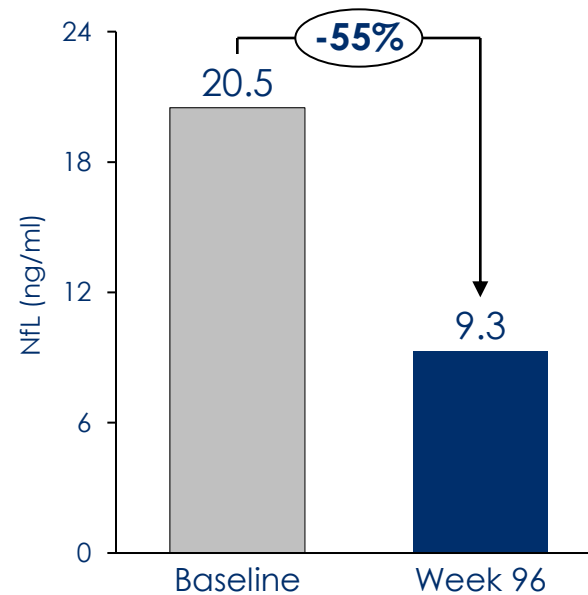


Orelabrutinib data out to 96-week support sustained clinical activity and potential impact on disability progression

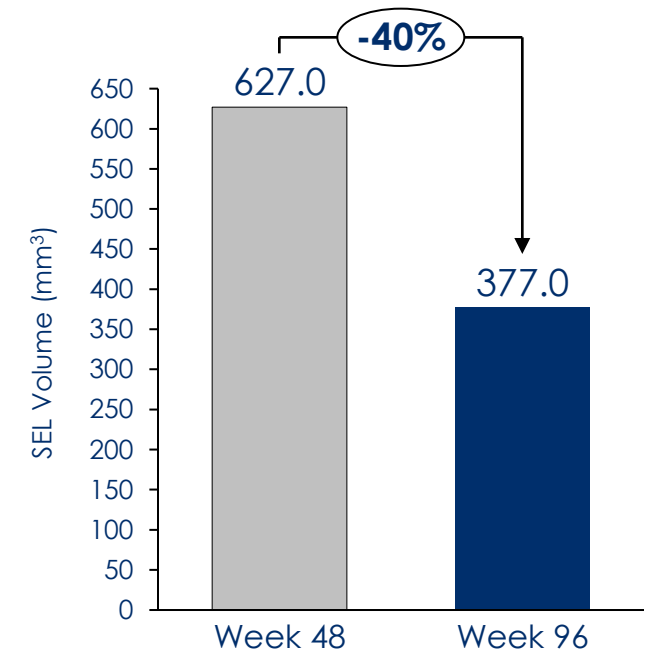
EDSS Score: Indicative of neurological disability and disease progression



Serum NfL: Indicative of disease activity and progression



SEL Volume: Indicative of smoldering disease and progression



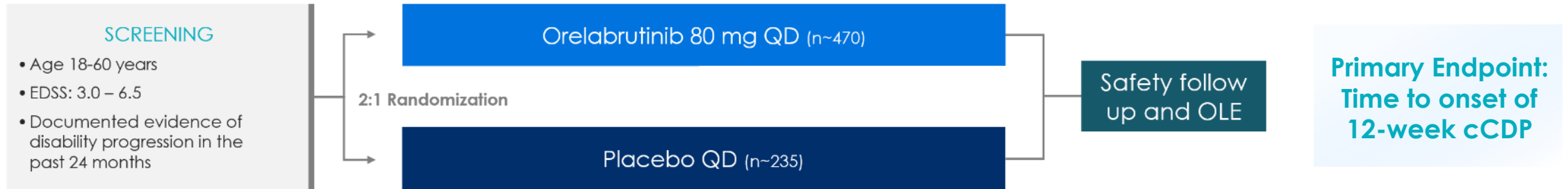
Data shown for 80 mg QD dose (switched to 50mg QD dose, week 24 through 96 for OLE, n=36-37)

Orelabrutinib was generally well tolerated with safety in-line with other BTKi in development for MS

