ACELYRIN

Accelerating Medicines to Transform Patients' Lives

Corporate Overview

Forward Looking Statements & Disclaimer

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Such 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 our successful completion of development and regulatory activities for our product candidates, maintaining and defending IP protection, ability to timely secure adequate supply of our product candidates, legal proceedings, government investigations, macroeconomic conditions, market volatility) and other risks and uncertainties described under the heading "Risk Factors" in the Company's most recent Quarterly Report on Form 10-Q for the three months ended June 30, 2023 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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“ACELYRIN Is A Leading Clinical-Stage Biopharma Company Focused On Identifying, Acquiring, And Accelerating The Development And Commercialization Of Transformative Medicines In Immunology”

Experienced Leadership Team

Successful Track Record of Delivering Some Of The Most Transformative Medicines For Patients

Shao-Lee Lin | MD, PhD
Founder and CEO

Melanie Gloria
COO

Gil Labrucherie
CFO

Paul M. Peloso | MD, MSc
CMO

Ron Oyston
CPO

Mina Kim
CL&AO

Ken Lock
CCO

Experienced Team

AMGEN · abbvie · HORIZON · GILEAD · MERCK · NEKTAR · zymergen · Pfizer

Leaders in Immunology

HUMIRA adalimumab · Skyrizi risankizumab-rzaa · TEPEZZA teprotumumab-trbw · RINVOQ upadacitinib · Enbrel etanercept · SILIQ (brodalumab) injection · KRYSTEXXA pegloticase

Board of Directors

Shao-Lee Lin · Bruce C. Cozadd · Dan Becker · Alan Colowick · Henry Gosebruch · Patrick Machado · Beth Seidenberg · Dawn Svoronos

Building With A Sense Of Urgency For Patients

Current cash and cash equivalents as of June 30, 2023:

$823 Million

2020

October 2020
Series A completed

July 2020
ACELYRIN founded

2021

December 2021
Positive Phase 2 top-line data for izokibep in PsA

October 2021
$250 million Series B

August 2021
First program, izokibep, licensed

2022

November 2022
Add'l Phase 2 RCT PsA Endpoint & QoL Data Presented at ACR

September 2022
$300M committed in Series C; accelerated PsA Phase 2b/3 into 2022

June 2022
Phase 2 RCT PsA Data Presented at EULAR

2023

May 2023
$621 million IPO

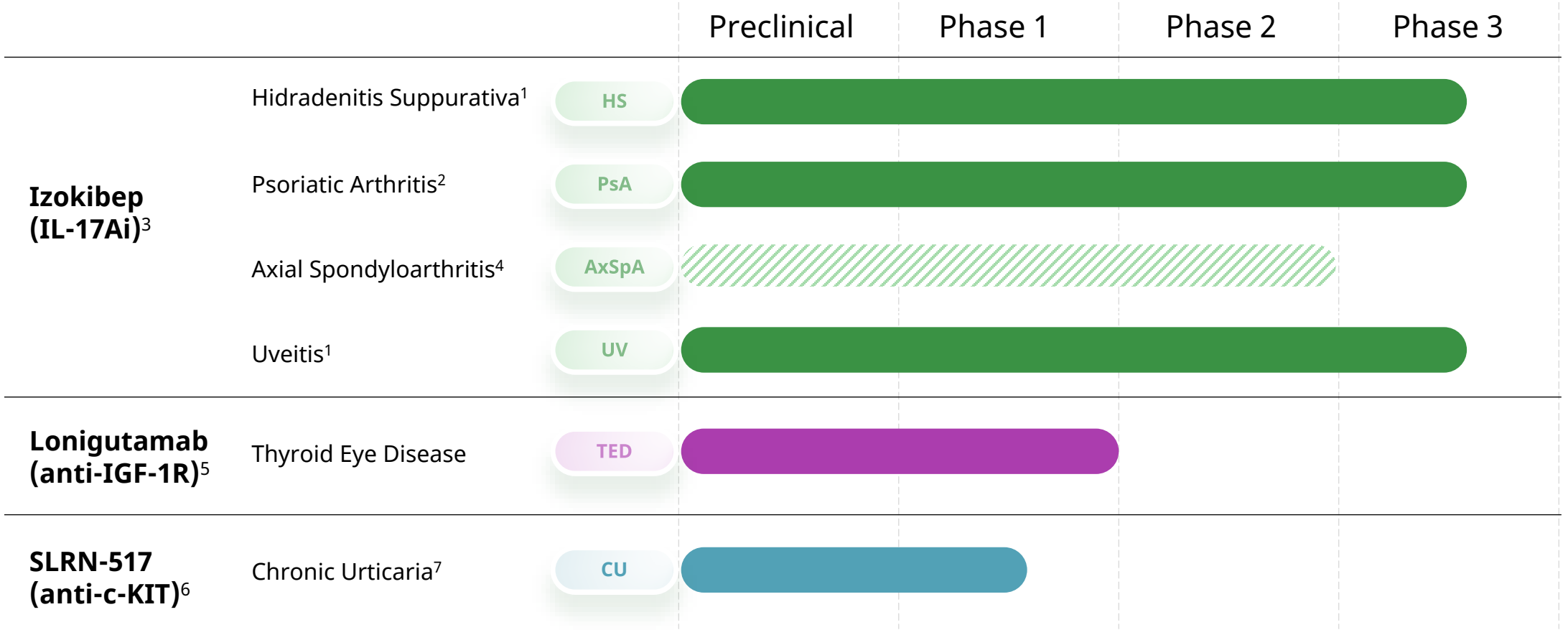
April 2023
Announced 46-week PsA P2 Data

March 2023
Positive Phase 2b/3 Part A data for izokibep in Hidradenitis Suppurativa; *accelerated Part B RCT top-line data to Q323*

January 2023
Expanded portfolio with an all-stock company acquisition, adding lonigutamab and SLRN-517

RCT: Randomized Controlled Trial; **QoL:** Quality of Life

Robust Portfolio Of Clinical Programs With Multiple Indications In Late Stage



1 Phase 2b/3 trial in moderate to-severe hidradenitis suppurativa (HS) and uveitis. Planned inclusion into registrational package for HS and non-infectious uveitis (as applicable) if granted orphan drug designation and following consultation with relevant heath authorities. We have not previously completed any clinical trials for uveitis and are currently conducting our first Phase 2b/3 trial.

2 Phase 2b/3 trial in PsA.

3 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.

4 Based on data from our Phase 2 and ongoing Phase 2b/3 trials in PsA, we intend to discuss with the FDA initiation of the Phase 3 program in AxSpA without completing earlier clinical trials in AxSpA. The FDA may require us to complete a Phase 2 trial in AxSpA prior to initiating our planned Phase 3 program.

