ACELYRIN

Accelerating Medicines to Transform Patients' Lives

Corporate Overview
November 13, 2024

Forward Looking Statements & Disclaimer

This presentation contains statements that are not of historical facts, considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements include, but are not limited to, statements about our expectations regarding the potential benefits, effectiveness, and safety of our product candidates including with respect to lonigutamab's potential for its composition and subcutaneous administration to provide for sustained and/or improved treatment over time, or potential for a longer-term treatment duration and generally well-tolerated safety profile; izokibep's ability to offer clinically meaningful, differentiated benefits, and/or deepening of response over time, and its safety profile; our expectations with regard to our research, development and regulatory plans, including the design (including, potentially registrational design) of preclinical and clinical trials, anticipated commencement of trials, the timing and availability of data from such trials, and the timing or likelihood of regulatory filings and approvals for our product candidates; our expectations with regard to our ability to explore selective pipeline expansion opportunities; the potential market size and size of the potential patient populations for our product candidates and any future product candidates and those indications we target; our expectations about our ability to maintain existing, and establish new, strategic collaborations, licensing, or other arrangements; the scope of protection we are able to establish and maintain for intellectual property ("IP") rights covering our product candidates and any future product candidates; our business strategy; and our future results of operations and financial position.

Such forward-looking statements reflect the current views of ACELYRIN with respect to future events, and are subject to known and unknown risks (including, without limitation, business, regulatory, economic and competitive risks), uncertainties, assumptions and contingencies about ACELYRIN, including, without limitation, those associated with: ACELYRIN's successful completion of development and regulatory activities for its product candidates, including the risk that future clinical trial results could differ materially and adversely from early clinical trial results and other data, and the risk that the U.S. Food and Drug Administration may not agree with ACELYRIN's planned registrational program for lonigutamab and may ultimately require more Phase 3 clinical trials prior to any regulatory submissions or approval; ACELYRIN's ability to achieve projected cost savings in connection with the suspension of further internal investment in the development of izokibep development in HS, PsA and AxSpA, and the corporate restructuring, and the potential failure to realize the expected benefits of the foregoing and unintended consequences from the foregoing that may impact ACELYRIN's business; maintaining and defending IP protection; the ability to timely secure adequate supply of its product candidates; and legal proceedings, as well as other risks and uncertainties described under the heading "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 filed with the U.S. Securities and Exchange Commission ("SEC") and in subsequent filings made by us with the SEC, which are available on the SEC's website at www.sec.gov.

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Our product candidates are currently under preclinical or clinical investigation, and no representation is made as to the safety or effectiveness of our product candidates. In addition to our own internal research and estimates, this presentation contains information related to or based on studies, publications, surveys and other data obtained from third-party sources, including without limitation relating to market size and growth. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness thereof. In addition, market data (e.g., market size) involves a number of projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate. There can be no guarantee of the accuracy or reliability thereof as they are necessarily subject to a high degree of uncertainty and risk.

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ACELYRIN is a Clinical-Stage Biopharma Company Focused on Identifying, Acquiring, and Accelerating the Development and Commercialization of Transformative Medicines

Experienced Leadership Team

Successful Track Record of Delivering Transformative Medicines for Patients

Mina Kim
CEO

Gil Labrucherie
CFO & CBO

Kelly Chow
CPO

Ken Lock
CCO

Shep Mpofu, MD, MRCP, FRCP
CMO

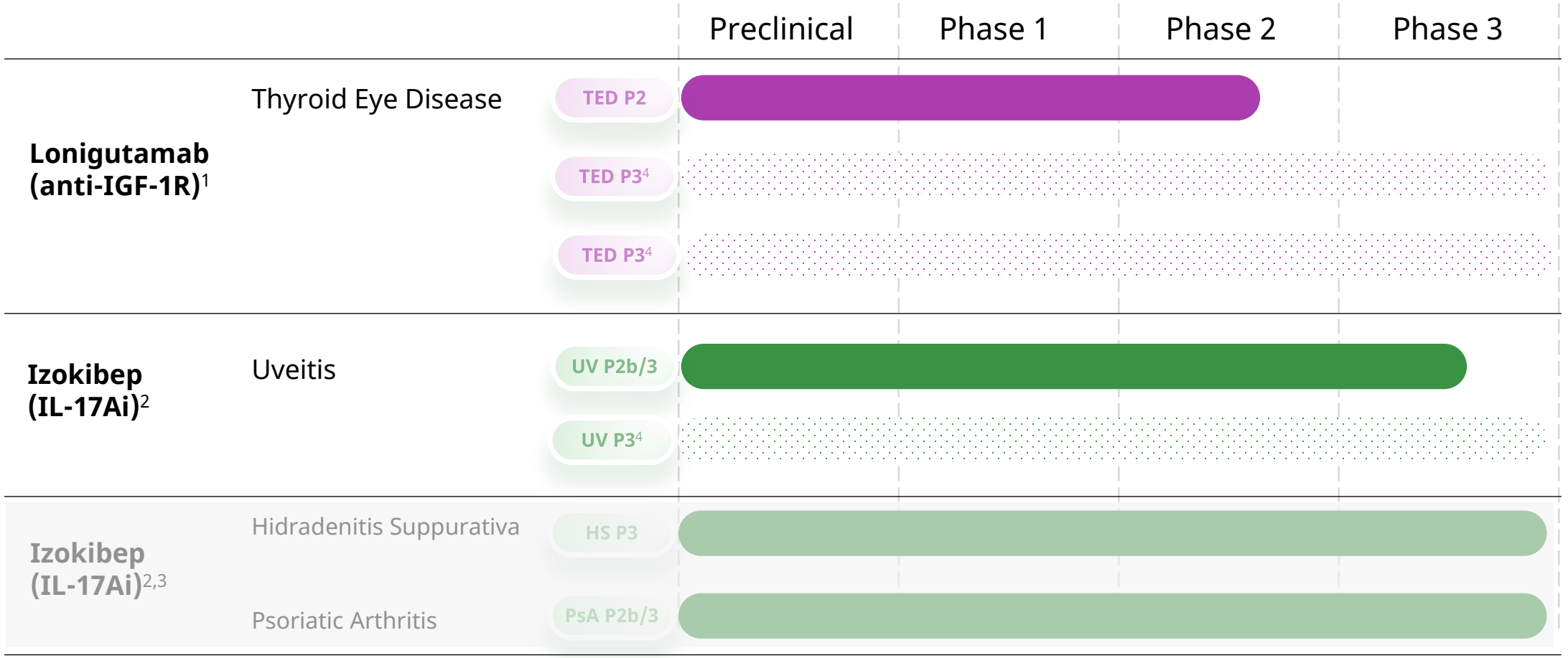
Amar Murugan
CLO

Patricia Turney
CTO

Board of Directors

Mina Kim | Bruce C. Cozadd | Dan Becker | Alan Colowick | Henry Gosebruch | Patrick Machado | Beth Seidenberg | Dawn Svoronos | Lynn Tetrault

Portfolio of Late-Stage Clinical Programs



[1] IGF-1R Inhibitor; Worldwide rights to non-oncology indications. Potential opportunity to extend certain IP protection into 2043.

[2] IL-17A Inhibitor; Excludes (i) development, commercialization and manufacturing rights in mainland China, Hong Kong, Macau, South Korea and Taiwan, and (ii) development rights in certain other Asia Pacific countries including, without limitation, Australia, India, New Zealand and Singapore. We retain decision making authority for izokibep global development. Potential opportunity to extend certain IP protection into early 2040's.

[3] On August 13, 2024, ACELYRIN announced plans to complete these two ongoing trials and suspend new investment in these two indications.

[4] Not yet initiated; denotes trials anticipated to be required for registration in the United States

Lonigutamab

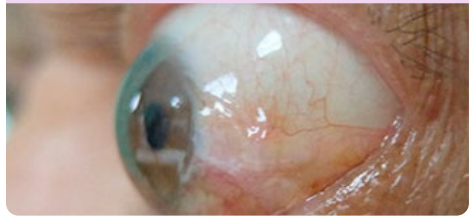
TED: Unmet Needs Persist for Greater Efficacy, Safety & Convenience

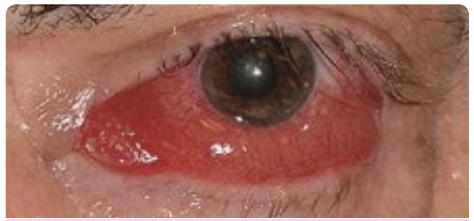
Multifaceted Disease Whose Impact Extends Beyond Visual Disfigurement

TED is a rare debilitating disease with many life-impacting manifestations

- Impacts >100,000 patients in the U.S.
- Characterized by progressive inflammation that can lead to **irreversible damage to tissues around the eye**, threatening vision

Proptosis





Redness

Diplopia

Patient QoL

Opportunities to improve on SoC to positively impact lives of patients living with chronic disease

Rapid & deeper responses across TED manifestations, resulting in **improved patient quality of life**

Minimize or delay retreatment by providing more **durable** responses and **patient-specific** treatment duration

Avoid risk of **serious, potentially long-term AEs** (e.g., hearing impairment) that result from high doses of SoC

Increase **convenience** through at-home **subcutaneous** administration and/or less frequent dosing

Lonigutamab TED

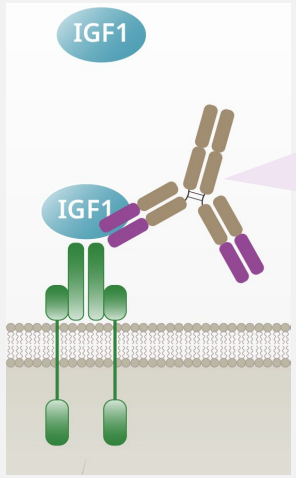
Next Generation Best-in-Class Anti-IGF-1R Designed to Optimize Patient Benefit

High Potency

20-75x more potent than other anti-IGF-1Rs[1,2]

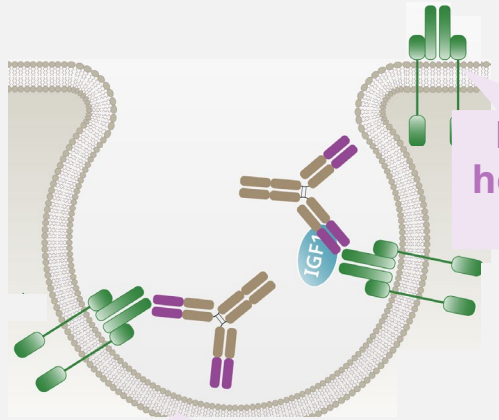
Lower drug exposure

Unique Binding Epitope



Peripheral IGF-1 binding site: does not compete with IGF-1 binding

IGF-1 Internalization



Maintains homeostatic IGF-1

IGF-1 internalization within minutes enables faster kinetics

Potential Patient Benefits

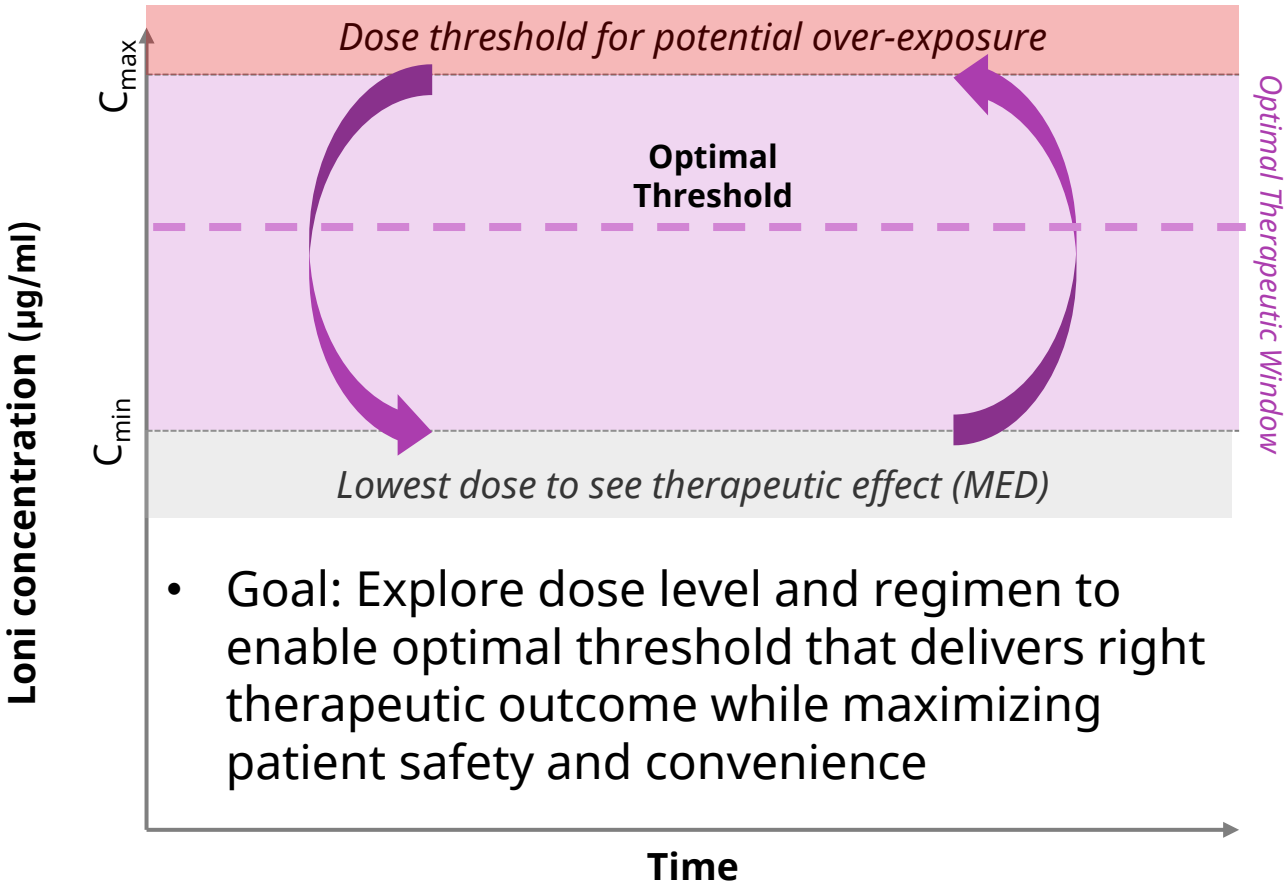
- **Faster Time to Response**
- **Deep & Durable Responses**
- **Minimize Safety Risks**
- **Patient-Centric Convenient Administration**

1. Akla, B. et al. Efficacy of the Antibody–Drug Conjugate W0101 in Preclinical Models of IGF-1 Receptor Overexpressing Solid Tumors. Mol. Cancer Ther. (2020).
2. Data on File

Applying Our Innovative Approach to Clinical Development

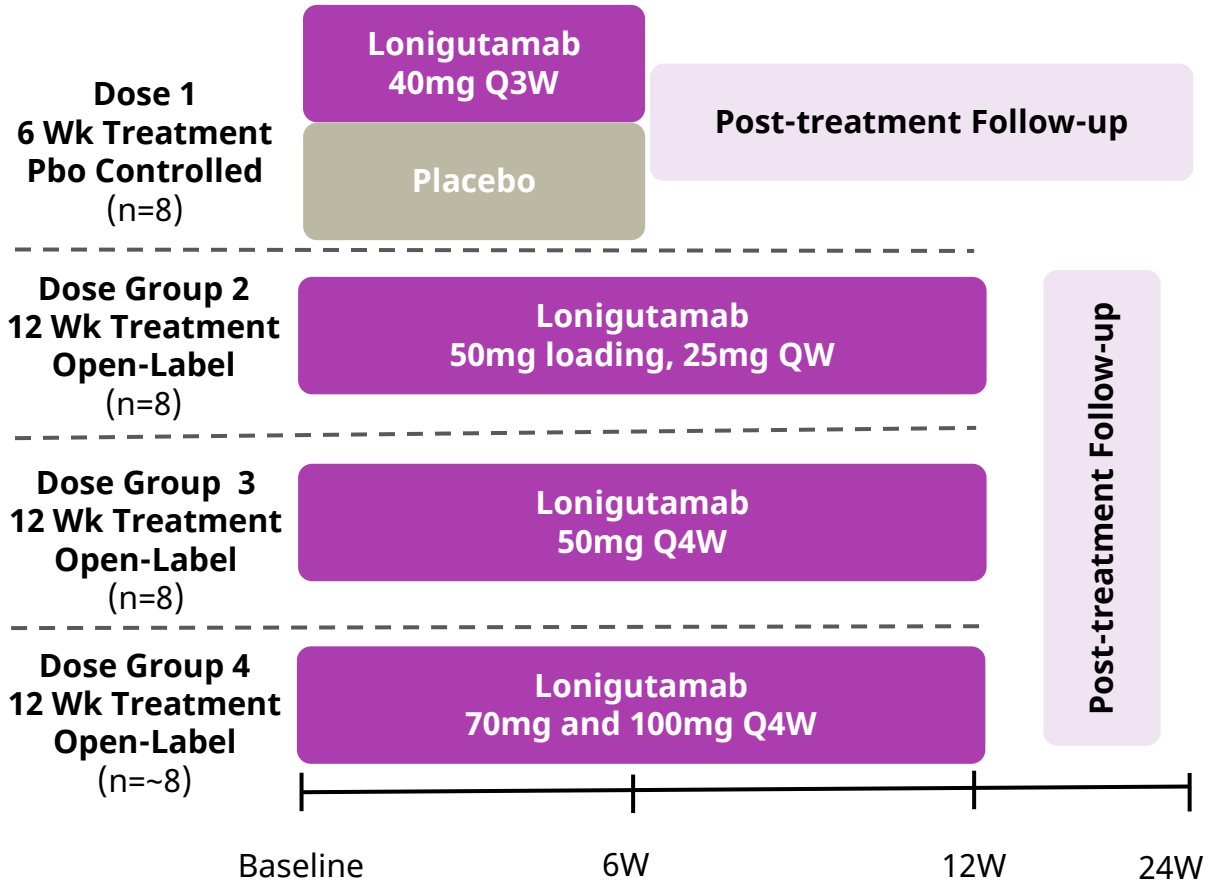
A Patient-Centric Approach Designed to Optimize Benefit-Risk

Iterative & robust approach to optimize anti-IGF-1R dosing…



- Goal: Explore dose level and regimen to enable optimal threshold that delivers right therapeutic outcome while maximizing patient safety and convenience

…targeting an optimal therapeutic benefit



MED, Minimally Effective Dose

Positive Proof-of-Concept Data for Lonigutamab

First Subcutaneous Anti-IGF-1R to Report Clinical Data in Thyroid Eye Disease[1]

Positive Proof of Concept for Lonigutamab

- Rapid and meaningful clinical responses for Proptosis, Clinical Activity Score, and Diplopia versus placebo
- Responses observed within 3 weeks after first subcutaneous dose and were maintained through 12 weeks; six weeks after last dose
- Well-tolerated safety profile

Potential for Differentiated Profile

- High potency anti-IGF-1R with unique impact on the IGF-1R Axis enabling the potential to optimize benefit-risk towards more complete resolution of disease
- Clinically meaningful responses achieved at lower exposures relative to standard of care:
  - Maximizing clinical benefit by enabling greater depth and durability of response with longer term treatment
  - Minimizing safety liability by reducing C_{max} compared to IV therapy and penetration to the inner ear which may drive hearing impairment