- Safety of orelabrutinib (n=118) vs. placebo (n=40) during the 12-week RCP
 - Serious TEAEs: 2% vs. 0%
 - Liver-related TEAEs: 10% vs. 7.5%
 - Occurred primarily in the first eight weeks of treatment, most were present as lab abnormalities only without clinical symptoms
- Orelabrutinib was placed on partial clinical hold by FDA (but not EMA) for studies in RRMS after 2 cases of DILI meeting Hy's Law criteria
- For high unmet need for progressive MS development, **FDA has cleared protocols** to proceed with risk mitigation including weekly LFTs and stopping rules
- Ocrevus (ocrelizumab) and multiple oral therapies for MS are also associated with elevated LFTs

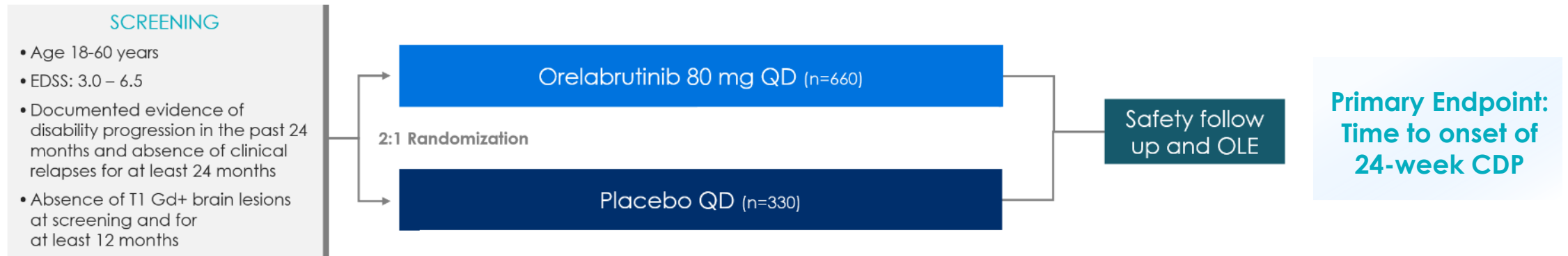
Orelabrutinib Phase 3 protocols cleared with FDA and positive EMA Scientific Advice

PPMS Study Design; trial initiated in U.S.



A total of 355 events would yield approximately 90% power to detect the superiority of orelabrutinib over placebo

non-active SPMS Study Design; trial initiated in U.S.



A total of 332 events would yield approximately 88% power to detect the superiority of orelabrutinib over placebo

Growing global MS market expected to reach >\$30B by 2030 with naSPMS and PPMS expected to represent >\$12B+

**>150K
Patients**

with naSPMS and PPMS in
U.S. alone representing a
commercial market¹ of

\$12B+



~640K diagnosed cases of MS in the U.S.¹

~150-185K diagnosed cases of naSPMS and PPMS²

~100-130K naSPMS and PPMS patients receiving
disease modifying therapies (DMT)

**Current naSPMS and PPMS commercial opportunity
in the U.S. projected to be >\$12B+³**

*Significant growth potential driven by increased
diagnosis and DMT use with approval of effective
therapies that impact disability progression*



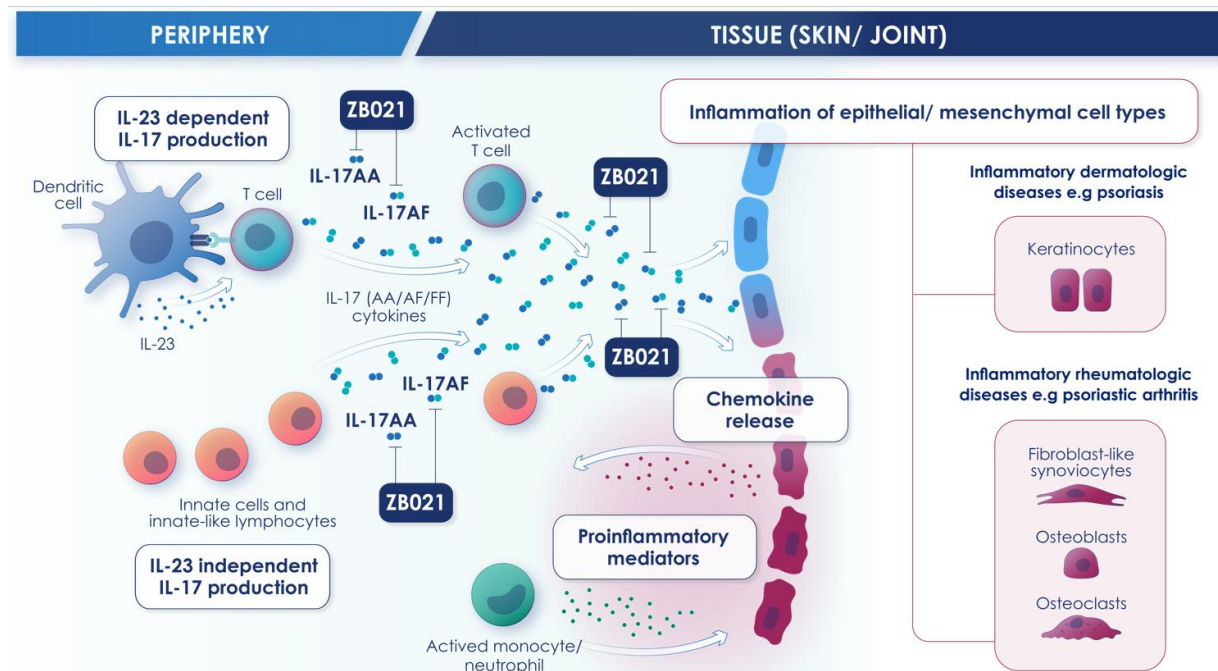
ZB021: An Oral IL-17 AA/AF Inhibitor With Best-in-Class Potential