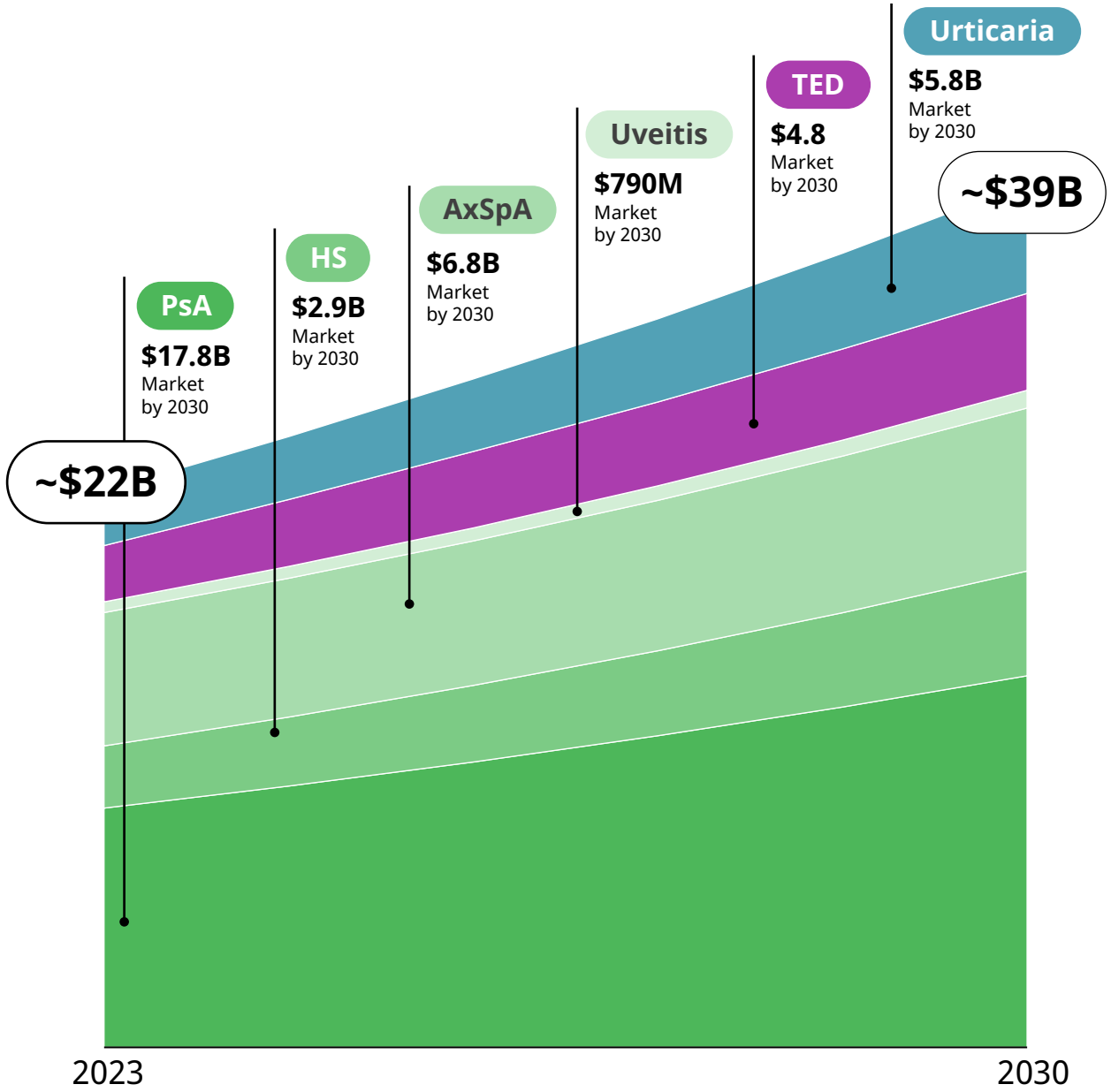
5 Worldwide rights to non-oncology indications. Potential opportunity to extend certain IP protection into 2043.

6 Potential opportunity to extend certain IP protection to 2039.

7 Based on preclinical studies demonstrating highly potent inhibition of the c-KIT pathway targeting mast cell proliferation and degranulation, our first indication of interest for SLRN-517 is chronic urticaria, an inflammatory disease that is driven by the release of histamine and other vasoactive molecules produced by mast cells

Total Addressable Markets Are Significant And Growing

- Opportunity to impact more than 12 million patients in the top 7 major markets[1]
- More than $16 billion in growth anticipated by 2030
- Significant unmet needs remain across each of these indications



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* HS: Hidradenitis Suppurativa; PsA: Psoriatic Arthritis; AxSpA: Axial Spondyloarthritis; TED: Thyroid Eye Disease
1 GlobalData Epidemiology Estimates; Helmick C. 2014; Perros P, 2017; Chin Y, 2020; Bartley GB, 1994