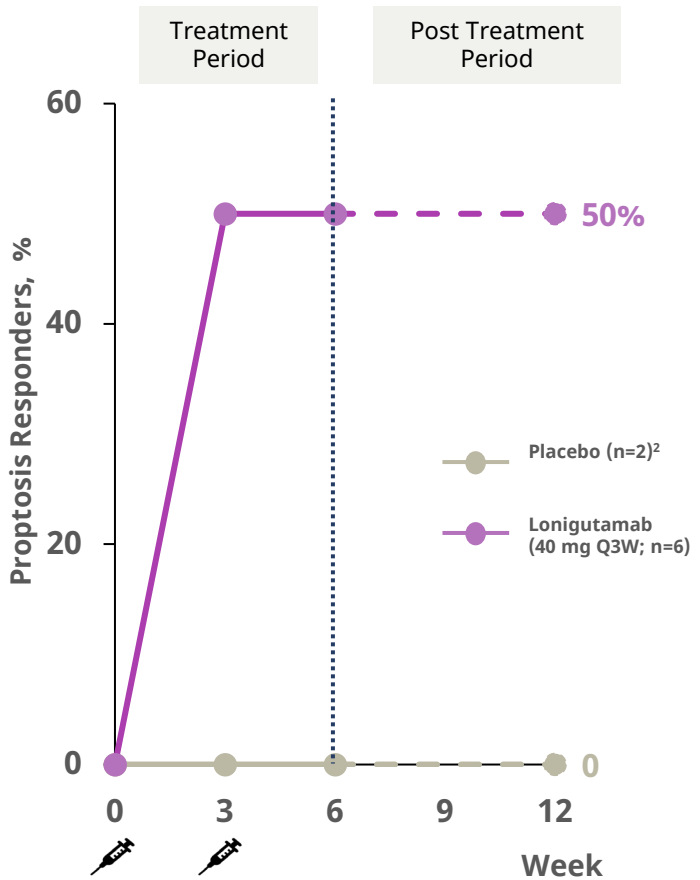
Next Steps

- Dose Group 3 completed; Dose Group 4 ongoing
- Positive EOP2 interaction with FDA completed
- Investor Event to be held in early 2025: updated Phase 2 trial data, FDA feedback and Phase 3 program design
- Plan to initiate Phase 3 program in Q1 2025

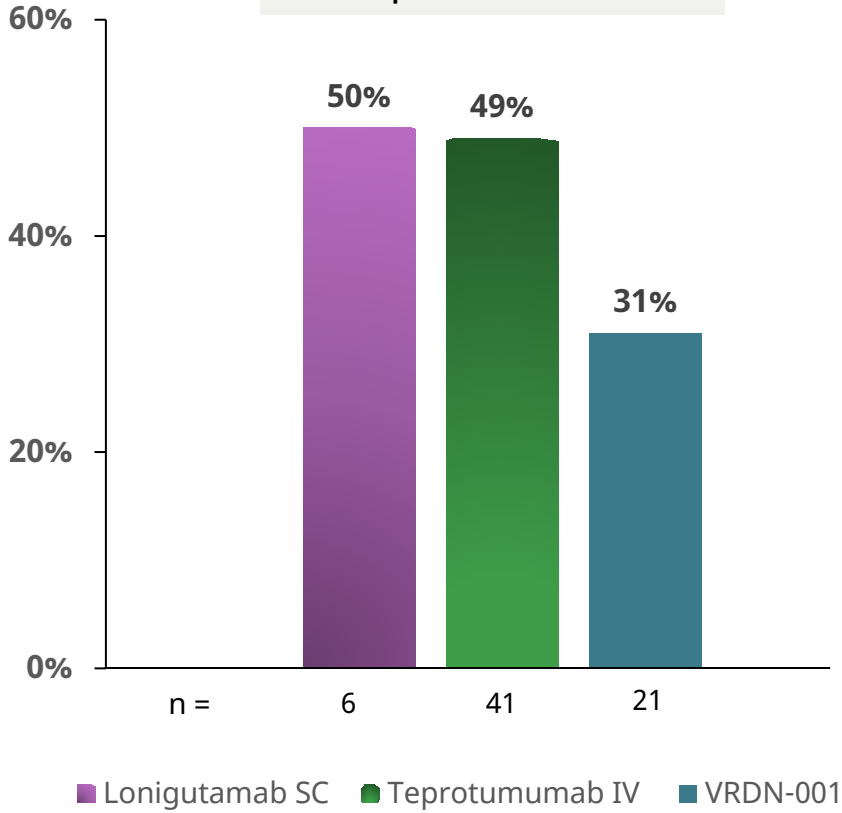
1 Based on publicly reported data in the U.S. and EU.

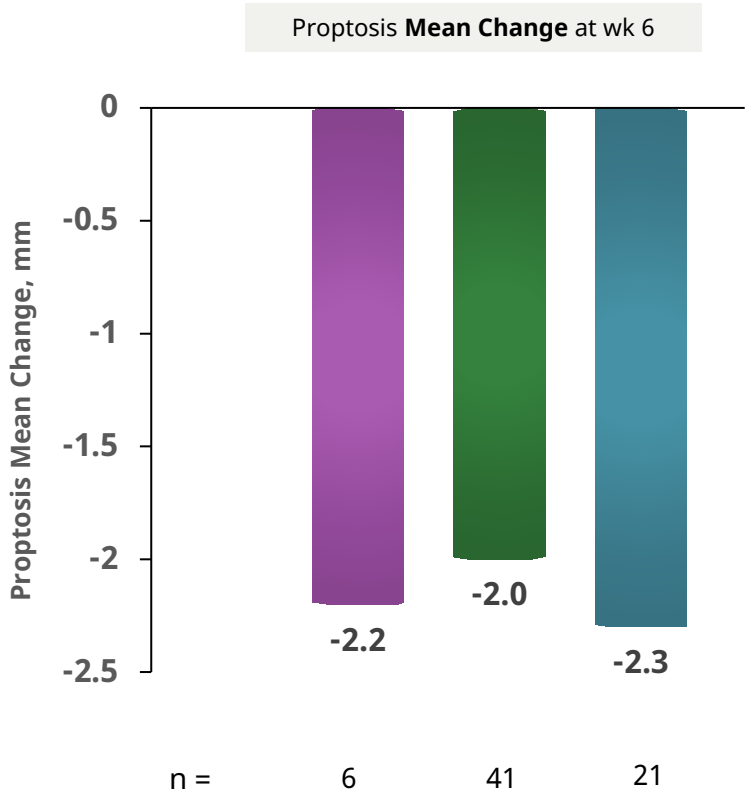
Cohort 1: Proptosis Response Maintained Through and Post Treatment Periods

50% of Patients Achieved Response Within 3 weeks After a Single 40mg Subcutaneous Injection



Proptosis Response[1]
(defined as ≥2-mm reduction in proptosis)

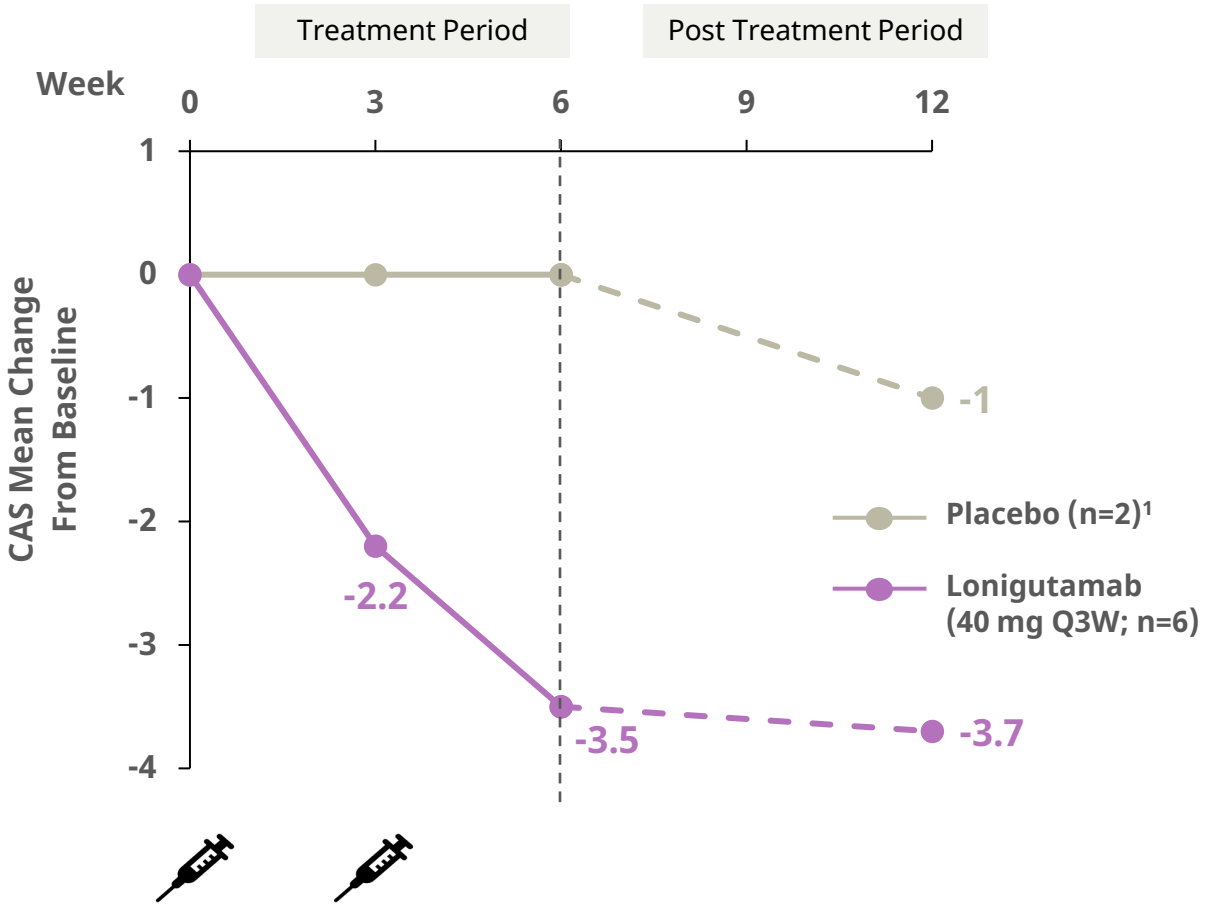


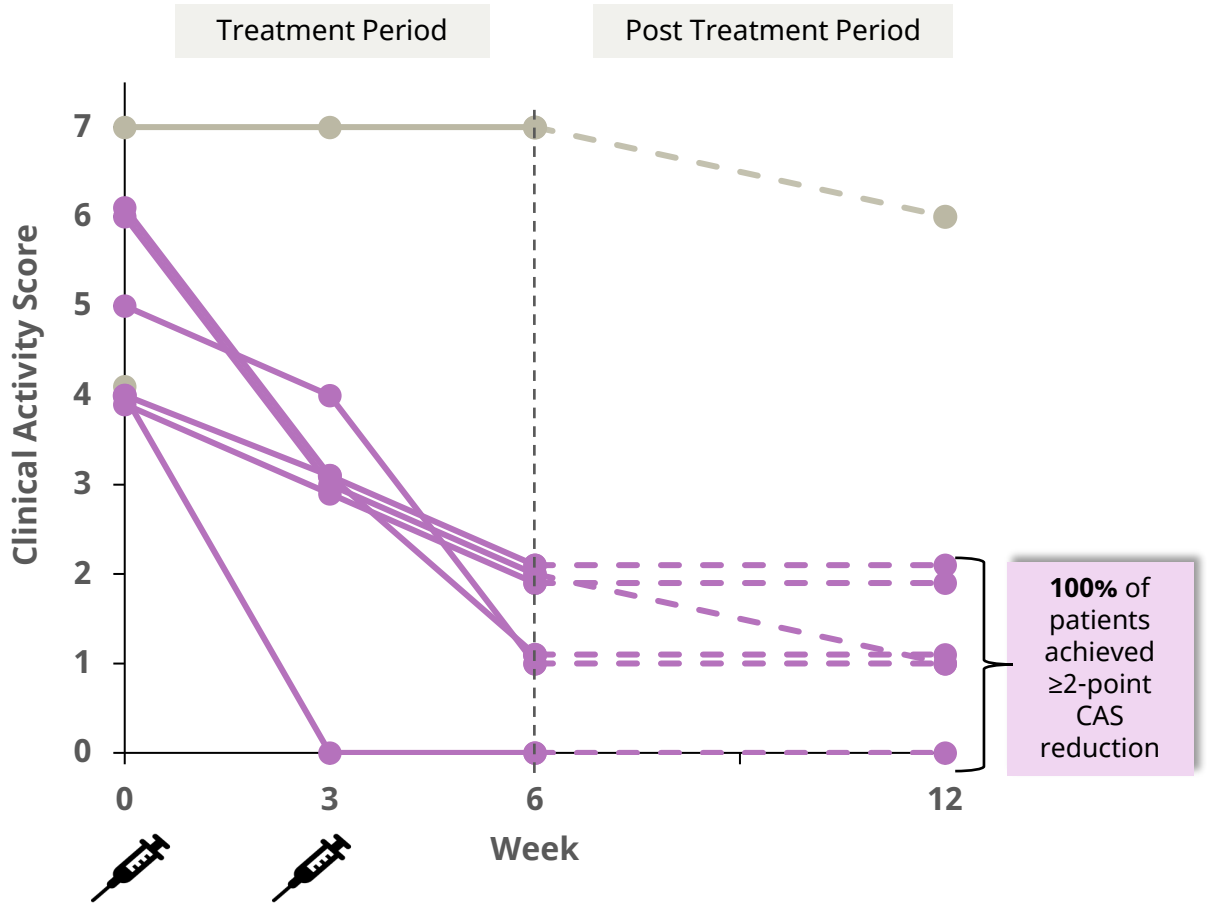


1 Proptosis was measured via Hertel exophthalmometer.
2 One patient in the placebo group had no post-baseline data and was imputed as a non responder. Q3W, every 3 weeks
3 Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: Douglas NEJM 2020 382:341:52. VRDN-001 data from public source: Kossler AAO 2023, pooled doses

Cohort 1: Clinical Activity Score – Changes From Baseline

100% of Patients Achieved Clinically Meaningful CAS Reduction Within 6 Weeks After 2 SC Injections

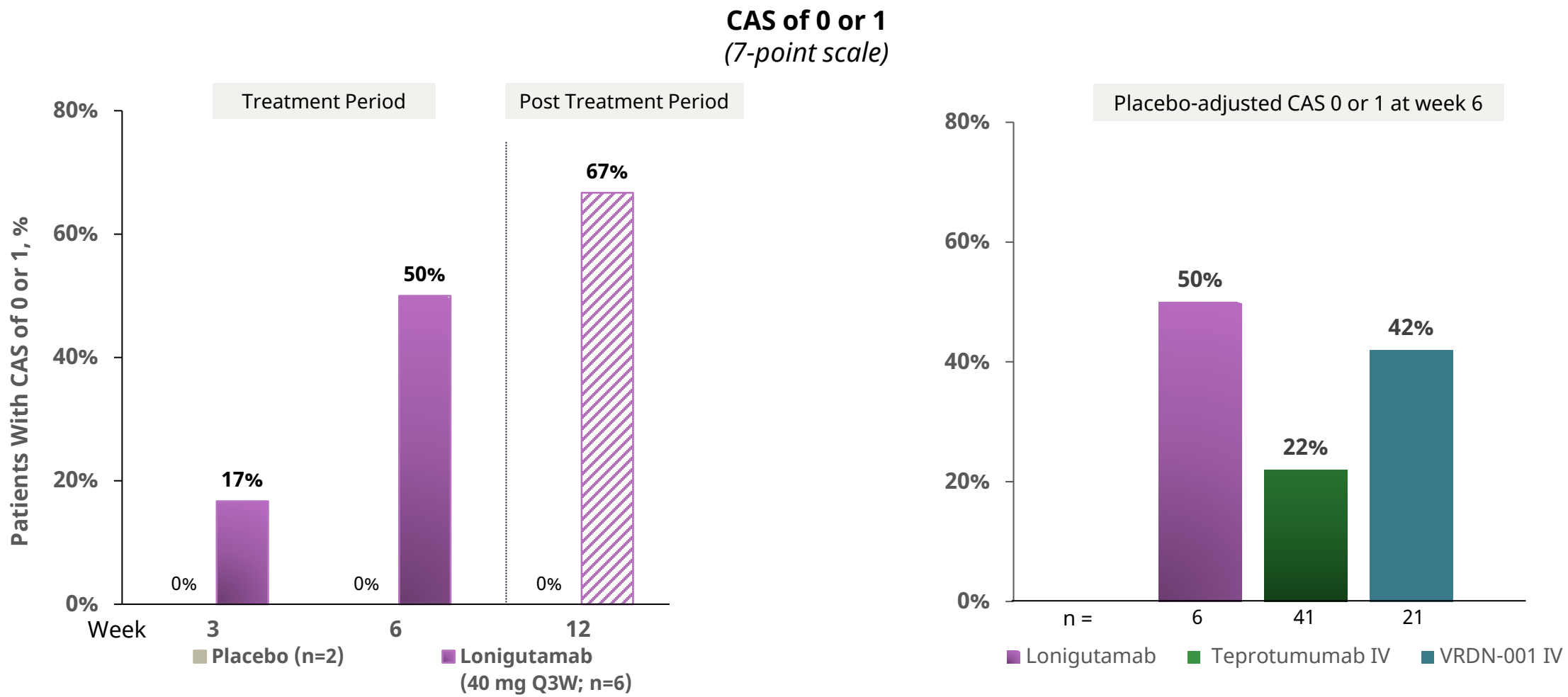




CAS Responders: patients with ≥2 pt CAS reduction considered clinically meaningful
1 One patient in the placebo group had no post-baseline data.
CAS, Clinical Activity Score; Q3W, every 3 weeks

Cohort 1: Clinical Activity Score – 0 or 1 Through Week 12

Low Disease Activity (CAS 0 or 1) Achieved at Week 6 and Improved Over Time

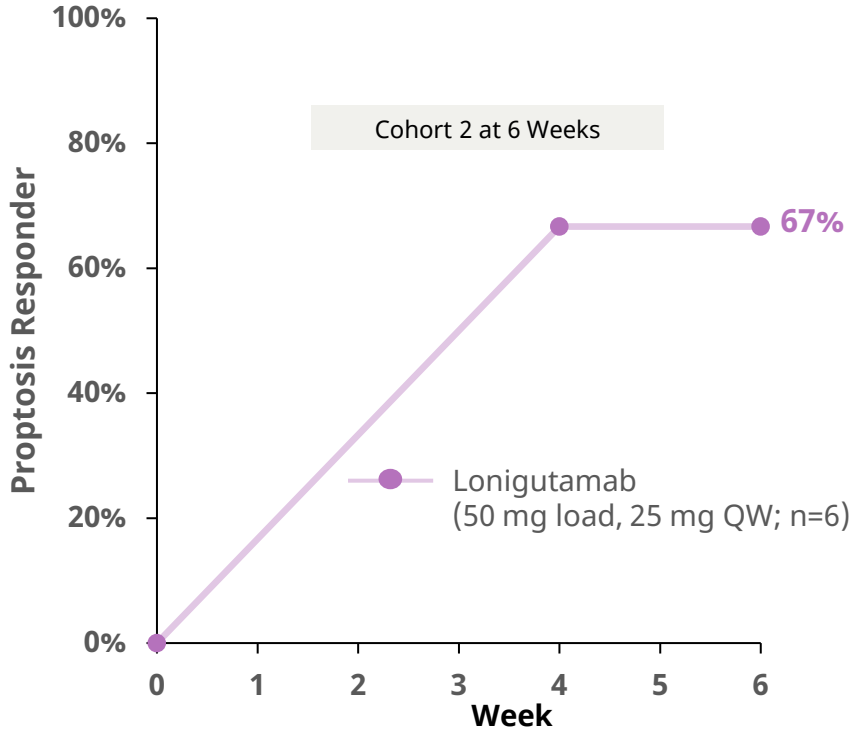


One patient in the placebo group had no post-baseline data and was imputed as a non responder. Q3W, every 3 weeks
Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: Douglas NEJM 2020 382:341:52. VRDN-001 data from public source: Kossler AAO 2023.