ZB021 is an oral IL-17 AA/AF inhibitor with significant opportunity in multiple inflammatory and autoimmune indications

IL-17 is a well-validated target for numerous dermatologic and rheumatologic diseases

- Focal point for **acute and chronic inflammation** in skin and joint-related diseases
 - Several upstream cytokines including IL-23 promote Th17 cells and innate-like lymphocytes to secrete **IL-17 as the primary driver of the inflammatory processes**
 - Cytokines, chemokines and other proinflammatory mediators can cause **dysfunction of cells in tissues**
 - Strong **clinical confirmation of role in pathogenesis** of multiple autoimmune and inflammatory diseases
 - Drug development to-date **focused on biologics**



Growing interest in small molecules against targets established by biologics

- Recent positive data and FDA approval of an oral IL-23 program for plaque psoriasis provides evidence that **oral therapies can match the safety and efficacy of established biologics**

The IL-17 market is substantial and growing

Multiple **biologic approvals validate IL-17** as a target for autoimmune and inflammatory diseases

- Three biologics are **approved for six indications** in rheumatology and dermatology

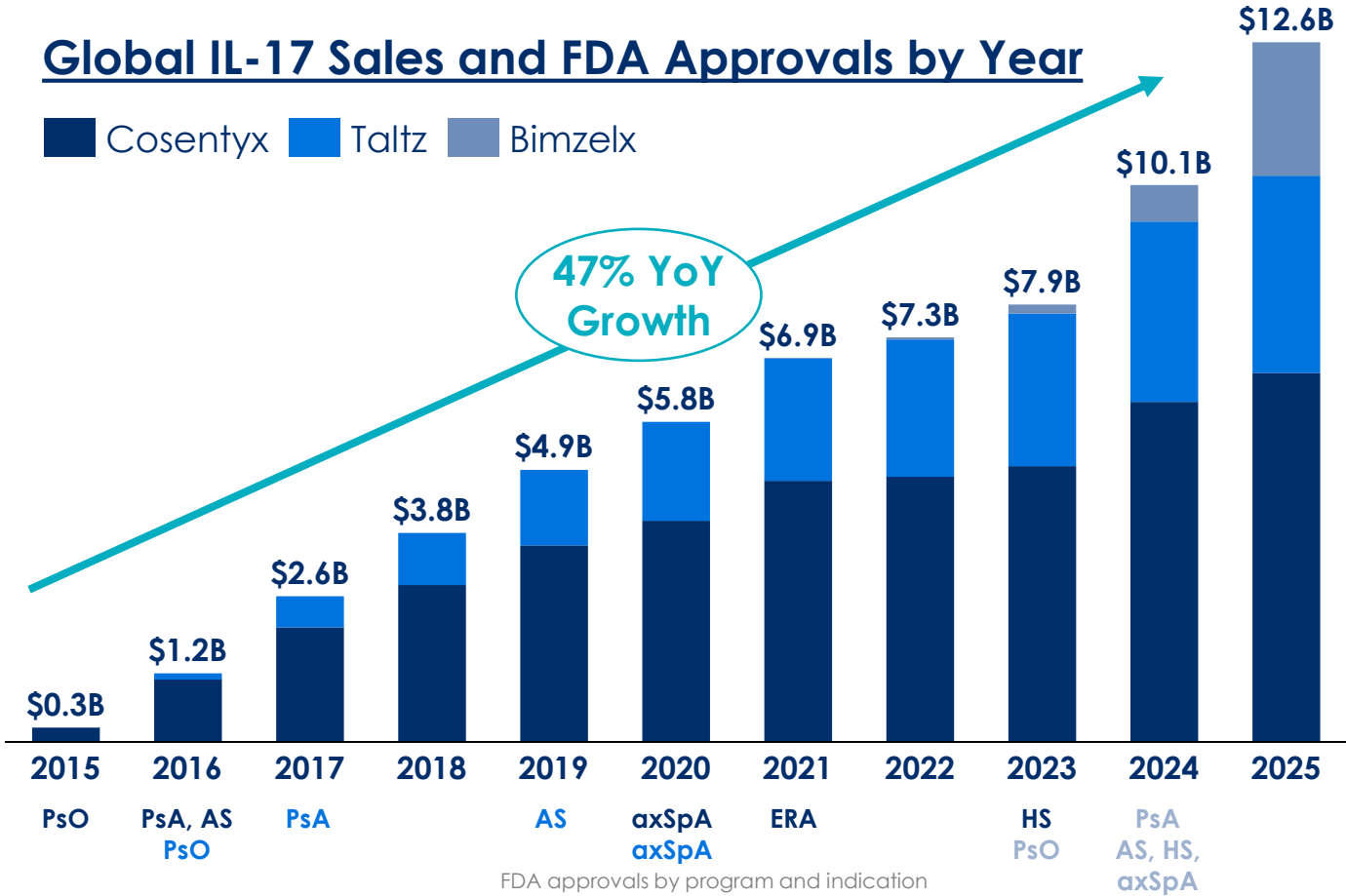
IL-17 currently represents a **\$12.6B global market**