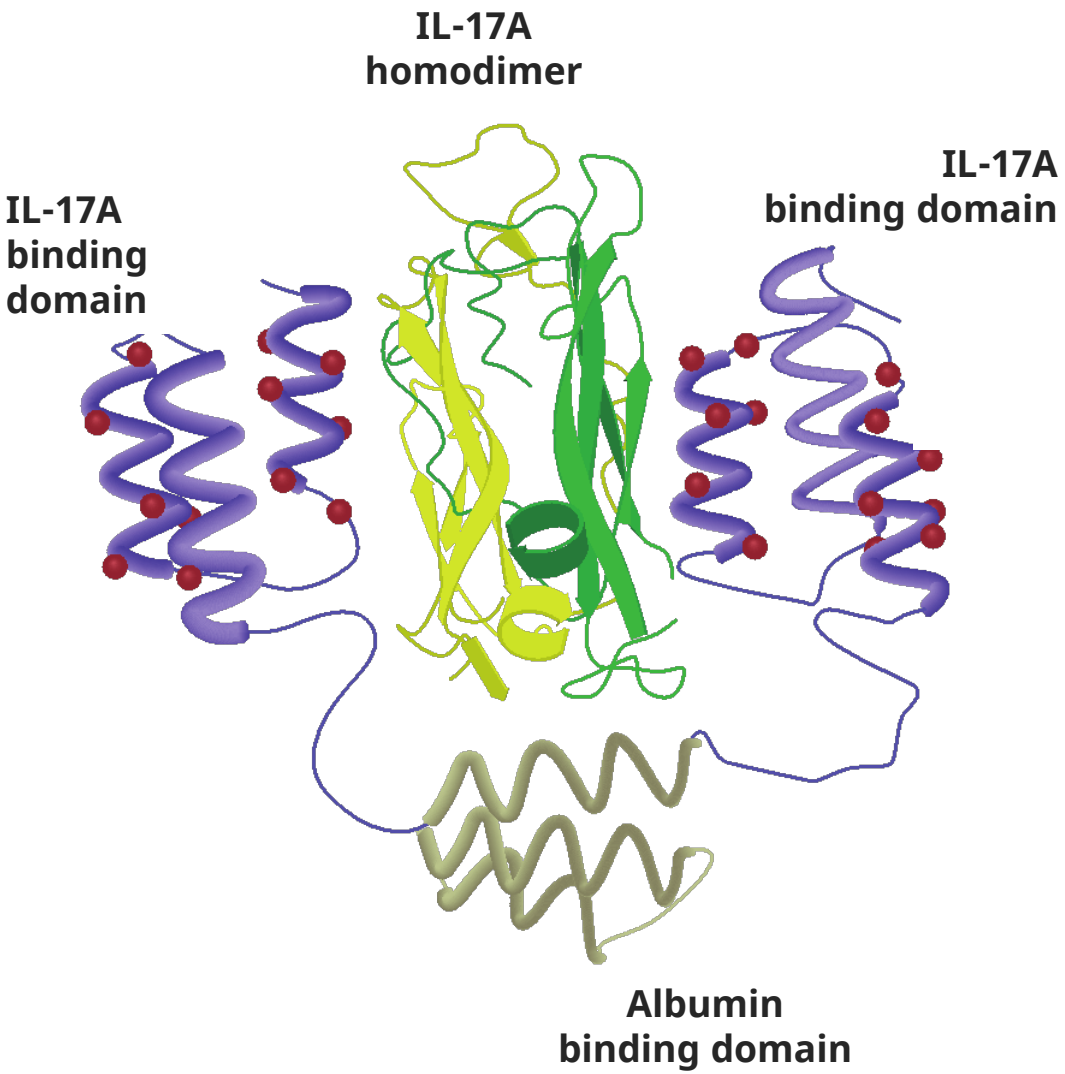
2 Active PsA Market - Emergen Research, 2022; Global AxSpA Market - iHealthcare Analyst, Nov 2022; HS Market Outlook - DelveInsight, Jan 2023; HS Opportunity Analysis - GlobalData 2019; CSU Market - DelveInsight, Dec 2022, Uveitis Global Drug Forecast - GlobalData, June 2021; Tepezza Consensus Sales Forecast compiled by GlobalData