Cohort 1 & 2: Proptosis and CAS Responses Seen at Week 6

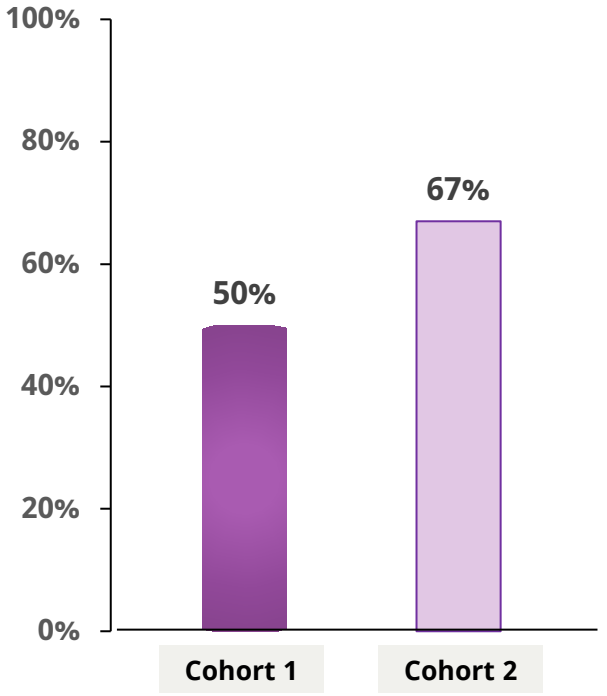
Data Consistent With Cohort 1 and Allows for Regimen Exploration

Treatment Period



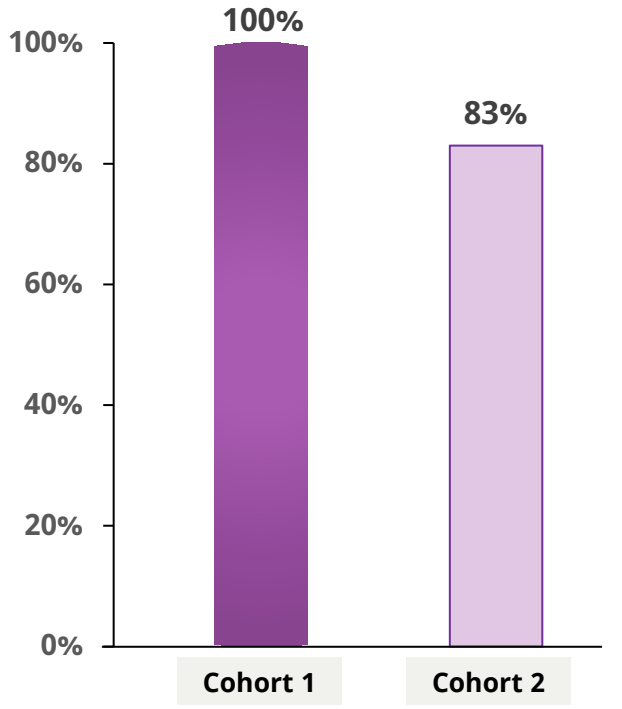
Proptosis Responder Rate at week 6

% patients with ≥2 mm reduction in proptosis



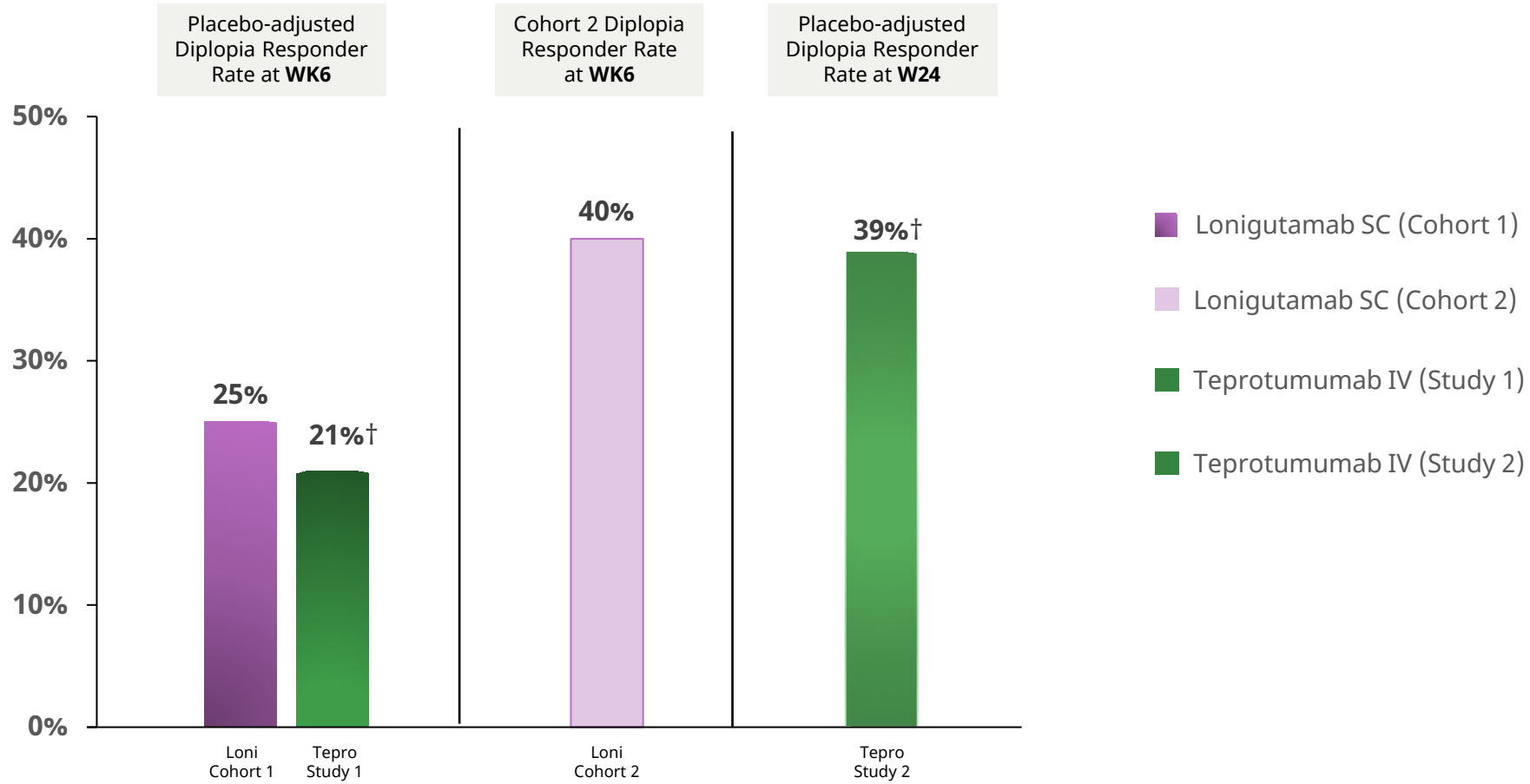
CAS Responder Rate at week 6

%: patients with ≥2 pt CAS reduction



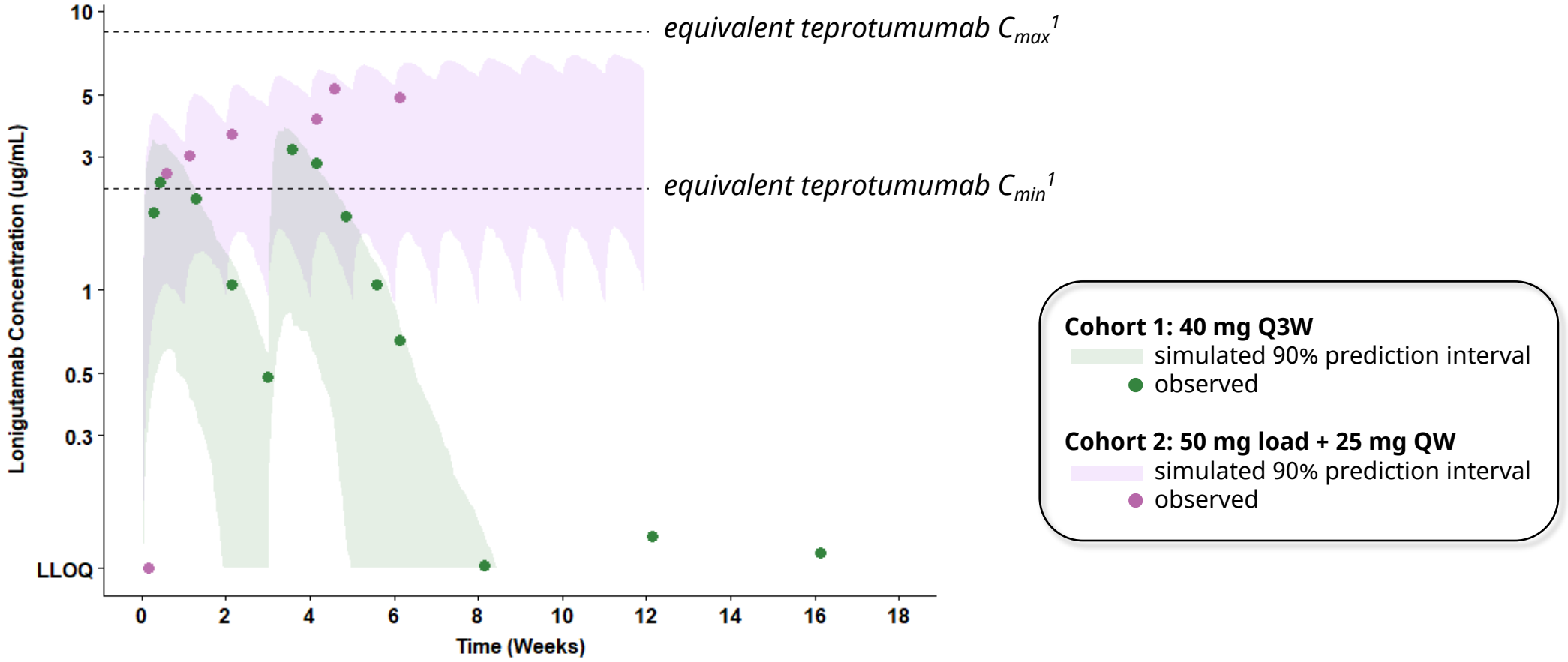
Proptosis was measured via Hertel exophthalmometer. Proptosis responder rate: % patients with ≥2 mm reduction in proptosis Q3W, every 3 weeks; QW, weekly.
CAS Responder rate: % patients with ≥2 pt CAS reduction considered clinically meaningful.

Clinically Meaningful Diplopia Responses Observed by Week 6[1]



1 Comparisons across trials, with inherent limitations. Diplopia Response defined as improvement in >1 Bahn Gorman grade.
†Teprotumumab: Ph2 Smith, et al NEJM 2017 376:1748-61, Ph3 Douglas NEJM 2020 382:341:52

Subcutaneous Exposure Achieves Responses Enabling Optimization of Benefit-Risk



1 Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: FDA Tepezza Clinical Pharmacology review, Teprotumumab Cmax and Cmin from approved dosing regimen (10 mg/kg followed by 20 mg/kg Q3W). Equivalence calculated by ~75x scaled potency. Cohort 1: intensive sampling, Cohort 2: Cmin, through W6. LLOQ, lower limit of quantitation for the assay. Preliminary PK data from an ongoing study.

Safety: Cohorts 1 and 2

No audiology changes, no hyperglycemia events, and no serious adverse events

n (%)	Placebo (Cohort 1) n=2	Lonigutamab (Cohort 1: 40 mg Q3W) n=6	Lonigutamab (Cohort 2: 50 mg load, 25 mg QW) n=6
Any TEAEs	2 (100.0)	4 (66.7)	5 (83.3)
Serious	0	0	0
Grade 2 or higher	0	1 (16.7)	2 (33.3)
Any treatment-related TEAEs	0	3 (50.0)	4 (66.7)
Any AESIs	0	3 (50.0)	0
Tinnitus	0	3 (50.0)	0
Inflammatory bowel disease	0	0	0
Hyperglycemia	0	0	0
TEAEs leading to study drug discontinuation	1 (50.0)	0	0
Dysthyroid optic neuropathy	1 (50.0)	0	0

- Most events were mild in severity, with no serious TEAEs
- Injection site reactions were all mild
- Three patients receiving lonigutamab had AESIs
  - All tinnitus (all mild): no changes on audiogram
- One patient receiving placebo discontinued due to dysthyroid optic neuropathy

Tinnitus Events Mild, Resolved With no Intervention

Events Not Associated With Changes on Audiogram or Treatment Interruption; Not Dose Related

COHORT*	Description	Symptom Onset	Resolution Outcomes	Audiogram
Cohort 1 (40 mg Q3W)	• 47 yo female with mild bilateral tinnitus • Subject also on amiloride and hydrochlorothiazide	1 day after dose 2	Resolved without intervention	*At baseline, week 6, 12, 16* No changes
	• 47 yo female, history of intermittent tinnitus/blocked ears from seasonal allergies, 1 mild R-sided tinnitus, 1 mild bilateral tinnitus	10 days after dose 2 32 days after dose 2	Resolved without intervention	*At baseline, week 6, 12, 16* No changes
	• 50 yo male with 2 events of mild bilateral tinnitus • Subject also on amlodipine	2 days after dose 1 1 day after dose 2	Resolved without intervention	*At week 6* No changes

*No tinnitus events observed in Cohort 2 (50 mg load, 25 mg QW)

Izokibep

Non-Infectious, Non-Anterior Uveitis (NINAU) is an Orphan Indication With Significant Unmet Need

Complex Disease

- Characterized by ocular inflammation, mainly affecting people of working age
- Heterogeneous with various etiologies - pathophysiology varies greatly and not well understood, even within a given anatomic site
- Significant challenges in diagnosis and management; patients at risk of retinal detachment, vision loss, cataracts and glaucoma[1]

Rare / Orphan

- ~70,000 people living with NINAU in US; >200,000 in Japan[2]
- A leading cause of blindness in the developed world with decades more lifetime risk of vision loss relative to age-related diseases
- Significant personal and economic impact of potential vision lost

Common Symptoms

- Redness, pain, blurred vision, sensitivity to light, corneal manifestations, pupil changes, and floaters[3]

1. Dick AD, Tundia N, Sorg R, Zhao C, Chao J, Joshi A, et al. Risk of ocular complications in patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis. *Ophthalmology.* 2016;123(3):655–662.
2. Thorne et al. Prevalence of Noninfectious Uveitis in the United States: A Claims-Based Analysis. JAMA Ophthalmol. 134(11):1237-1245;2016; Umazume et al, 2021
3. Rosenbaum JT, Bodaghi B, Couto C, Zierhut M, Acharya N, Pavesio C, et al. New observations and emerging ideas in diagnosis and management of non-infectious uveitis: A review. *Semin Arthritis Rheum.* 2019;49(3):438–445.

Current Treatment Paradigm Highlights Need for New Therapeutics; Most Patients do not Receive Biologic Tx; ~50% of Biologic Tx Relapse

	Steroids	Immunomodulators	Biologics
Current Therapeutic Approaches	Corticosteroids are effective first line therapy in ~ 60% of patients	Added for patients who do not respond (or relapse) during corticosteroid therapy	Adalimumab (anti-TNF) is only approved biologic Delays time to treatment failure in 39–55% of patients[1]
Limitations	Should be **tapered over time to prevent long-term adverse effects**	**Slow acting**, often administered in conjunction with high-dose corticosteroids	Predominantly used in tertiary care settings, in **more complex and difficult-to-treat (severe/refractory) patients**

Need for Rapid, Deep, Durable, Safe Therapies

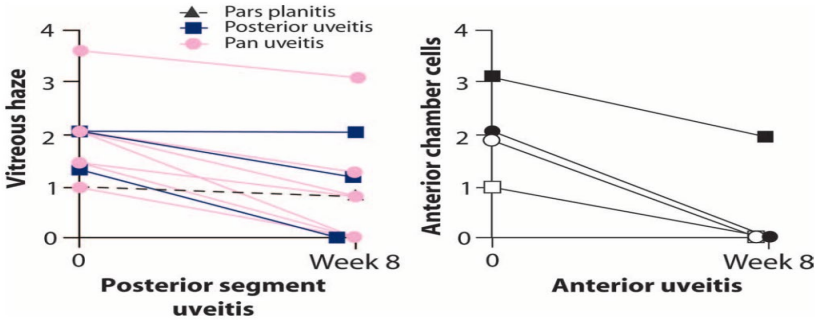
- **Fast-acting**, non-steroid therapies to rapidly control disease without adverse effects
- **Novel mechanisms of action** to address heterogeneity of UV
- Use in **anti-TNF failures**
- Inducing **durable remissions**
- Therapies that specifically **target macular edema** – a major cause of blindness in uveitis

1. Humira® *USPI*

Secukinumab Experience Suggests Targeting IL-17A Could Achieve Efficacy in Uveitis, But Requires High Serum Exposures

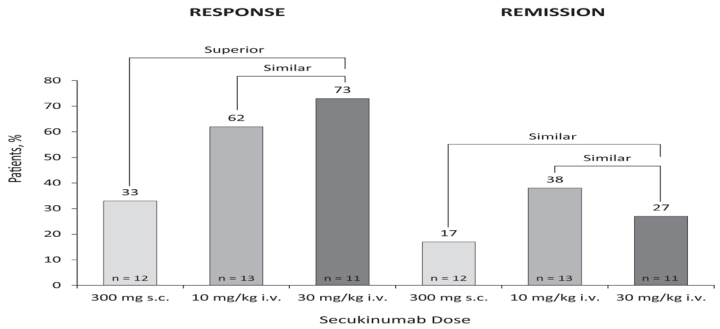
IV

Ph. 2
Hueber et al 2010



Efficacious
Secukinumab 8W
10 mg/kg IV Q3W

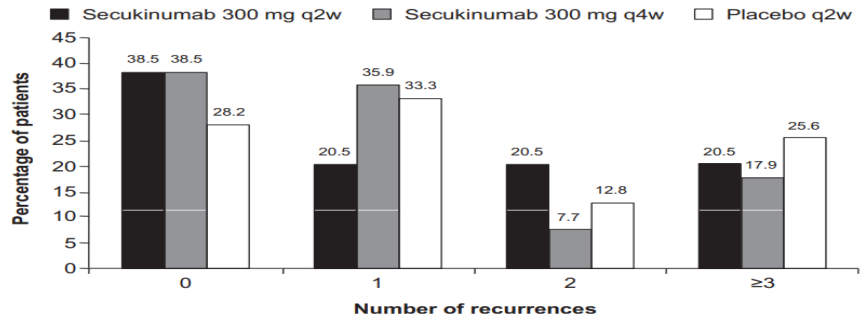
IIS
Letko et al 2015



Efficacious
Secukinumab 8W
300 mg SC Q2W
10 mg/kg IV Q2W
30 mg/kg IV Q4W

SC

Ph. 3
Dick et al 2013



NOT efficacious
Secukinumab 24W
300 mg SC dose (~4 mg/kg)

Izokibep's High Potency & Small Size Enables Potential to Improve Clinical Response With SC Exposures Others Require IV to Achieve

Validated Target

IL-17A is associated with autoimmune inflammation. Marketed monoclonal antibodies have demonstrated targeting IL-17A results in dose-responsive increases in efficacy without dose-limiting toxicity.