- **Market growth** driven by new entrants; **further expansion expected** to be driven by additional launches and approvals for new indications

Strong **patient preference for oral therapies** highlights unmet need within IL-17 class

- No oral IL-17 agents are later than Phase 2

Global IL-17 Sales and FDA Approvals by Year

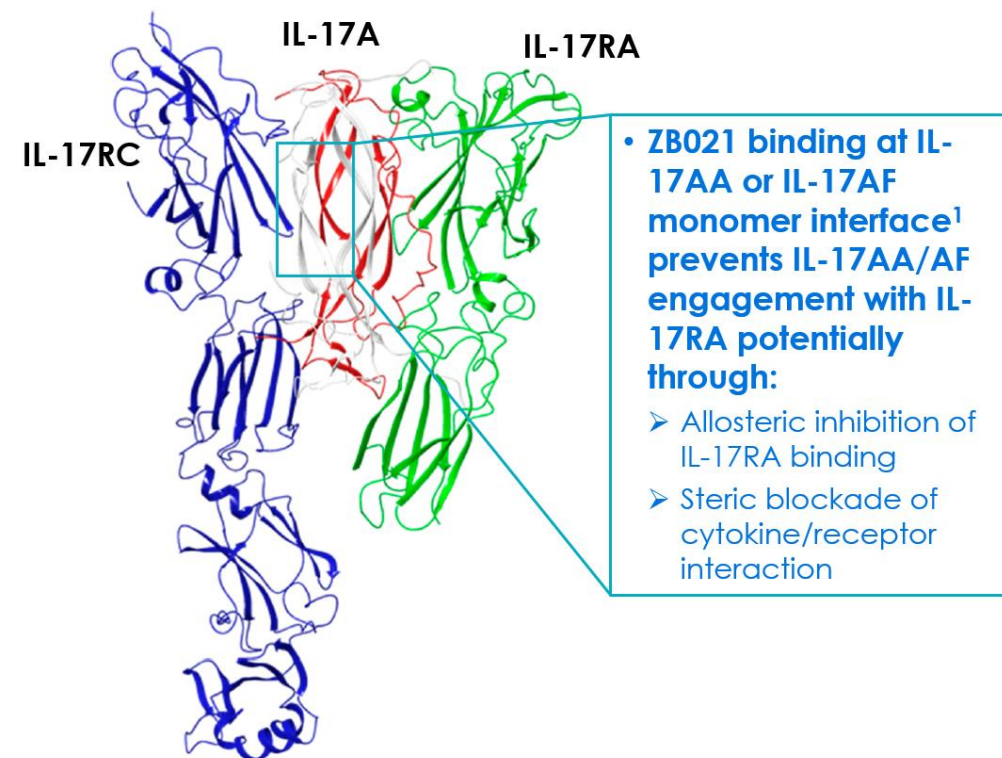


ZB021: a differentiated approach to targeting IL-17 with potential for biologic-like efficacy combined with improved access, compliance and patient convenience