Izokibep

(Small protein inhibitor of IL-17A)

Characteristics Of Izokibep Drive Hypothesis For Differentiated Efficacy

- **High Potency**
  Blocks the homodimeric IL-17A target protein by binding to both sub-units simultaneously with high affinity (K_D: 0.3 pM)
- **Small Size**
  ~1/10th the size of a mAb (~18.6 kD) enabling potential to reach difficult to treat tissues
- **Extended Plasma Half-Life**
  Albumin binding domain increases plasma half-life to 12 days and also enhances targeting to sites of inflammation
- **Generally Well Tolerated Safety Profile**
  Demonstrated in more than 400 participants; some for up to 3 years. No observed impact of ADAs on PK or efficacy and no increased risk of infection[1]



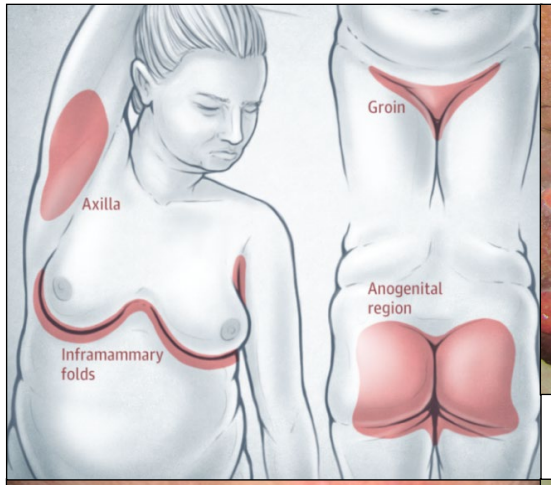
1. Based on Phase 2b/3 HS Part A, Phase 2 PsA trial and Phase 2 PsO trial
pM, picomolar; **kD,** kilodalton