Targeting more broadly than IL-17A as a means to more effectively inhibit the IL-17 axis has demonstrated risk for increased fungal infection, suicidal ideation & behavior, and liver toxicity with a requirement for routine monitoring – all raising the potential of association specifically with inhibition of IL-17F.

Hitting IL-17A the hardest may be the sweet spot of achieving increased exposure/efficacy without introducing additional or new safety liability. The high potency and small size of izokibep has the potential to impact clinical response.

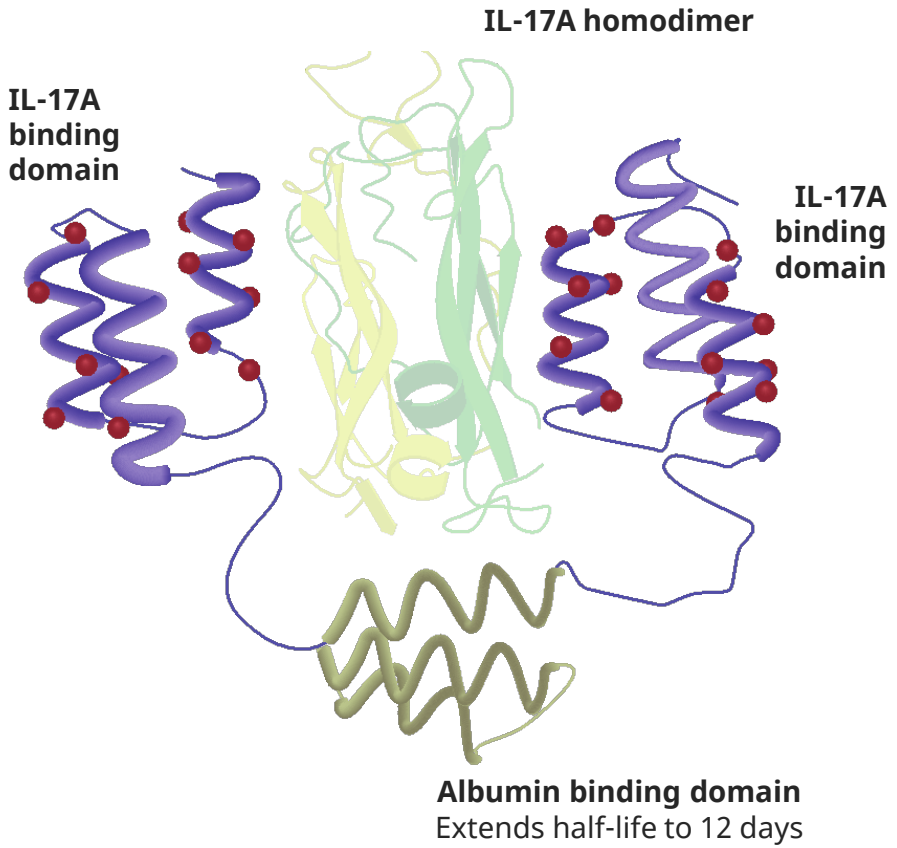
High Potency

Blocks the homodimeric IL-17A target protein by binding to both sub-units simultaneously with the high affinity (KD: 0.3 pM) versus other IL-17A inhibitors.

Small Size

~1/10th the size of a mAb (~18.6 kD) enabling potential to reach difficult to treat tissues.

pM, picomolar; kD, kilodalton



IZOKIBEP (~18.6 kDa)

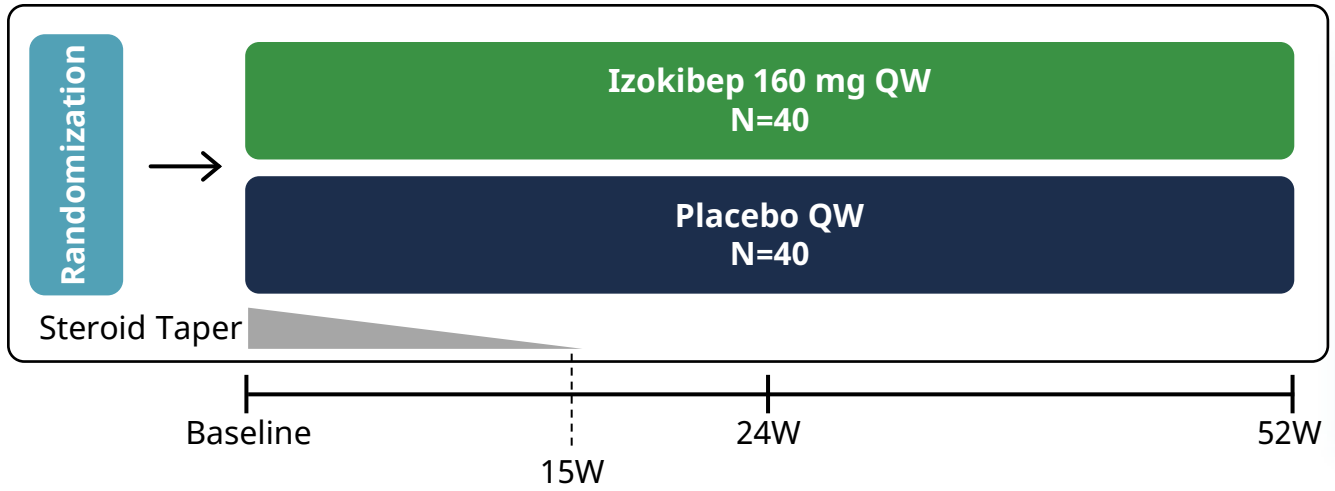
Izokibep UV

Ongoing Phase 2b/3 Trial

Enrollment Completed with Topline Data Expected in December 2024

Screening/ Eligibility

- Active non-infectious uveitis
- Macular edema on CT
- Anterior chamber cells
- Abnormal fluorescein angiogram
- Failure of corticosteroids or TNFi



Efficacy Endpoints

Primary: Time to treatment failure at 24 Weeks

Secondary:

- BCVA
- NEI VFQ-25 score
- Central retinal thickness
- Quiescence

Safety Endpoints*

- TEAEs, events of special interest and SAEs
- Laboratory values and vital signs at collected timepoints

*Secondary endpoint

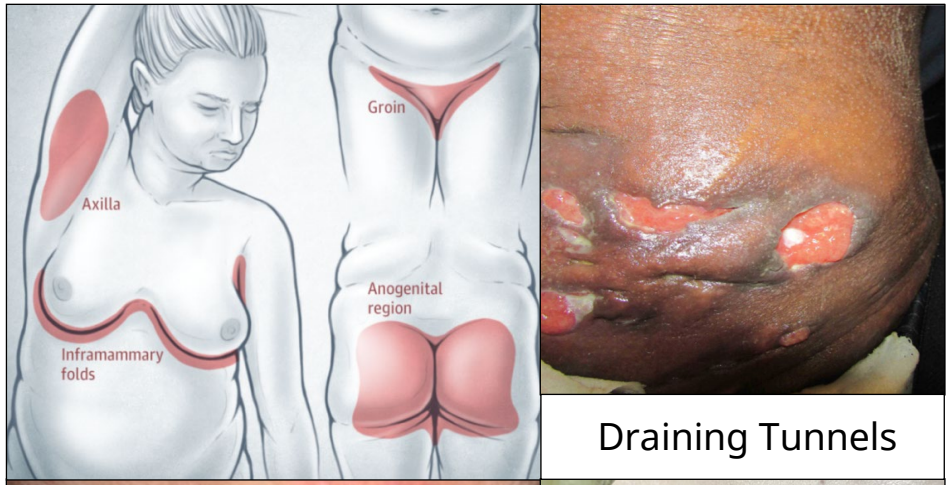
Stratification: TNFi, systemic inflammatory disease

BCVA, best corrected visual acuity, change from best state < W10; NEI VFQ-25, National Eye Inst. Visual Function Questionnaire-25, change from best state <10W; *Change from baseline and change from best <W10 by SD-OCT (Spectral-Domain Optical Coherence Tomography)

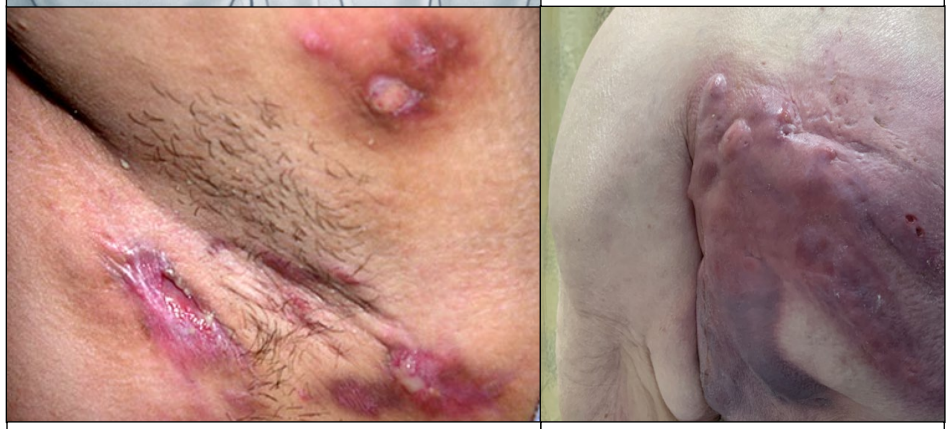
Hidradenitis Suppurativa

Hidradenitis Suppurativa is a Devastating Disease Where Exposures Matter

High Potency and Small Size of Izokibep Could Improve Patient Outcomes



Draining Tunnels



Inflammatory Nodules

Abscesses

- Chronic Inflammatory disease characterized by skin abscesses, inflammatory nodules, fistulae, scar tissue, malodor and pain, often resulting in permanent disfigurement and social stigma negatively impacting quality of life
- **~370,000 HS patients in the U.S.**; approximately half of patients are considered to have moderate-to-severe disease
- Diagnosis rates are estimated to **increase 1-3% annually**
- **Current therapy options are limited**; more complete and faster resolution of disease symptoms remain an unmet need for patients

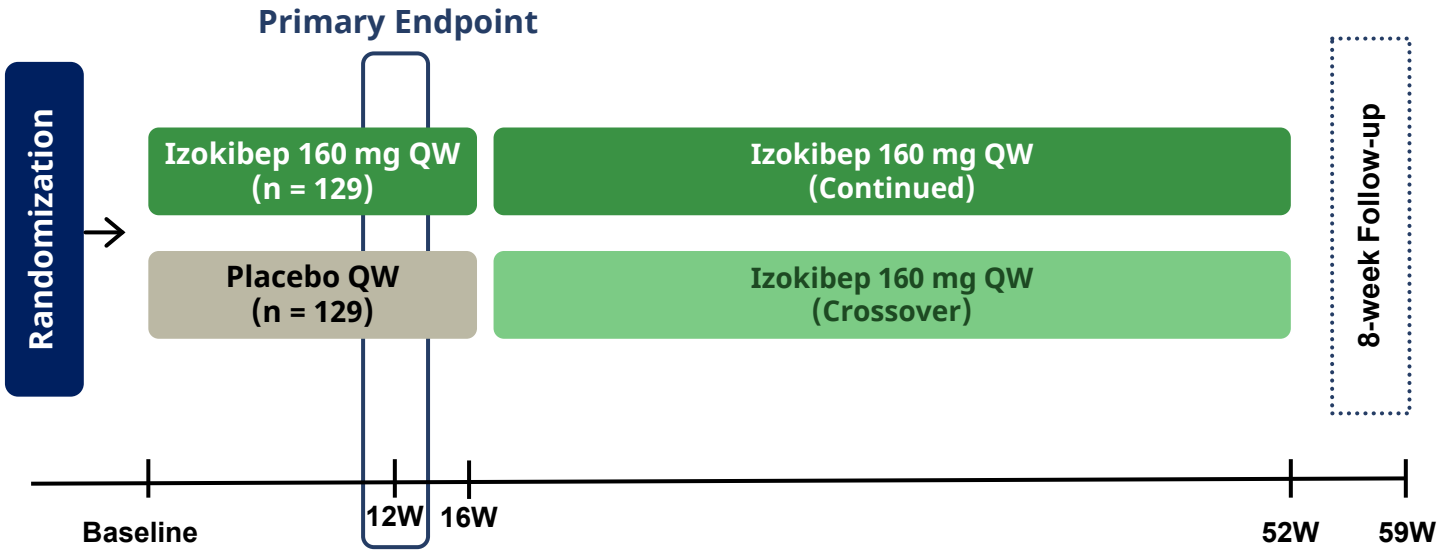
Izokibep HS

Izokibep Phase 3 Hidradenitis Suppurativa Trial

Randomized, Double-blind, Placebo-controlled

Screening/ Eligibility

- Moderate-to-severe HS
- HS > 6 months
- HS lesions in ≥2 distinct anatomic areas, one of which is Hurley Stage II or III
- Minimum abscess/nodule (AN) count of 5
- Inadequate response, intolerance or contraindication to oral antibiotics allowed in up to 30% of enrolled patients



Efficacy Endpoints

Primary & secondary endpoints wk 12

- HiSCR75 (primary)

Secondary

- HiSCR90/100/50
- Flares (%)
- DLQI
- AN = 0, 1 or 2 (%)
- Skin Pain 3 pt reduction (%)

Safety Endpoints

All secondary endpoints wk 12

- AEs, SAEs, AESIs
- Safety laboratory, vital signs, physical examination

Exploratory

- Presence of ADAs

Statistical Analysis

- Multiple Imputation
- Use of antibiotics that treat HS imputed as NR
- Stratified by prior TNFi use for HS (Yes/No) and Hurley Stage (II or III)

ACELYRIN

ADA, anti-drug antibodies; **AE,** adverse event;; **AESIs,** adverse events of special interest; **AN**, total abscess and inflammatory nodule count; **HiSCR**, Hidradenitis Suppurativa Clinical Response; **HS,** hidradenitis suppurativa; **QW**, once every week; **SAE**, serious adverse event; **DLQI**, Dermatology Life Quality Index; **TNFi,** tumor necrosis factor inhibitor. Primary endpoint at week 12, Placebo Crossover at 16 wks

Positive Results for Global Phase 3 in Hidradenitis Suppurativa

Positive topline results

- Study met primary endpoint of HiSCR75 at 12 weeks with statistical significance
- Izokibep demonstrated rapid onset of action within 2 weeks and achieved statistical significance as early as week 4
- Rapid and significant responses achieved for the higher hurdles of HiSCR90/100

Differentiated profile

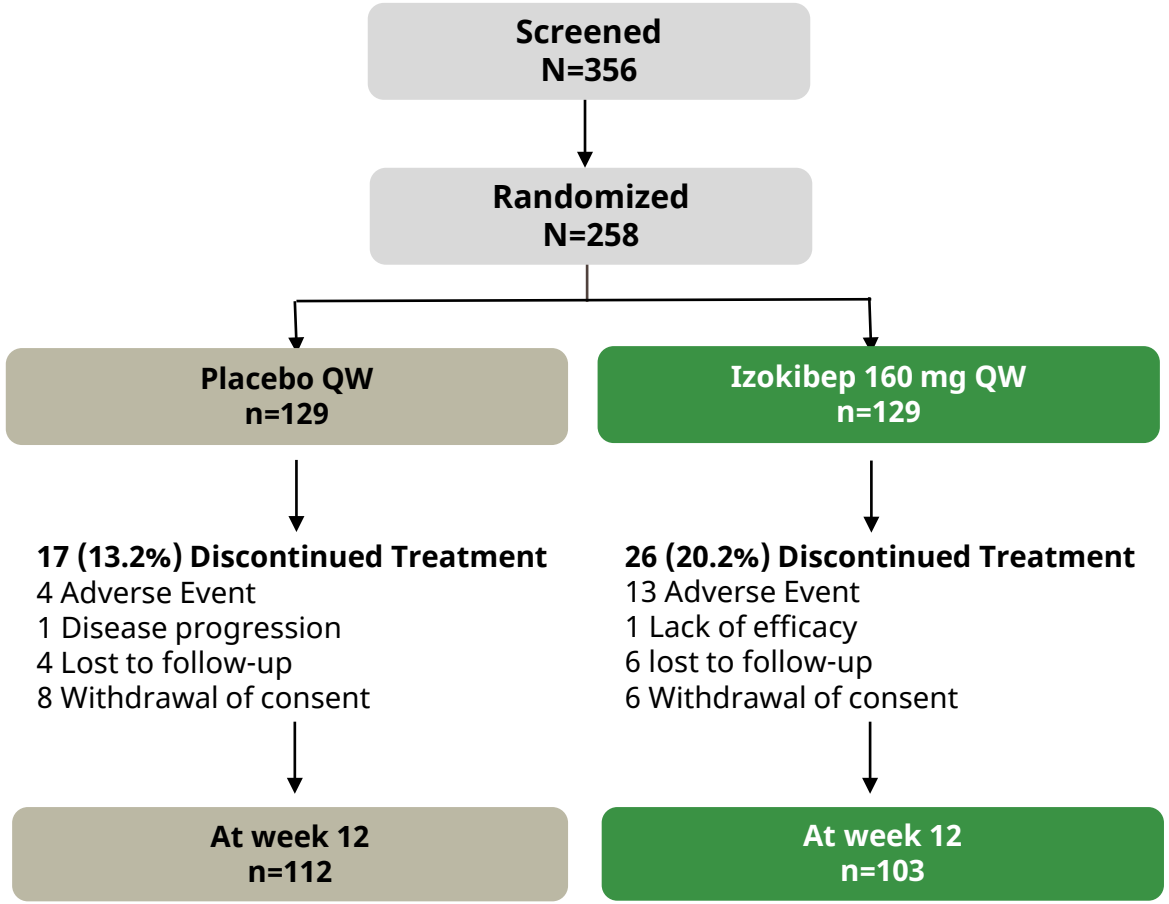
- Izokibep IL-17A inhibition achieves rapid improvement across HiSCR, pain and disability endpoints
- 1 out of 4 patients achieve HiSCR90/100 within 12 weeks
- Continued deepening of HiSCR responses over time observed in preliminary Week 16 data (2/3 of patients)
- Safety consistent with previous experience – notably no cases of candidiasis, liver toxicity or suicidal ideation

Regulatory Pathway

- Based on EOP2 FDA guidance, single additional trial of approximately 400 patients required for registration