IL-17AA/AF is a proven therapeutic approach balancing safety with strong disease control across multiple indications

High ZB021 potency observed *in vitro*

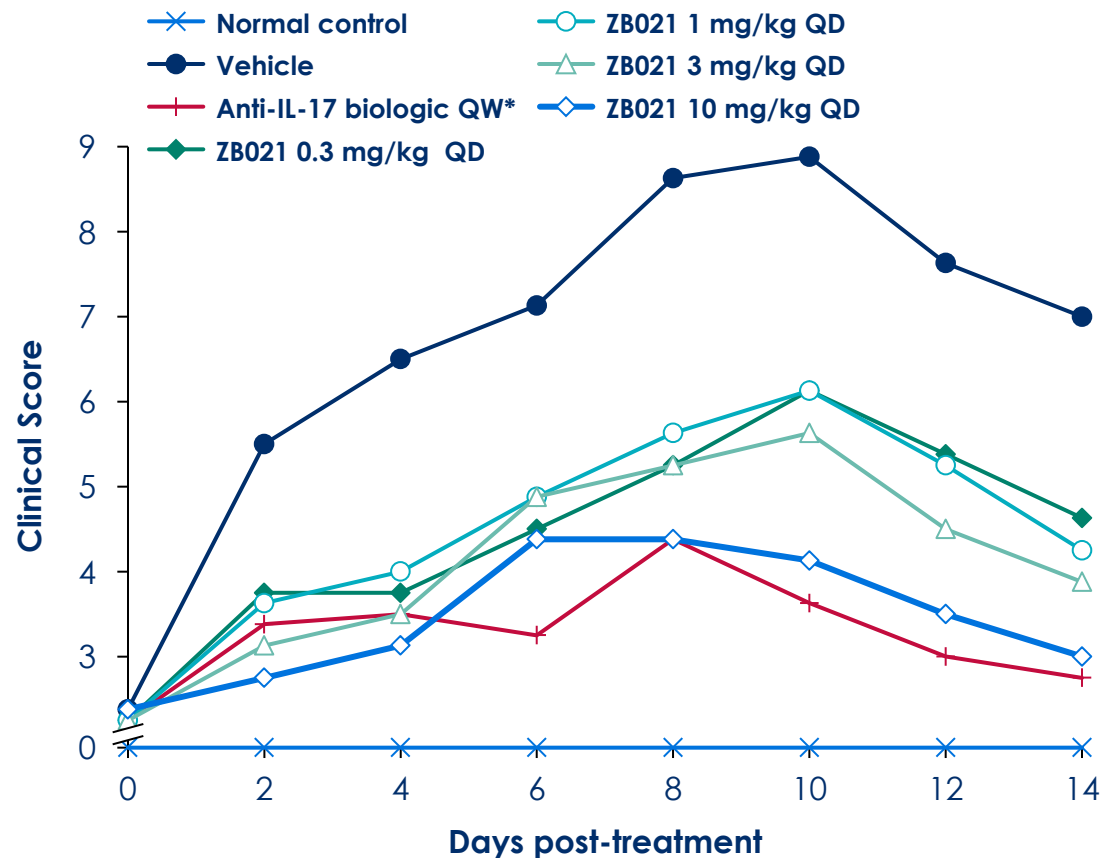
	Target engagement	IL-17–IL17RA binding inhibition	$2.6 \pm 1.7 \text{ nM}$
	Functional inhibition	IL-17 signaling inhibition	AA: $6.5 \pm 3.1 \text{ nM}$ AF: $18.4 \pm 16.2 \text{ nM}$
	Disease-relevant activity	IL-17 signaling inhibition from Th17 supernatant	$2.8 \pm 2.4 \text{ nM}$



Based on approved products, IL-17AA/AF inhibition demonstrates strong clinical activity while avoiding safety risks observed with IL-17FF inhibition²

The ZB021 biologic-matching preclinical activity combined with favorable ADME properties support best-in-class potential