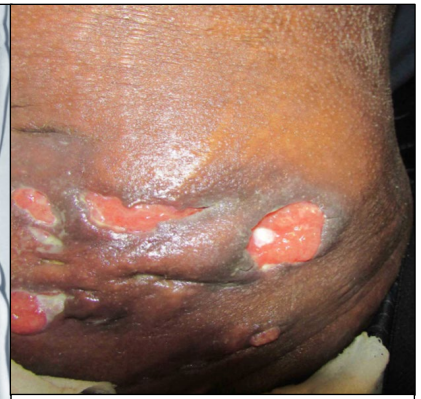
Izokibep

Hidradenitis Suppurativa

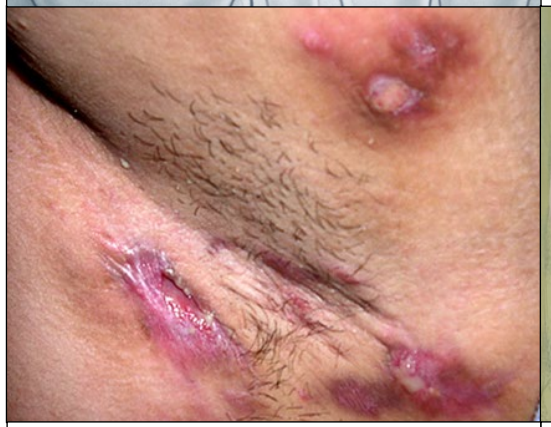
Izokibep HS

Hidradenitis Suppurativa Is A Devastating Disease With Limited Treatment Options

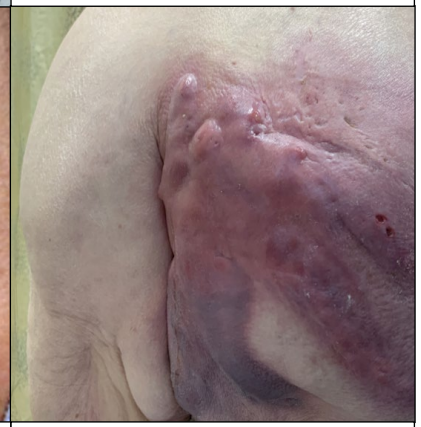




Draining Tunnels



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

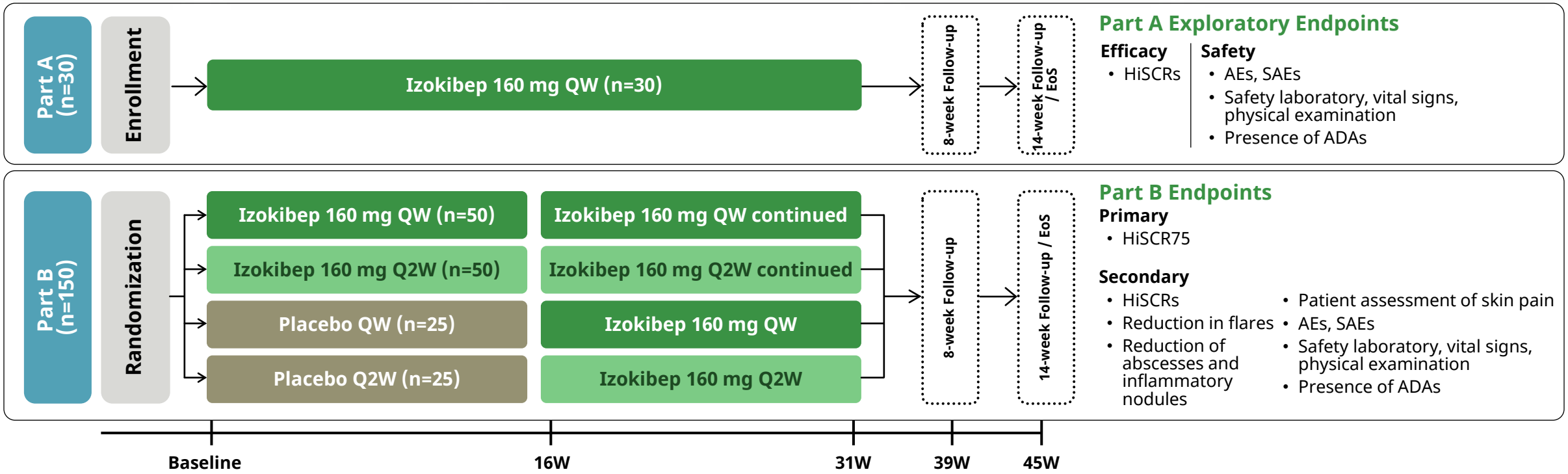
Izokibep HS

Izokibep Phase 2b/3 Hidradenitis Suppurativa Trial

Open Label Part A; Randomized, Double-blind, Placebo-controlled Part B

Screening/ Eligibility

- Moderate-to-severe HS
- Diagnosis of HS for ≥ 1 year prior to first dose
- HS lesions present in ≥ 2 distinct anatomic areas, one of which is Hurley Stage II or III
- Minimum abscess/ nodule (AN) count of 3 (Part A) or 5 (Part B)
- Inadequate response, intolerance or contraindication to oral antibiotics



ADA, anti-drug antibodies; **AE,** adverse event; **AN**, total abscess and inflammatory nodule count; **EoS**, end of study; **HiSCR**, Hidradenitis Suppurativa Clinical Response; **HS,** hidradenitis suppurativa; **QW**, once every week; **Q2W**, once every 2 weeks; **SAE**, serious adverse event.