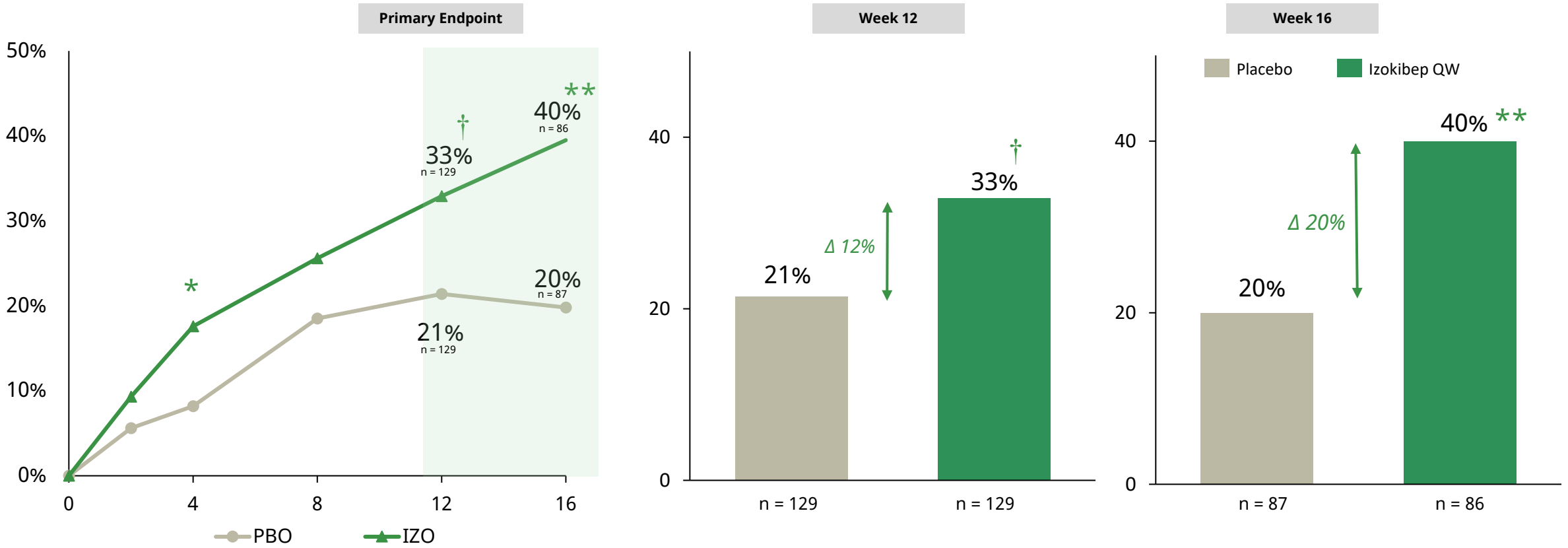
Baseline Characteristics & Patient Disposition Through Week 12

	Overall N = 258	Placebo N = 129	160mg QW N = 129
Mean age (years)	37.3	37.4	37.1
White (%)	69.8	70.5	70.2
Black (%)	19.0	21.7	16.3
Female (%)	69.0	69.0	69.0
Mean BMI	34.0	34.1	34.0
Smoking status current (%)	43.0	45.0	41.1
Mean disease duration (years)	10.2	10.2	10.2
Mean AN count	13.4	13.2	13.5
Mean abscess count	2.5	2.7	2.4
Mean inflammatory nodule count	10.8	10.5	11.1
Mean Draining Tunnels	2.2	2.2	2.2
Hurley Stage (%)			
Stage II	62.0	63.6	60.5
Stage III	38.0	36.4	39.5
Mean DLQI Score	11.9	11.4	12.3
Prior TNFi (%)	14.7	15.5	14.0



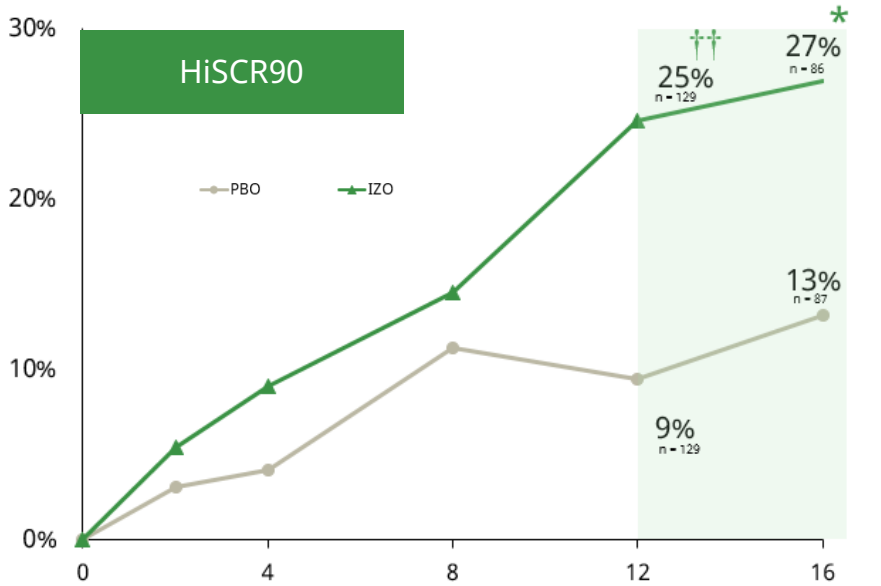
Primary Endpoint : HiSCR75

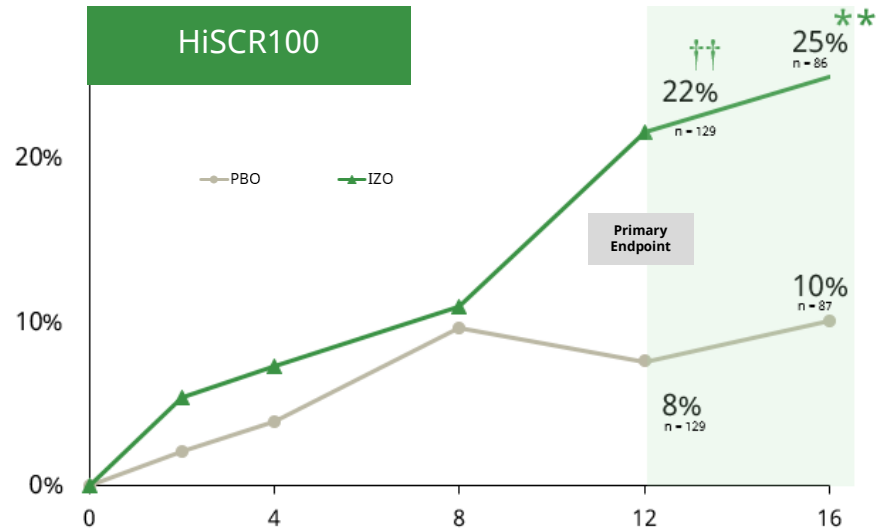
HiSCR75 Week 12 (1) and 16 (2) - Placebo Controlled

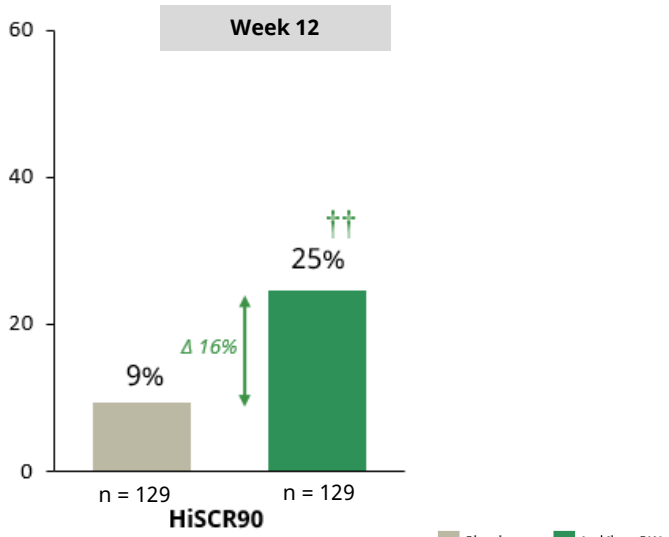


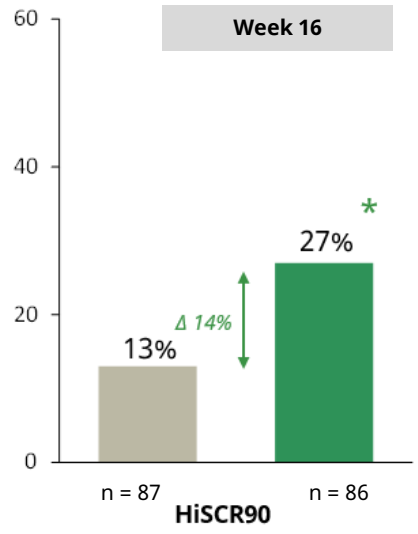
(1) Week 12 data are from the full analysis set (n=129) using prespecified multiple imputation; Significance per prespecified statistical hierarchy: †P<0.05 vs placebo; ††P<0.01 vs placebo
(2) All patients have reached Week 16. Interim Week 16 data using prespecified multiple imputation, of 2/3 of patients (n = 86 active and n = 87 placebo), is presented. This interim data is not necessarily indicative of, and could materially differ from, complete Week 16 results. Nominal p value: *p<0.05 vs placebo; **P<0.005 vs placebo

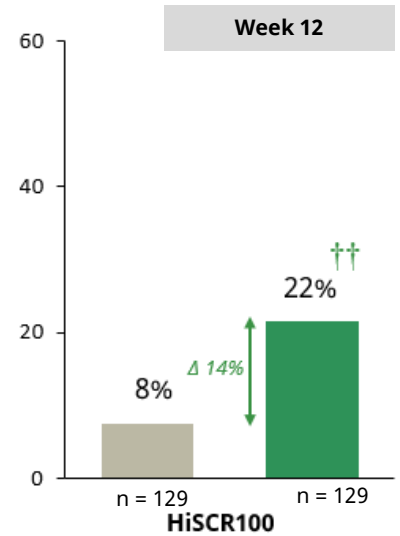
HiSCR90 and HiSCR100 - Week 12 (1) and Week 16 (2) - PBO Controlled

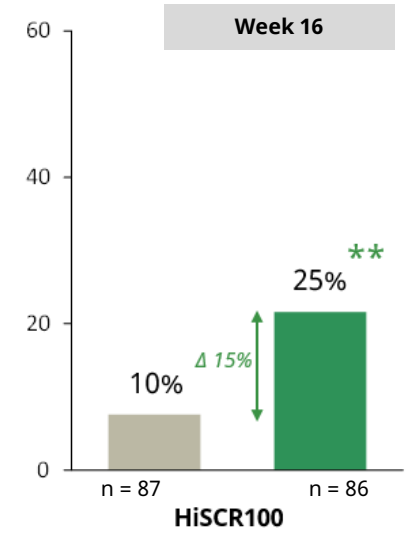










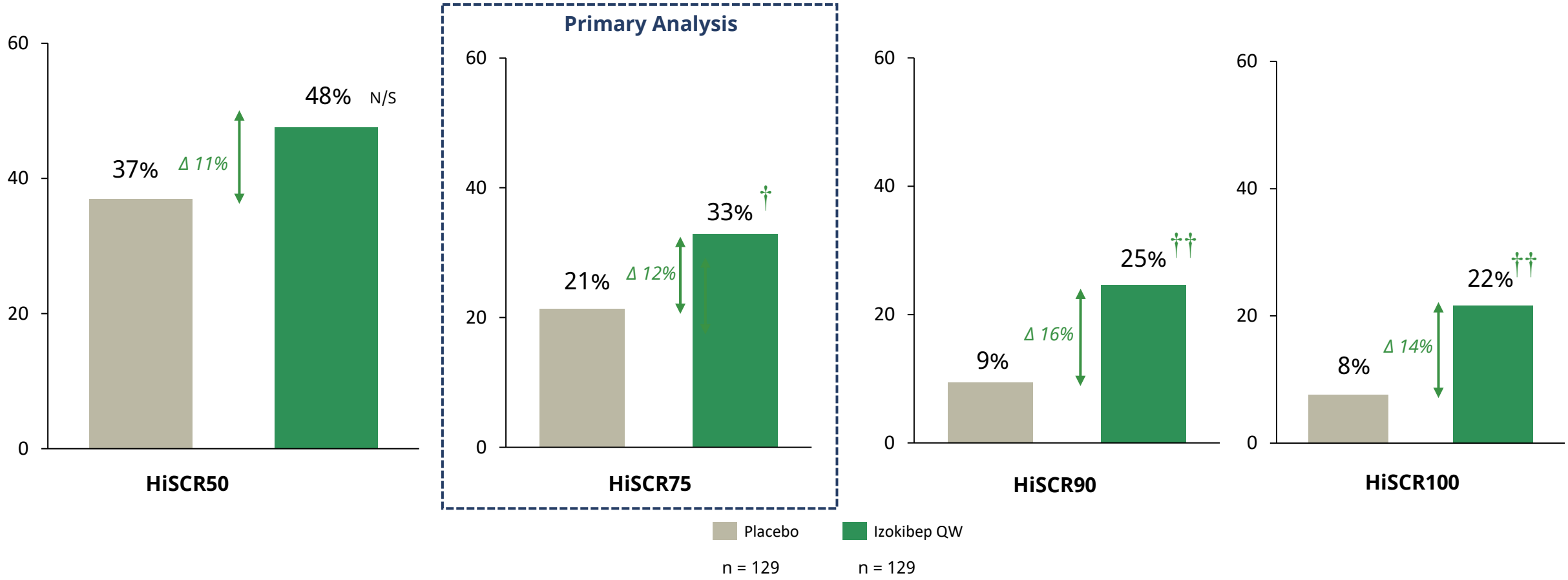


(1) Week 12 data are from the full analysis set using prespecified multiple imputation; Significance per prespecified statistical hierarchy: †P<0.05 vs placebo; ††P<0.01 vs placebo

(2) All patients have reached Week 16. Interim Week 16 data using prespecified multiple imputation, of 2/3 of patients (n = 86 active and n = 87 placebo), is presented. This interim data is not necessarily indicative of, and could materially differ from, complete Week 16 results; Nominal p value: *P<0.05 vs placebo; **P<0.01 vs placebo.

Summary of HiSCR Responses At Week 12

Approx. 1 of 4 Patients achieved HiSCR90/100 by week 12

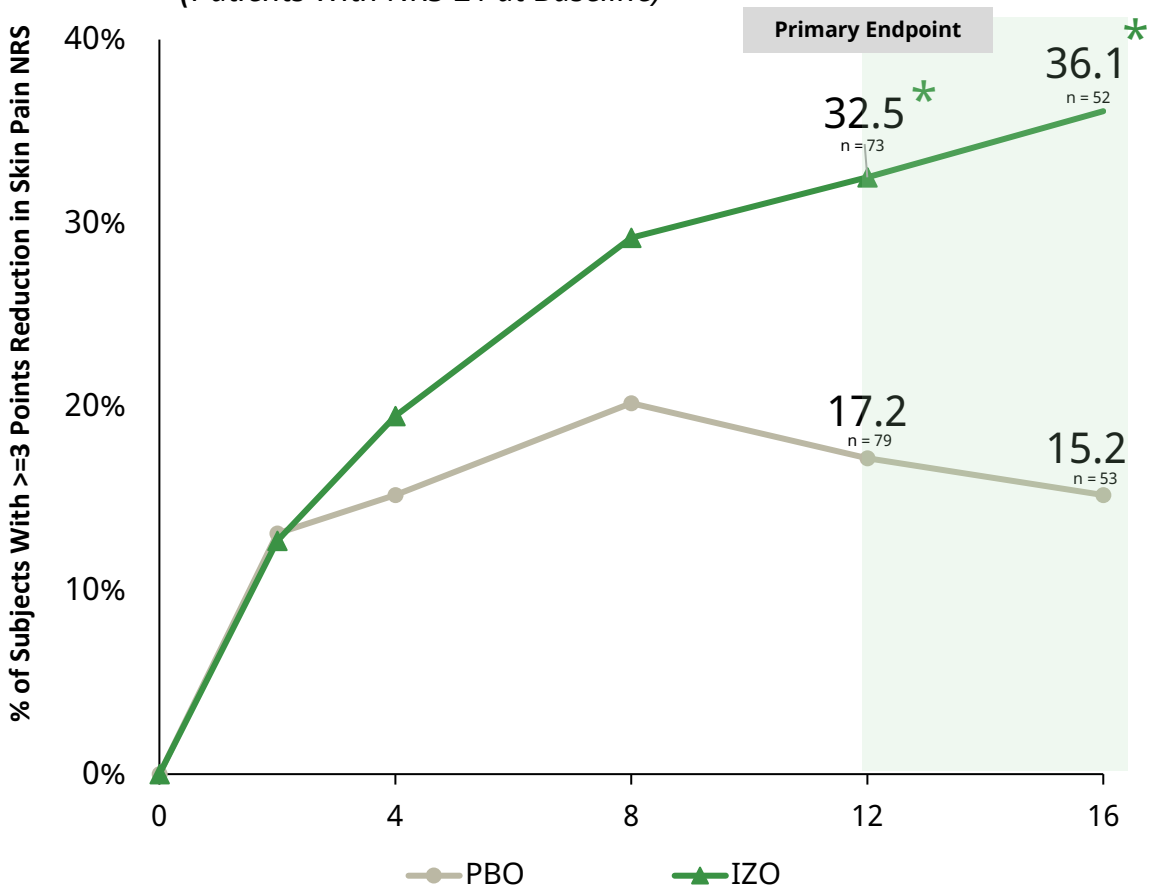


Week 12 data are from the full analysis set using prespecified multiple imputation. Significance per prespecified statistical hierarchy: †P<0.05 vs placebo; ††P<0.01 vs placebo. **N/S,** not significant.