Robust efficacy demonstrated: comparable activity *in vivo* to a reference anti-IL-17 biologic in rat CIA model



Strong preclinical ADME properties support best in class oral IL-17 potential

Low clearance observed in multiple species



High metabolic stability in liver microsomes



High oral bioavailability observed in multiple species; ~80% in non-human primates

ZB021 development program designed for rapid dose evaluation and to establish proof-of-concept in patients

Multiple Ascending Dose Evaluation in Healthy Volunteers

Up to 4 Dose Levels (n=8 per dose*)

Single Ascending Dose Evaluation in Healthy Volunteers; First Subject Dosed in May 2026

Up to 6 Dose Levels (n=8 per dose*)

Proof of Concept Study at 2 Dose Levels

Evaluate efficacy and PD biomarkers

PK and safety data expected by year-end 2026

Patient data expected in 2027

The established mechanism and clinical activity of IL-17 in autoimmune and inflammatory diseases may enable rapid advancement into multiple registration-directed trials



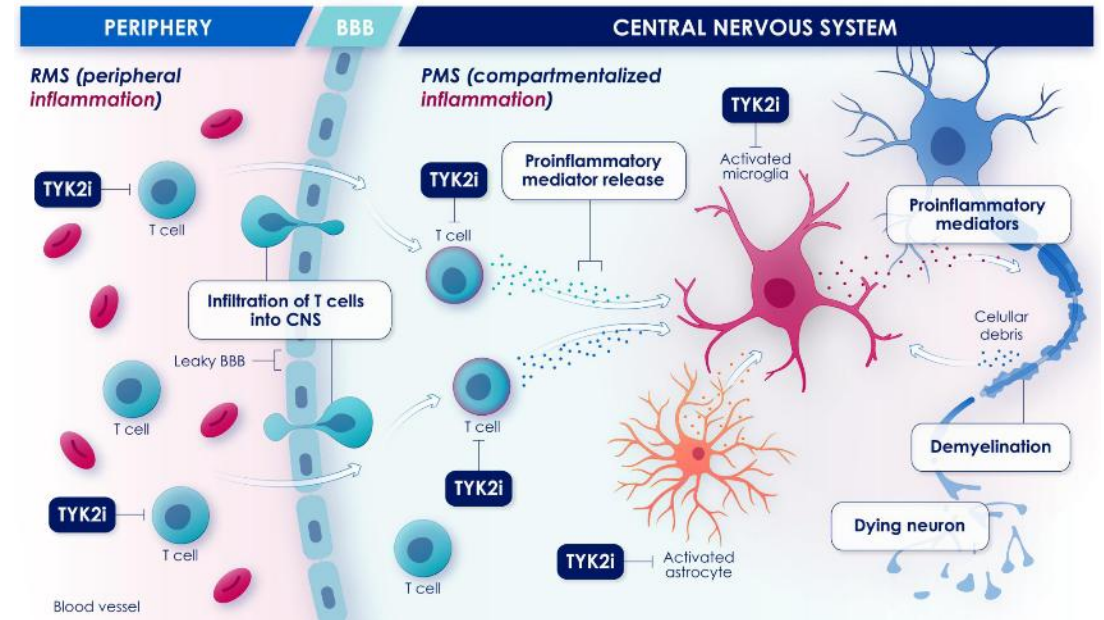
ZB022: A Brain Penetrant TYK2 Inhibitor With Best-in-Class Potential



ZB022: a brain-penetrant TYK2 inhibitor with substantial opportunity in neuroinflammatory and neurodegenerative diseases

TYK2 is a well-established mechanism across a range of autoimmune diseases

- Brain penetrant molecules may provide opportunity to extend benefit to neurological diseases
 - Increasing evidence implicating **TYK2's role in neuroinflammatory and neurodegenerative diseases**
 - Partial loss-of-function variants protect against various autoimmune diseases including MS
 - TYK2 shown to stabilize tau in Alzheimer's disease



ZB022: a brain-penetrant TYK2 inhibitor with best-in-class potential

- Complementary mechanism to **expand upon potential neurology franchise** led by orelabrutinib
 - **Allosteric JH2 inhibition** improves selectivity and specificity
 - **Favorable PK/PD** observed in preclinical studies
 - **High activity** in preclinical neurological disease model
- IND enabling studies ongoing



Zenas BioPharma

Enabling patients with autoimmune diseases to reimagine life