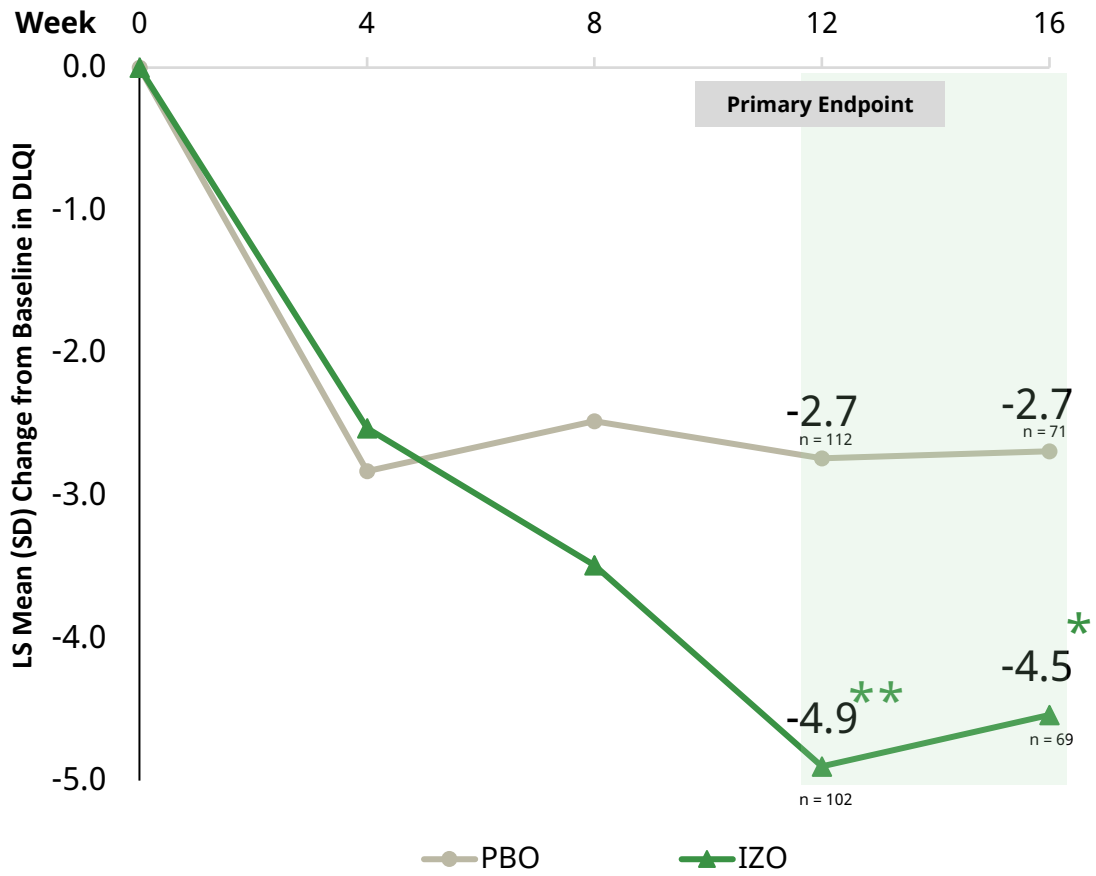
Reduction in Skin Pain and Improvement in DLQI

Skin Pain Reduction Week 12 (1) and 16 (2) - Placebo Controlled

(Patients With NRS ≥4 at Baseline)



DLQI through Week 12 (1) and 16 (2) - Placebo Controlled



(1) Week 12 data are from the full analysis set using prespecified multiple imputation : Nominal P value: *P<0.05 vs placebo; **P<0.01 vs placebo

(2) All patients have reached Week 16. Interim Week 16 data using prespecified multiple imputation, of 2/3 of patients (n = 86 active and n = 87 placebo), is presented. This interim data is not necessarily indicative of, and could materially differ from, complete Week 16 results; Nominal P value: *P<0.05 vs placebo; **P<0.01 vs placebo

Safety Results at Week 12

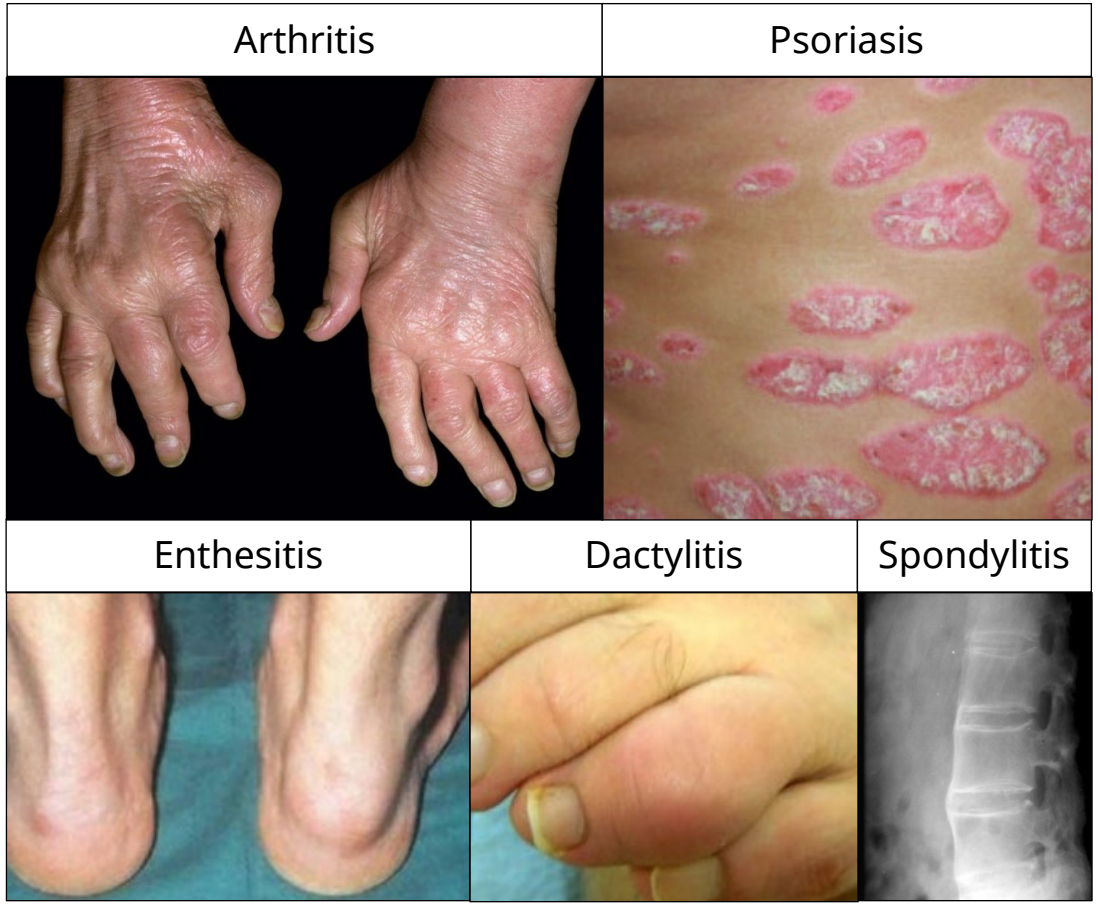
	Placebo N = 129 N (%)	160mg QW N = 129 N (%)
Any TEAE	68 (52.7)	102 (79.1)
Serious TEAE	4 (3.1)[1]	1 (0.8)[2]
TEAE leading to discontinuation of study treatment	4 (3.1)	10 (7.8)
Injection Site Reactions leading to discontinuation	0	7 (5.4)
Death	0	0
Infections and Infestations	31 (24)	27 (20.9)
TEAE Preferred Term (≥5%)		
Injection Site Reactions	10 (7.8)	84 (65.1)[4]
Headache	12 (9.3)	13 (10.1)
Nasopharyngitis	9 (7)	9 (7)
Fatigue	3 (2.3)	7 (5.4)
Diarrhea	2 (1.6)	7 (5.4)
AE of Special Interest		
Candidiasis	3 (2.3)[3]	0
Inflammatory bowel disease	0	0
Suicidal ideation behavior	0	0

[1] Abdominal pain, pelvic fracture, hepatic enzyme increased, urinary retention, hidradenitis; [2] Vasculitis ; [3] Two vulvovaginal, one undefined [4]Two injections of 80mg Izokibep administered weekly [5] No new safety findings observed in the preliminary Week 16 data

Psoriatic Arthritis

Psoriatic Arthritis is a Disease With Multiple Manifestations

Addressing Totality of Manifestations is Necessary to Achieve Disease Control & Restore Quality of Life



- Psoriatic arthritis (PsA) is **a chronic, inflammatory disease with multiple clinical manifestations** including arthritis, psoriasis, enthesitis (inflammation of dense, non-vascular tissues that connect ligaments and tendons to bone), spondylitis, and dactylitis
- **~1.6M PsA patients in the U.S.**
- Among moderate-to-severe PsA patients, **over a third fail non-biologic therapy**
- **More complete and faster resolution of disease symptoms** manifesting in dense tissues (e.g., enthesitis) remain an unmet need
- **Addressing totality of manifestations is the goal** for patients

Addressing All Manifestations Particularly Those That are Historically Difficult to Treat is Important to Improving Quality of Life for Patients

Peripheral Arthritis

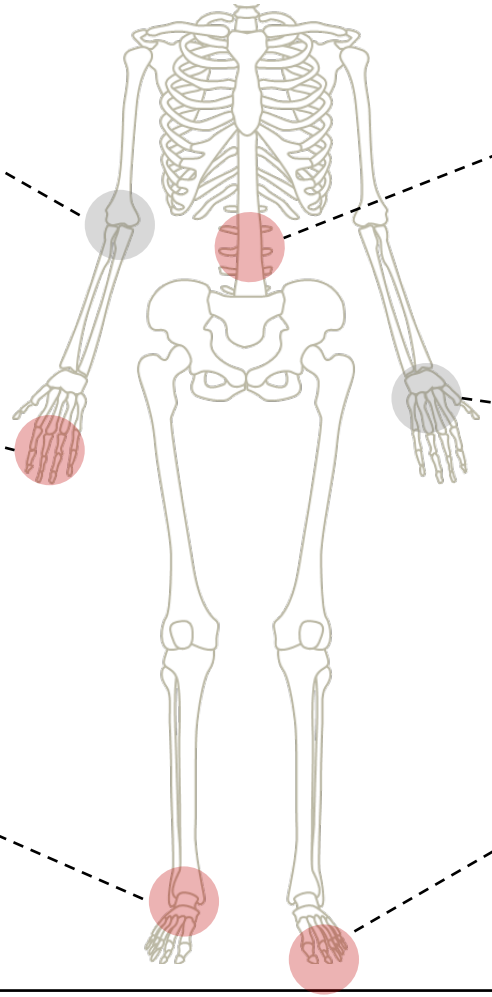
Painful swelling and stiffness of the joints of the arms and legs, including the elbows, wrists, hands and feet

Dactylitis

A hallmark symptom of PsA characterized by diffuse swelling along the entire length of fingers leading to "sausage-like" digits

Enthesitis

An early sign of PsA leading to a disabling and painful inflammation at sites where tendons, ligaments, or fascia insert into bones



Spondylitis

Inflammation of the axial skeleton (sacroiliac joints and spine) leading to severe back pain and stiffness

Skin Psoriasis

Chronic, inflammatory skin lesions (psoriasis), usually red, scaly thickened plaques on scalp, trunk, and extremities.

Nail Psoriasis

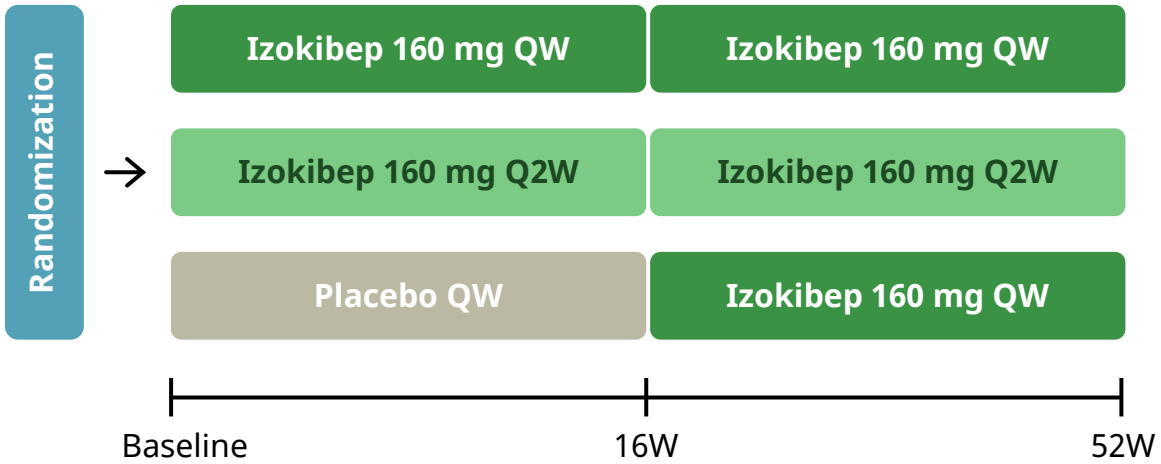
A serious functional impairment that affects a patient's quality of life and cause pitting, crumbling, and loosening of the nail plate

Historically difficult to treat

Positive Topline Data From Global Phase 2b/3 Announced 1Q24

Screening/ Eligibility

- Moderate-Active PsA (CASPAR criteria)
- > 3 TJC68 and > 3 SJC66
- RF and anti-CCP negative at screening
- Previous failure to NSAID or csDMARD or TNFi



Efficacy Endpoints

Primary & secondary endpoints, all week 16

- ACR50 (primary)
- PASI90
- Resolution of enthesitis (LEI=0)
- MDA
- ACR20
- PsAID response
- HAQ-DI change from baseline

Safety Endpoints

All secondary endpoints

- TEAEs, events of interest, and SAEs
- Laboratory values and vital signs at collected timepoints
- Treatment-emergent ADAs

Note: A fourth trial arm evaluating izokibep at 80 mg Q4W (equivalent to ~20 mg Q2W) was also included in study design to enable dose modeling but not shown here due to small sample size, n=8

CASPAR, Classification criteria for Psoriatic Arthritis; **QW,** Every Week; **Q2W,** Every Two Weeks; ; **SJC/66,** swollen joint count, assessing 66 joints; **TJC/68,** tender joint count, assessing 68 joints; **RF,** Rheumatoid Factor; **CCP**, Cyclic Citrullinated Peptide; **NSAID,** non-steroidal anti-inflammatory drugs; **csDMARD,** conventional synthetic disease modifying anti-rheumatic drug; **TNFi,** TNF inhibitor; **ACR50,** ≥50% improvement based on American College of Rheumatology criteria; **PASI90**, ≥90% improvement based on Psoriasis Area and Severity Index; **LEI,** Leeds Enthesitis Index; **MDA**, minimal disease activity; **ACR20,** ≥50% improvement based on American College of Rheumatology criteria; **PsAID**, PsA Impact of Disease; **HAQ-DI**, Health Assessment Questionnaire Disability Index; **TEAE**, treatment-emergent adverse event; **SAE**, serious adverse event; **ADA**, anti-drug antibodies

Positive Results for Global Phase 2b/3 in Psoriatic Arthritis

Positive topline results

- Study met primary endpoint of ACR50 at 16 weeks with high statistical significance
- Significant, multidomain responses achieved for the high hurdles of ACR70, PASI90, PASI100 and MDA
- Improvement in magnitude of responses relative to Phase 2 notable given higher burden of disease in Phase 2b/3

Differentiated profile

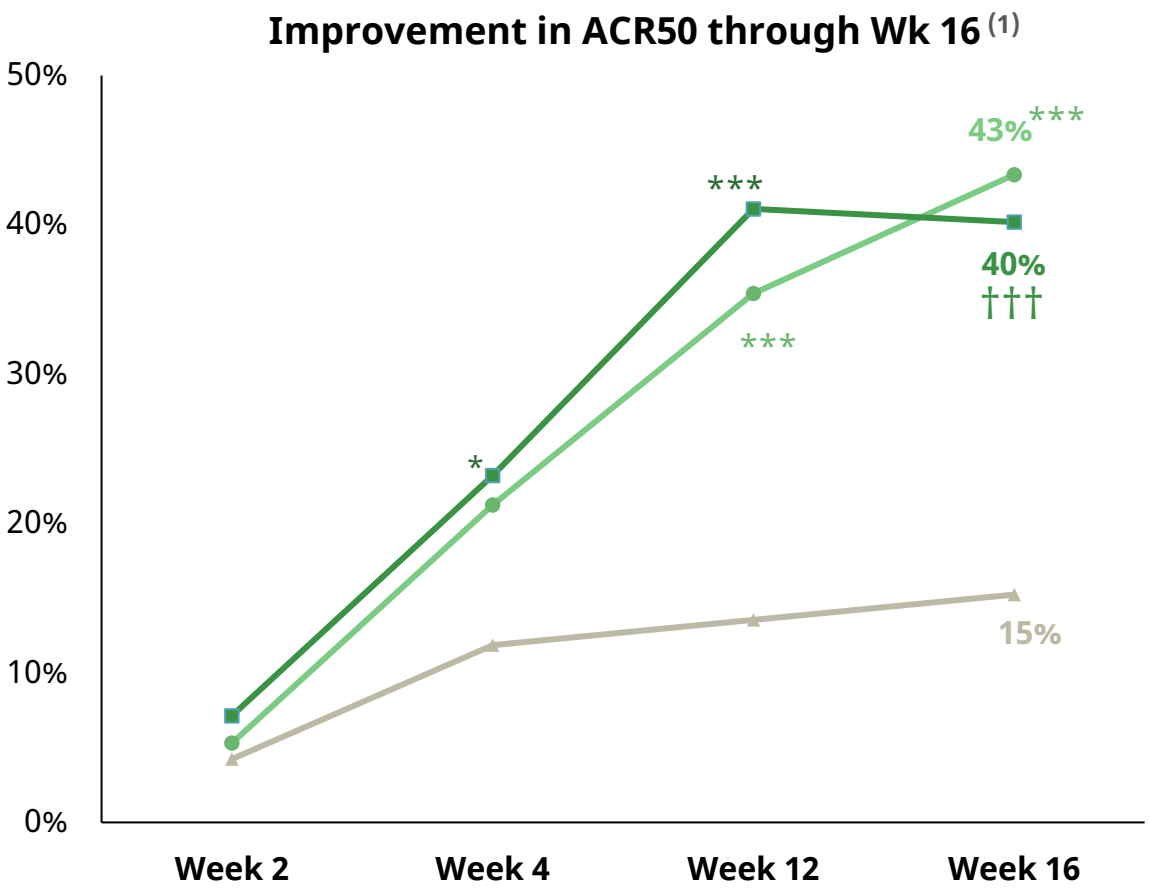
- Izokibep IL-17A inhibition alone achieves rapid improvement in resolution across manifestations of disease
- Pre-specified analyses support the potential for differentiation in enthesitis resolution
- Higher clinical responses than reported by the IL-17A agents
- Results comparable to those reported by the IL-17A&F agents but without the associated safety liabilities

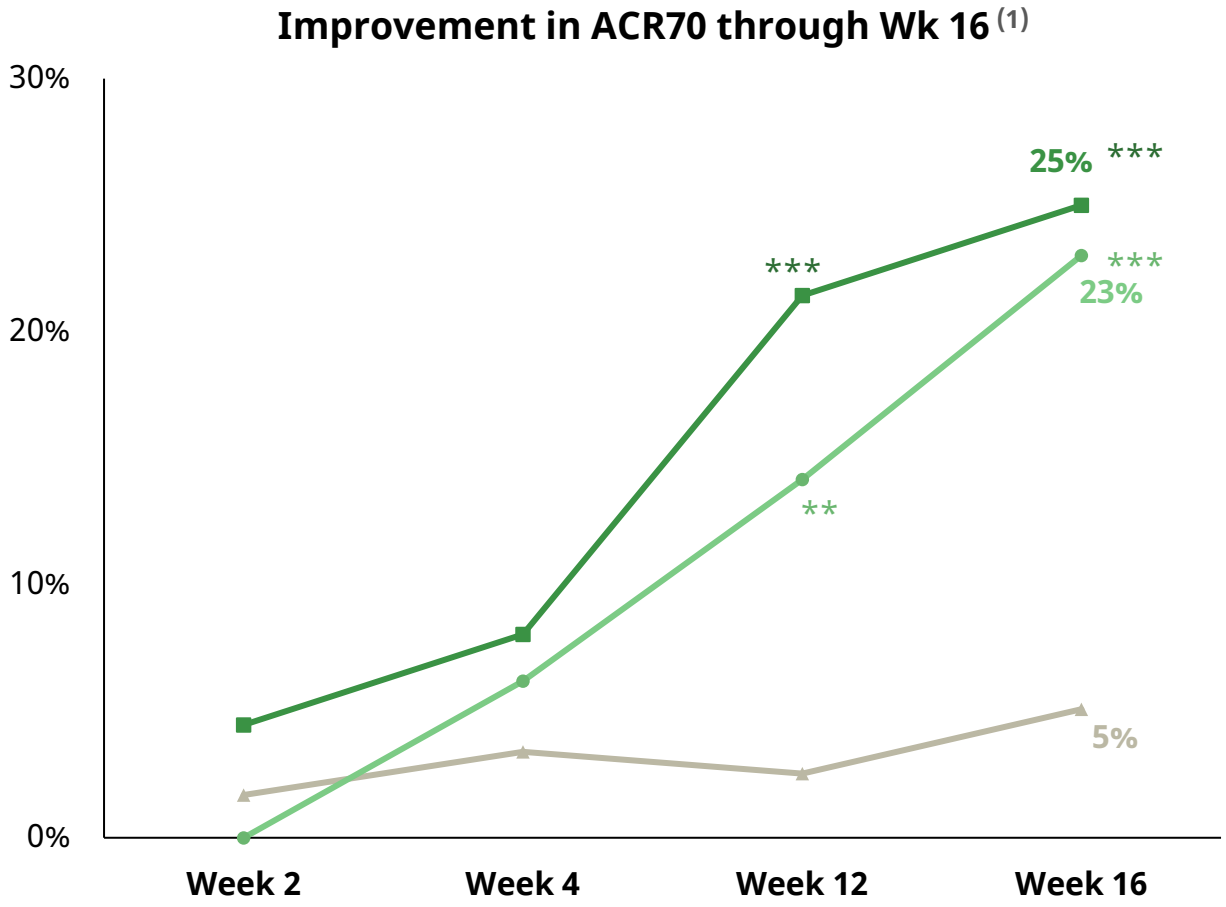
Deep and durable responses

- Robust clinical responses in high hurdle composite endpoints (ACR50/PASI100 and MDA)
- No safety limitation to long term treatment seen to date
- Longer duration of therapy has previously demonstrated the potential for even further improvements over time

ACR50 and ACR70 at Primary Endpoint

ACR50 in Joints Showed Rapid and Robust Improvement; Achievement of ACR70 Demonstrates Even Deeper Levels of Response





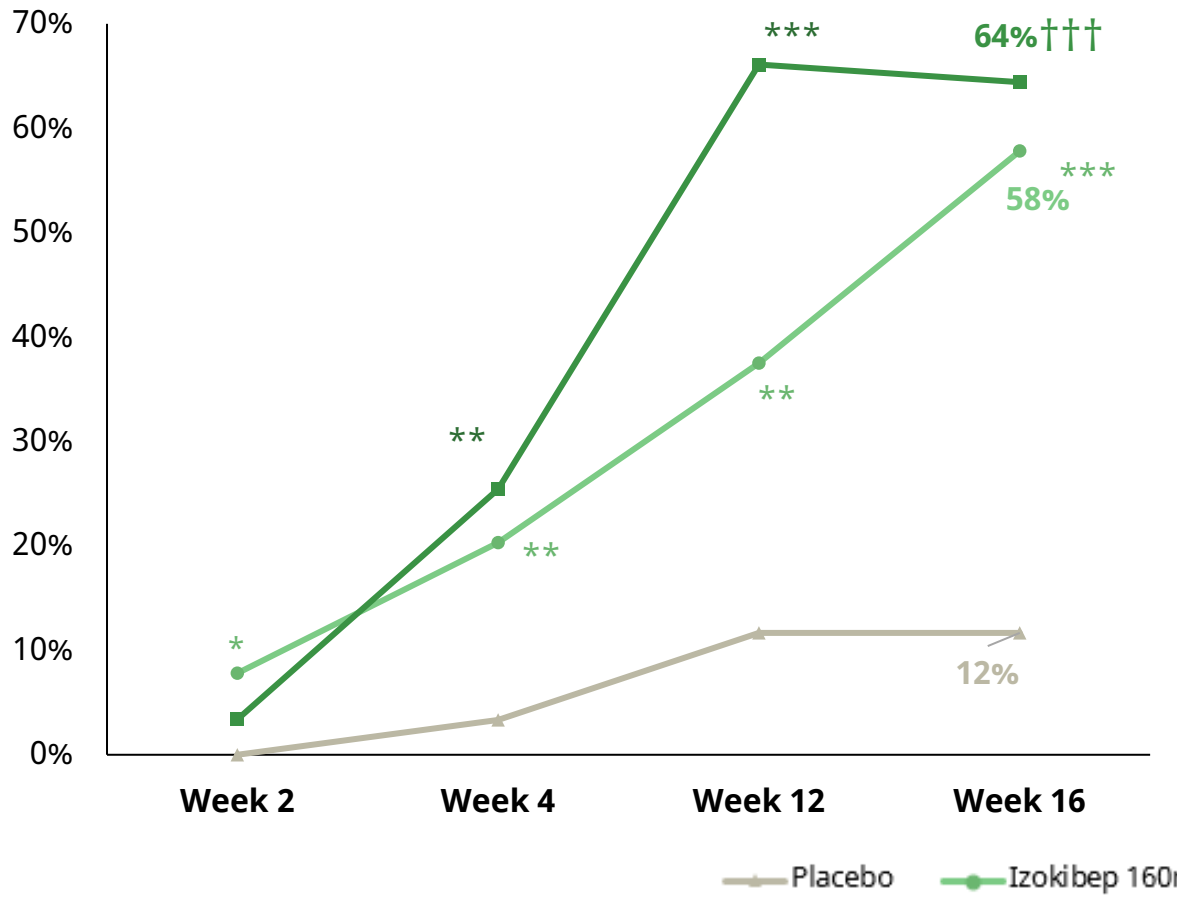
Placebo | Izokibep 160mg Q2W | Izokibep 160mg QW

(1) Week 16 data are from the full analysis set using non-responder imputation (NRI). Significance per prespecified statistical hierarchy: †††P<0.0001 vs placebo. Nominal significance: *P<0.05, **P<0.01, ***P<0.0001 vs placebo (stratified test of risk differences).

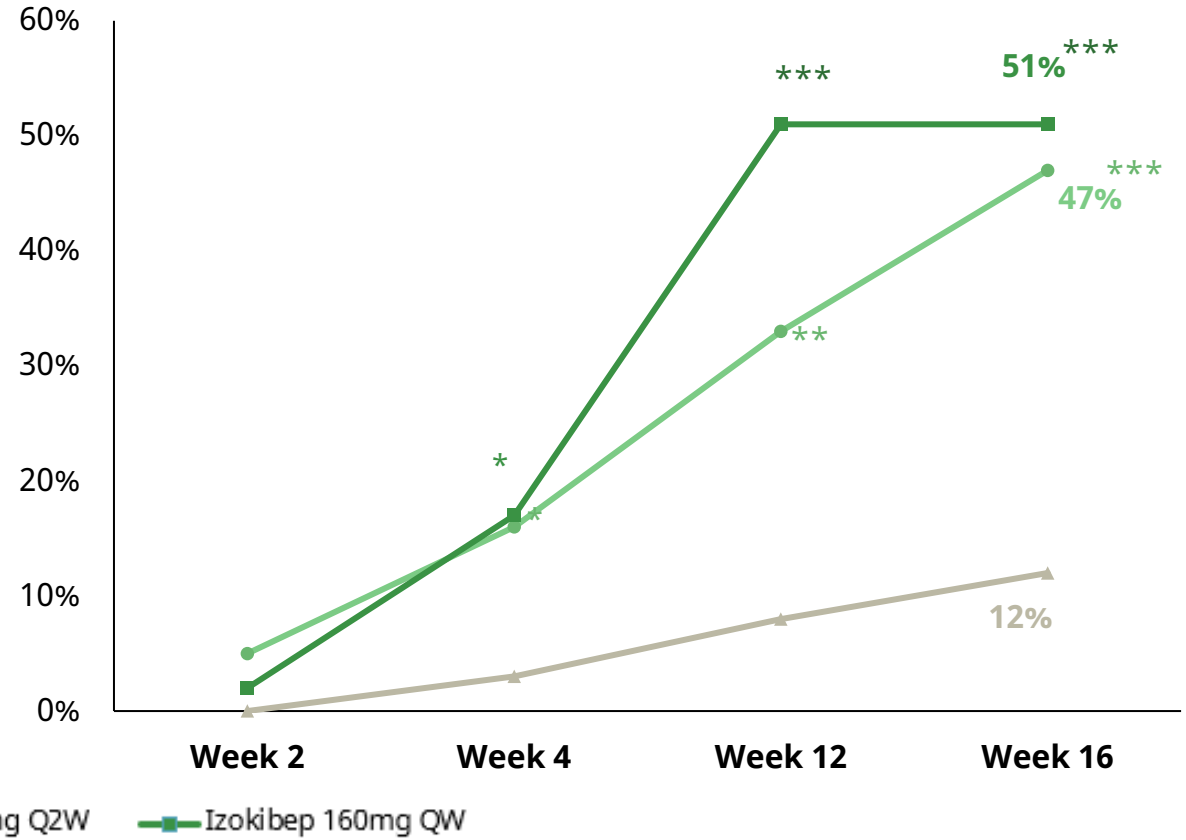
PASI90 and PASI100 at Primary Endpoint

Rapid and Robust Achievement of All-Clear Skin

Improvement in PASI90 through Wk 16 (1)



Improvement in PASI100 through Wk 16 (1)



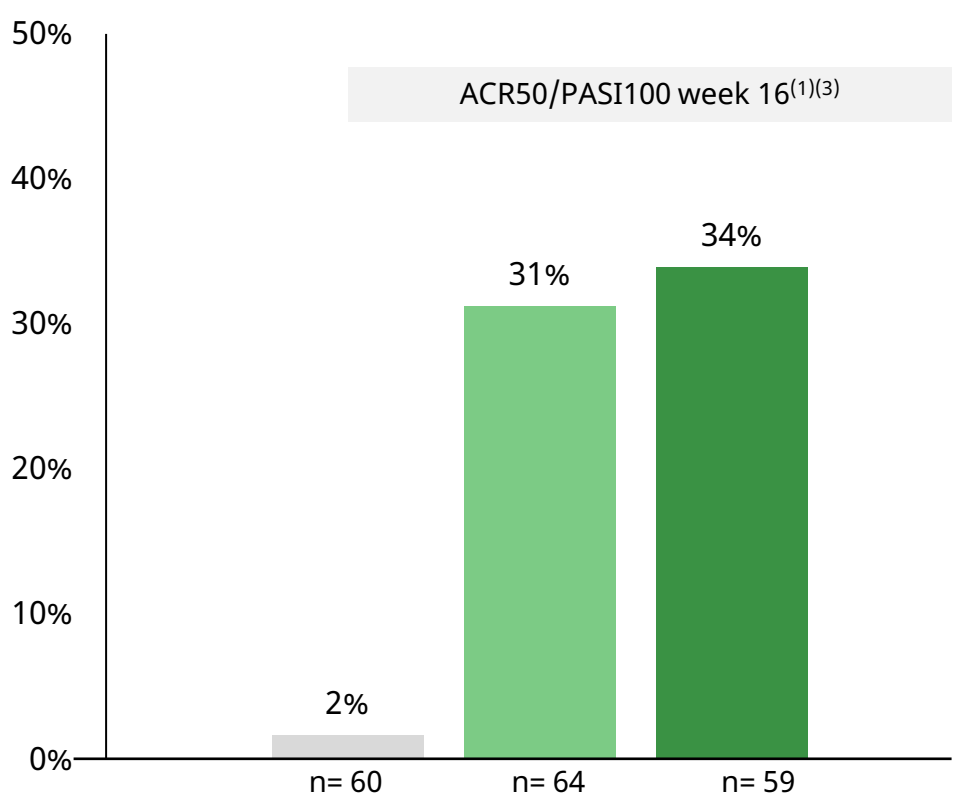
Placebo — Izokibep 160mg Q2W — Izokibep 160mg QW

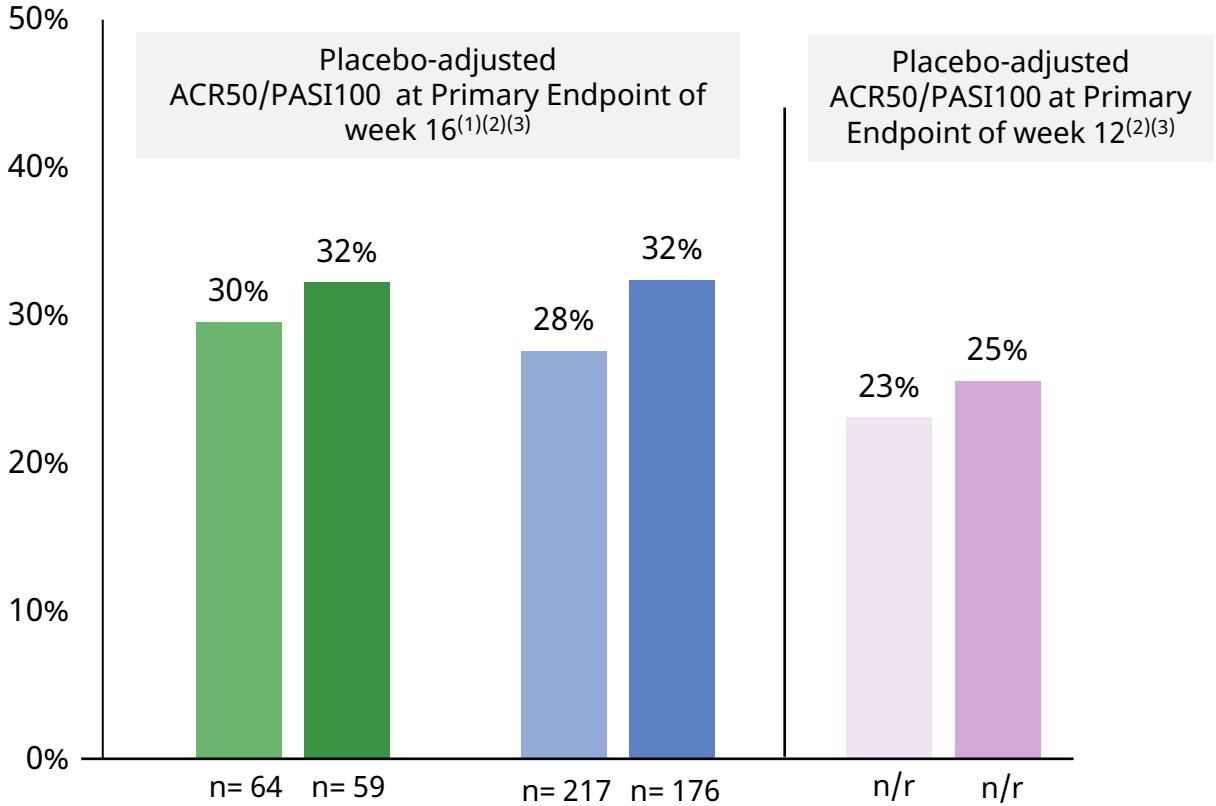
(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI) in patients with BSA ≥3% at baseline. Significance per prespecified statistical hierarchy: †††P<0.0001 vs placebo. Nominal significance: *P<0.05; **P<0.01; ***P<0.0001 vs placebo (stratified test of risk differences).

BSA, body surface area; **PASI90/100**, ≥90%/100% reduction from baseline in Psoriasis Area and Severity Index.

ACR50 and PASI100 Composite at Primary Endpoint

Robust Composite Responses of Joint and Skin Without the Safety Liabilities of IL-17 A&F Inhibition



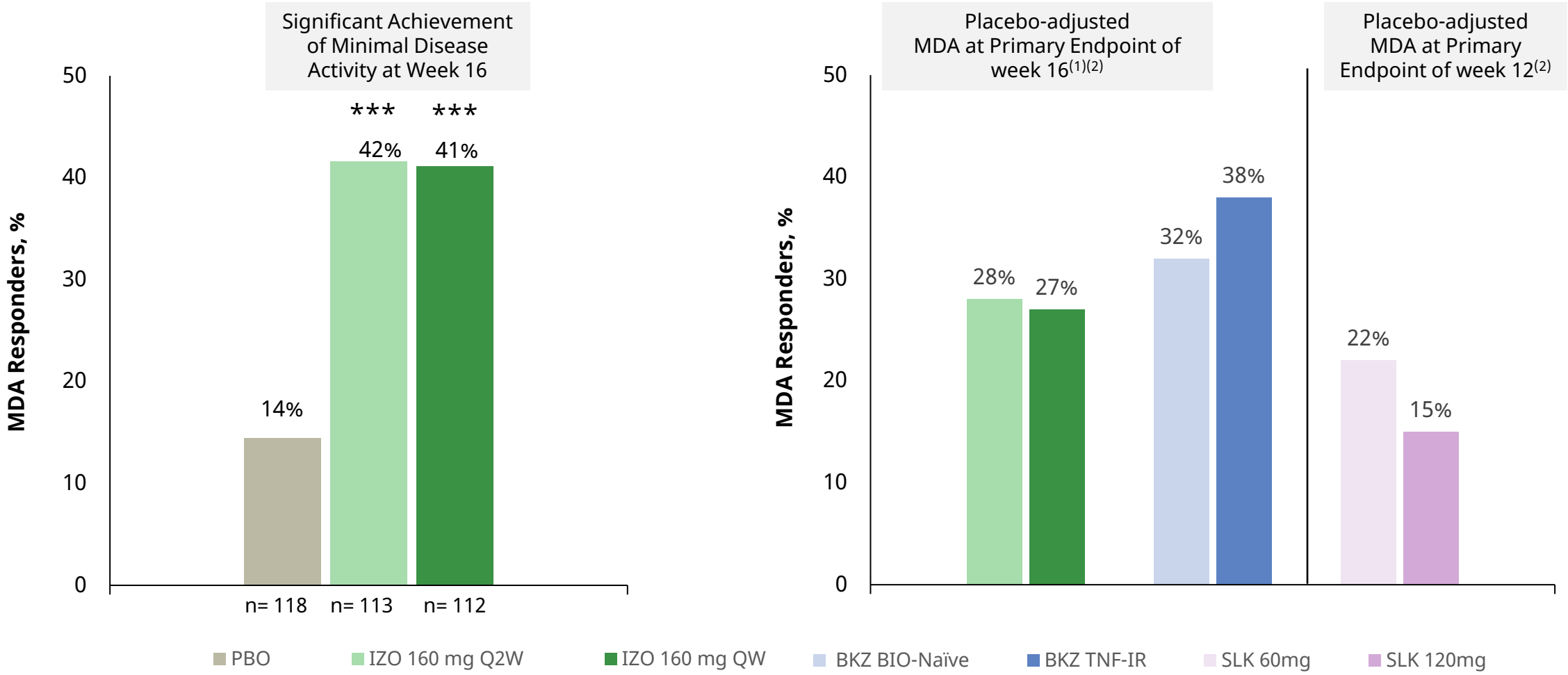


PBO IZO Q2W IZO QW BKZ BIO-naïve BKZ TNF-IR SLK 60mg SLK 120mg

(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI).
(2) Comparisons across trials, with inherent limitations. Not head-to-head trials. Bimekizumab and Sonelokimab data from public source: Ritchlin CT, Coates LC, McInnes IB, et al. Ann Rheum Dis 2023;82:1404–1414 BE OPTIMAL; Merola et al Lancet 2023 401: 38–48 BE COMPLETE. Moonlake R&D day March 10, 2024.
(3) In patients with psoriasis involving at least 3% body surface area (BSA) at baseline

Minimal Disease Activity at Primary Endpoint

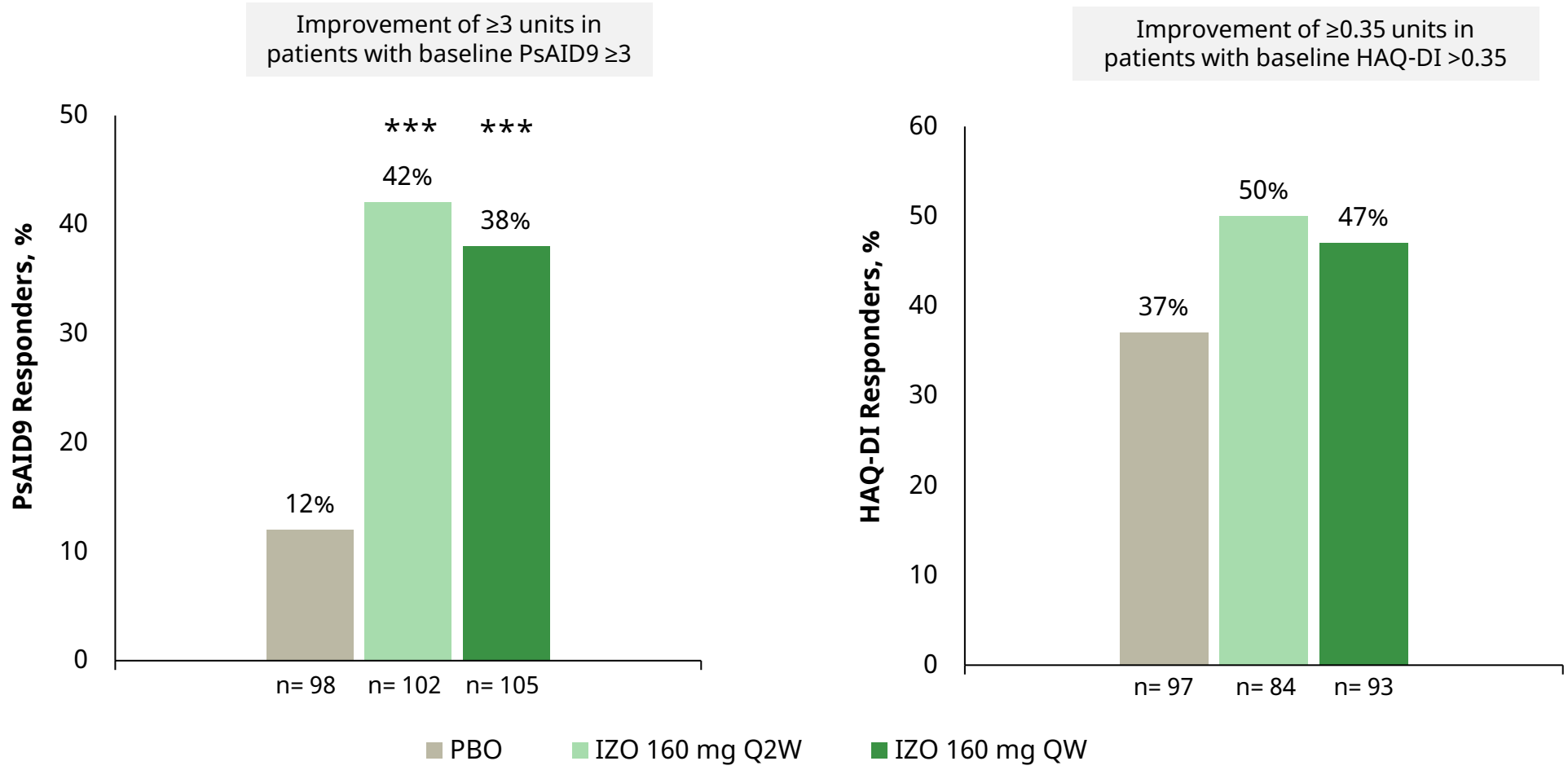
Improving the Totality of Manifestations is the Goal for Minimizing Disease Activity for Patients



(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI). Nominal significance: ***P<0.0001 vs. placebo (stratified test of risk differences)
(2) Comparisons across trials, with inherent limitations. Not head-to-head trials. Bimekizumab and Sonelokimab data from public source: Ritchlin CT, Coates LC, McInnes IB, et al. Ann Rheum Dis 2023;82:1404–1414 BE OPTIMAL; Merola et al Lancet 2023 401: 38–48 BE COMPLETE. Moonlake R&D day March 10, 2024.

Patient-Reported Disease Burden and Physical Function

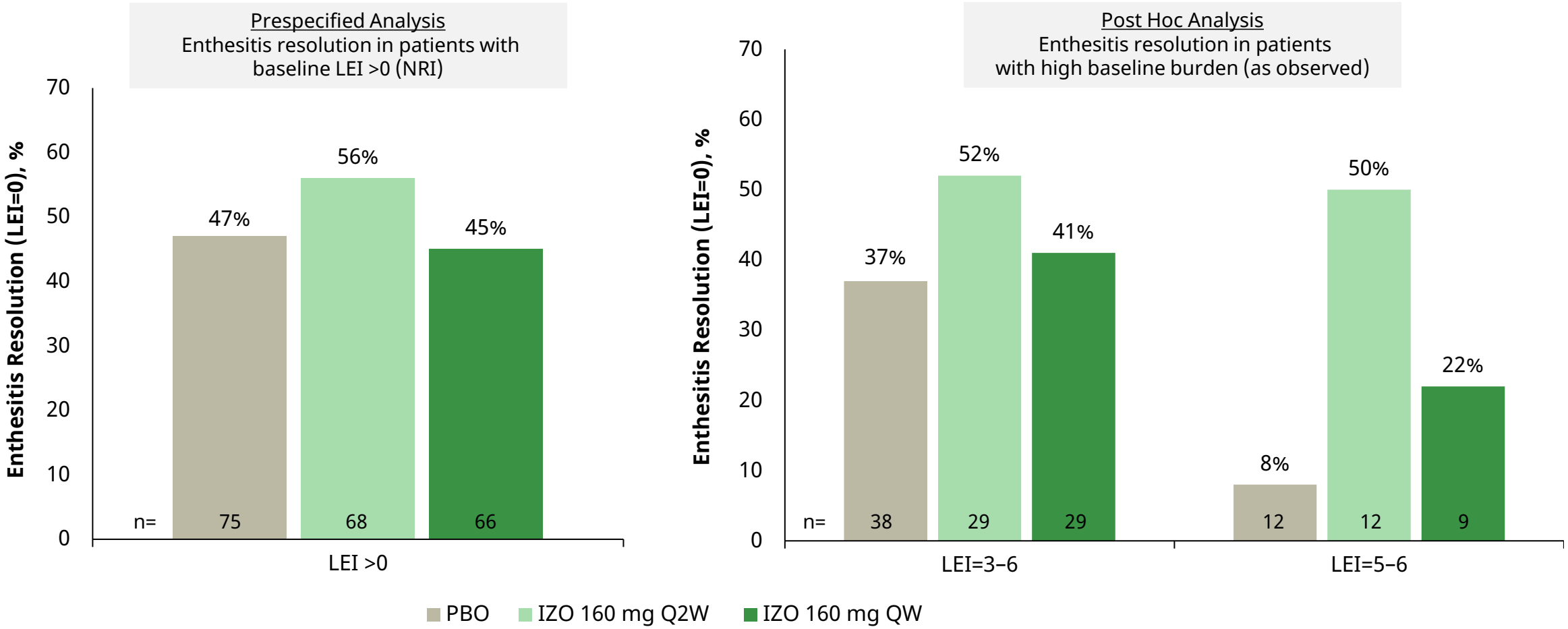
Clinically Meaningful Improvement in PsAID9 and HAQ-DI at Week 16



Data are from the full analysis set using nonresponse imputation. Nominal significance: ***P<0.0001 vs placebo (stratified test of risk differences)
PsAID9, Psoriatic Arthritis Impact of Disease based on 9 numerical rating scales

Izokibep Demonstrated Resolution Despite Highest Burden Of Enthesitis[1]

Improvement Relative to PBO in Highest Burden of Disease not Previously Reported by Other Agents[2]



(1) Enthesitis resolution overall in Phase 2b/3 was not statistically significant due to high placebo response
(2) Coates et al. Arthritis Research & Therapy (2019) 21:266 - Secukinumab demonstrated no difference between placebo and active in higher burden enthesitis subgroups. Data for Bimekizumab not available.
Data are from the full analysis set.

Summary Of Safety Through Week 16

n (%)	Placebo n=118	Izokibep 160 mg Q2W n=113	Izokibep 160 mg QW n=112
Any TEAEs	48 (40.7)	75 (66.4)	81 (72.3)
Serious	1 (0.8)	2 (1.8)	3 (2.7)
TEAEs leading to study discontinuation	0	5 (4.4)	8 (7.1)
General disorders and administration site conditions leading to study discontinuation[a]	0	1 (0.9)	5 (4.5)
Deaths	0	0	0
Preferred Term (≥5%)[b]			
Injection site erythema	0	44 (38.9)	60 (53.6)
Injection site pruritus	1 (0.8)	19 (16.8)	24 (21.4)
Injection site swelling	0	8 (7.1)	9 (8.0)
Injection site pain	1 (0.8)	6 (5.3)	7 (6.3)
Upper respiratory tract infection	4 (3.4)	3 (2.7)	6 (5.4)
Injection site rash	0	7 (6.2)	2 (1.8)
Injection site reaction	1 (0.8)	2 (1.8)	6 (5.4)
Fatigue	0	7 (6.2)	2 (1.8)
Any TEAEs of special interest[c]	2 (1.7)	5 (4.4)	6 (5.4)
Oral candidiasis	0	0	1 (0.9)
Skin candidiasis	1 (0.8)	0	0
Colitis ulcerative	0	1 (0.9)	1 (0.9)

Safety Set. [a] Include Injection site reaction, erythema, and pruritus. [b] Most commonly reported TEAEs occurring in ≥5.0% of patients in any group to week 16. [c] Only select TEAEs of special interest are shown.

SLRN-517

SLRN-517 Targets Mast Cell-Driven Diseases

Phase 1/2 Single Ascending Dose Trial in Healthy Volunteers Completed

Fully Human IgG1
No agonism of mast cell degranulation, potential for reduced immunogenicity potentially limiting acute reactions to the drug itself, and potent antagonism of mast cell proliferation and degranulation

High Potency to Maximize Efficacy and Convenience Blocks stem cell factor by binding to c-KIT with high affinity (K_D ~1.55 pM) enabling low volume SC dose and potential for greater exposures

Minimize On-Target Safety Impact
Combined with high potency, human half-life anticipated to be ~16 days, potentially enabling rapid depletion of mast cells while limiting opportunity for other effects on c-KIT or other sensitive tissues (spermatogenesis, hair color, hematopoietic cells (neutropenia))

SAD Screening/ Eligibility

- Healthy Subjects: 18-65 years
- Males and Females
- No chronic medical conditions or con meds

SAD

Cohort 1: Single dose SC
Healthy Subjects N=8 (incl 2 placebo)

Cohort 2: Single dose SC
Healthy Subjects N=8 (incl 2 placebo)

Cohort 3: Single dose SC
Healthy Subjects N=8 (incl 2 placebo)

Cohort 4: Single dose SC
Healthy Subjects N=8
(incl 2 placebo)

Efficacy Endpoints

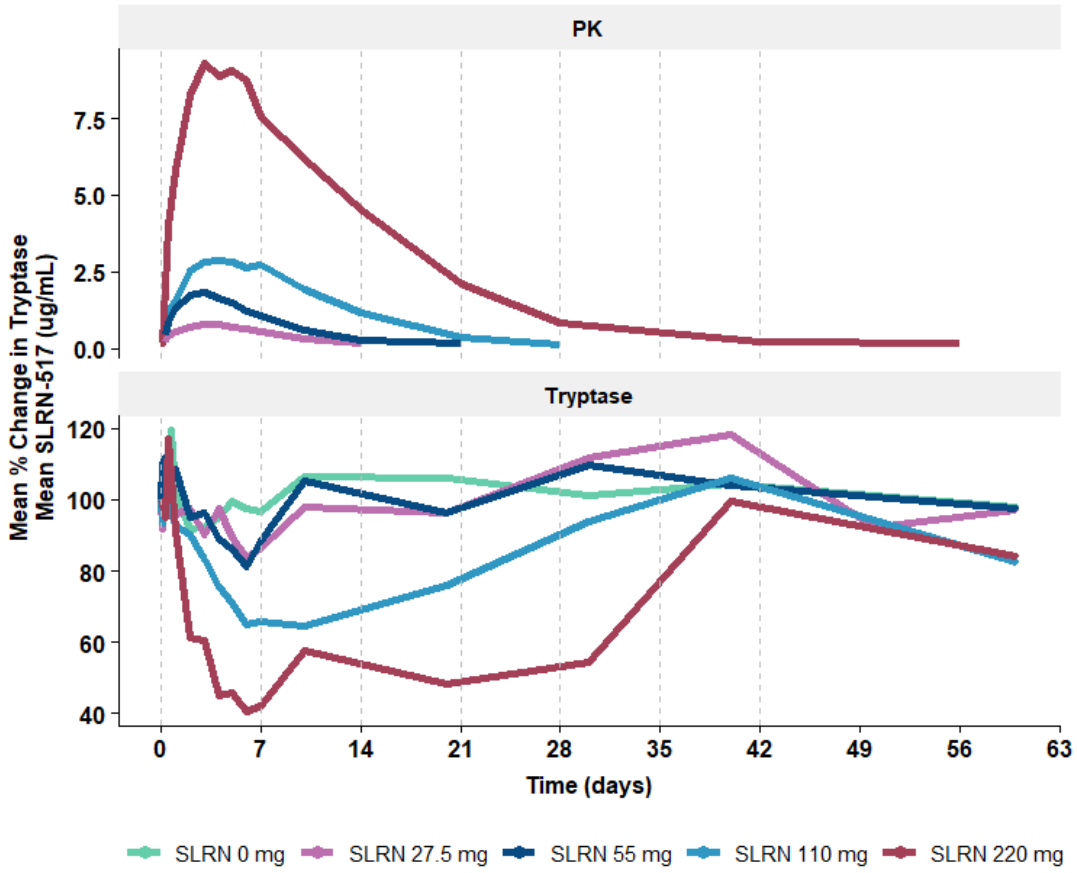
- Tryptase Levels

Safety Endpoints

- Incidence and characterization of nonserious and serious treatment emergent adverse events (TEAEs)

SLRN-517 Targets Mast Cell-Driven Diseases

Pharmacodynamic and Safety Data from Phase 1/2 Trial in Healthy Volunteers



PK

- Dose dependent increases in exposure
- Exposure levels lower than anticipated
  - TMDD and/or bioavailability

Tryptase

- Highest dose tested (220 mg) achieved mean ~70% nadir in tryptase
- Skin mast cell number decreased at day 8; returned by days 57 & 99

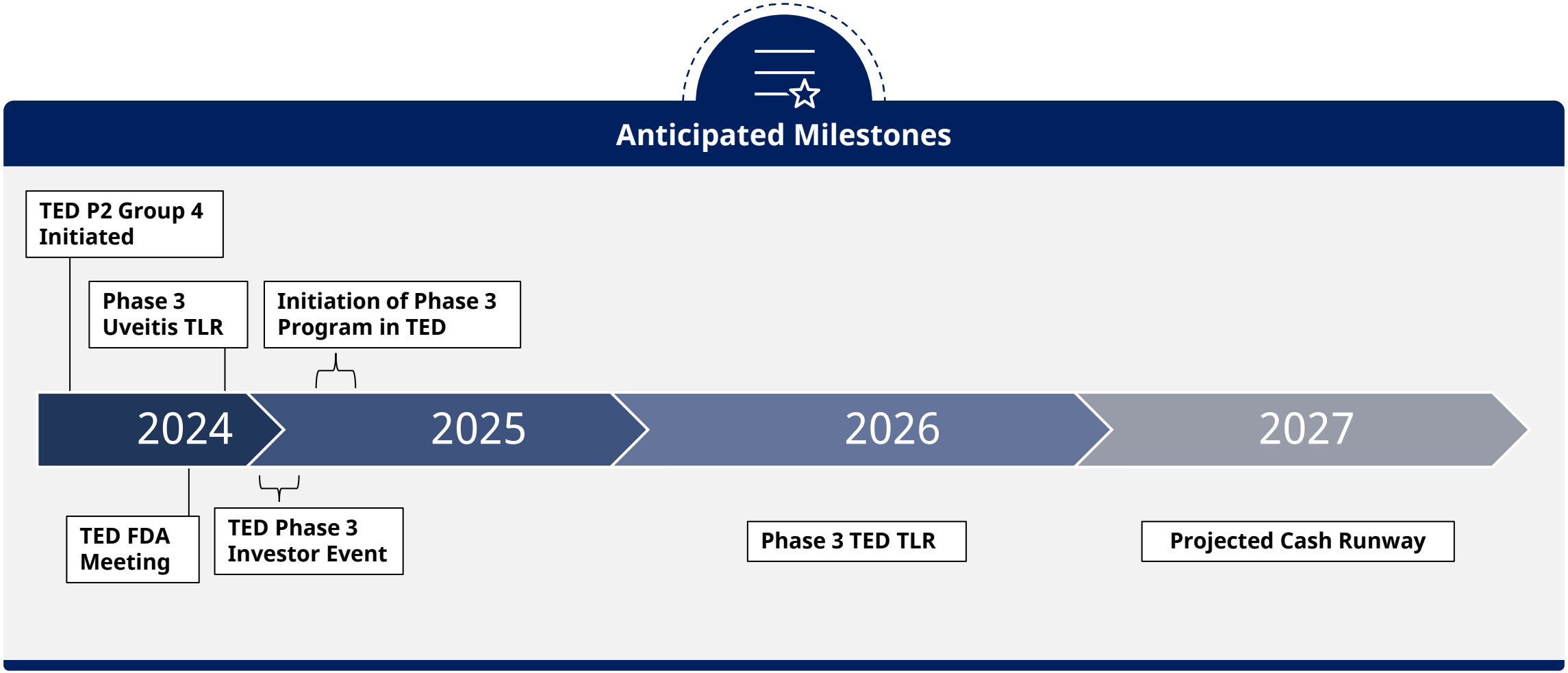
Safety

- No deaths or SAEs
- No subjects discontinued due to an AE
- Adverse events of special interest based on MoA and/or reported events to date include the following:
  - Sperm count reduction, skin and subcutaneous tissue disorders, neutropenia, hypopigmentation

4 Single-Ascending Dose cohorts: 6 active: 2 placebo

Strategic Initiatives Enable 3-Year Runway to Mid-2027

Existing ~$562M Projected to Fully Fund Lonigutamab Phase 3 Trials & Potential Pipeline Expansion



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Thank You

Contact

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