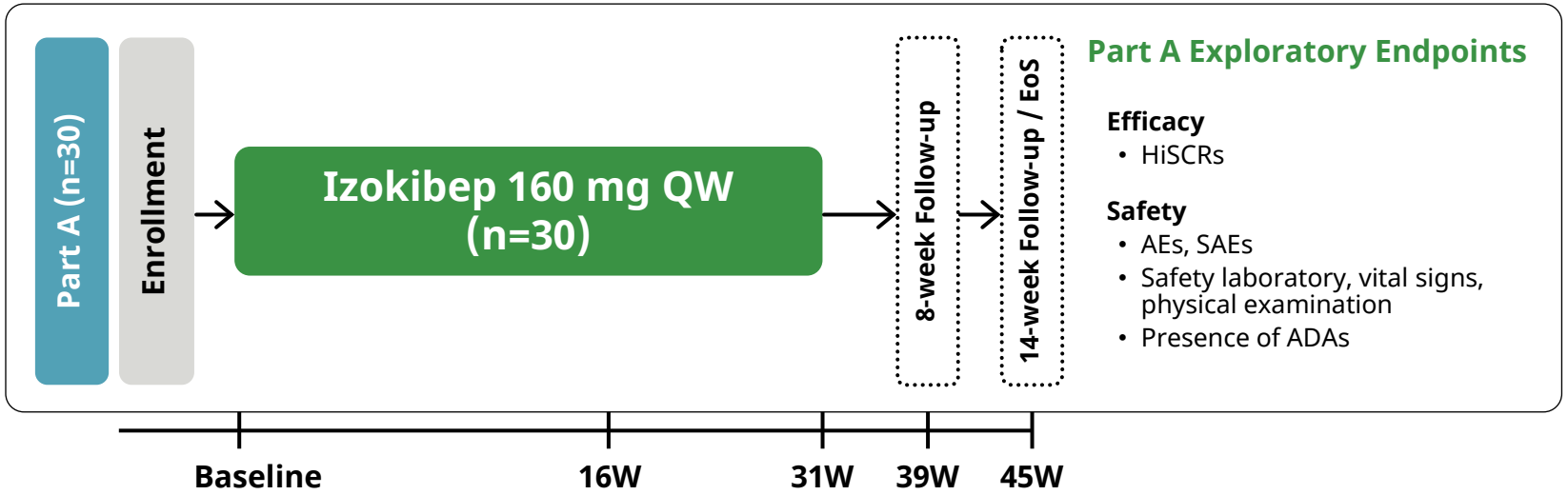
Izokibep HS

Izokibep Phase 2b/3 Hidradenitis Suppurativa Trial – Part A

Open Label Part A; Randomized, Double-blind, Placebo-controlled Part B

Screening/ Eligibility

- Moderate-to-severe HS
- Diagnosis of HS for ≥ 1 year prior to first dose
- HS lesions present in ≥ 2 distinct anatomic areas, one of which is Hurley Stage II or III
- Minimum abscess/ nodule (AN) count of 3
- Inadequate response, intolerance or contraindication to oral antibiotics



Part A Exploratory Endpoints

Efficacy
- HiSCRs

Safety
- AEs, SAEs
- Safety laboratory, vital signs, physical examination
- Presence of ADAs

Rationale for Part A

- Designed for internal decision-making
- Open-label design most efficient approach in terms of time / cost and attractive for patients in established MOA
- Bar for success was to be equal to, or better than, best agent at the time (bimekizumab Phase 2) without introducing new safety liability
- Looking for higher-order HiSCR responses, where placebo effect is historically low-to-none

ADA, anti-drug antibody; **AE,** adverse event; **AN**, total abscess and inflammatory nodule count; **EoS**, end of study; **HiSCR**, Hidradenitis Suppurativa Clinical Response; **HS,** hidradenitis suppurativa; **MOA**, mechanism of action; **PBO,** placebo; **QW**, once every week; **SAE**, serious adverse event.

Izokibep HS

Izokibep Phase 2b/3 Hidradenitis Suppurativa Trial – Part A

Baseline Characteristics Are Consistent With Historical HS Trials

	N = 30
Mean age (years)	38
Black (%)	46.7
Female (%)	70.0
Mean disease duration (years)	12.8
Mean AN count	9.7
Mean abscess count	1.5
Mean inflammatory nodule count	8.2
Hurley Stage (%)	
Stage II	67
Stage III	33

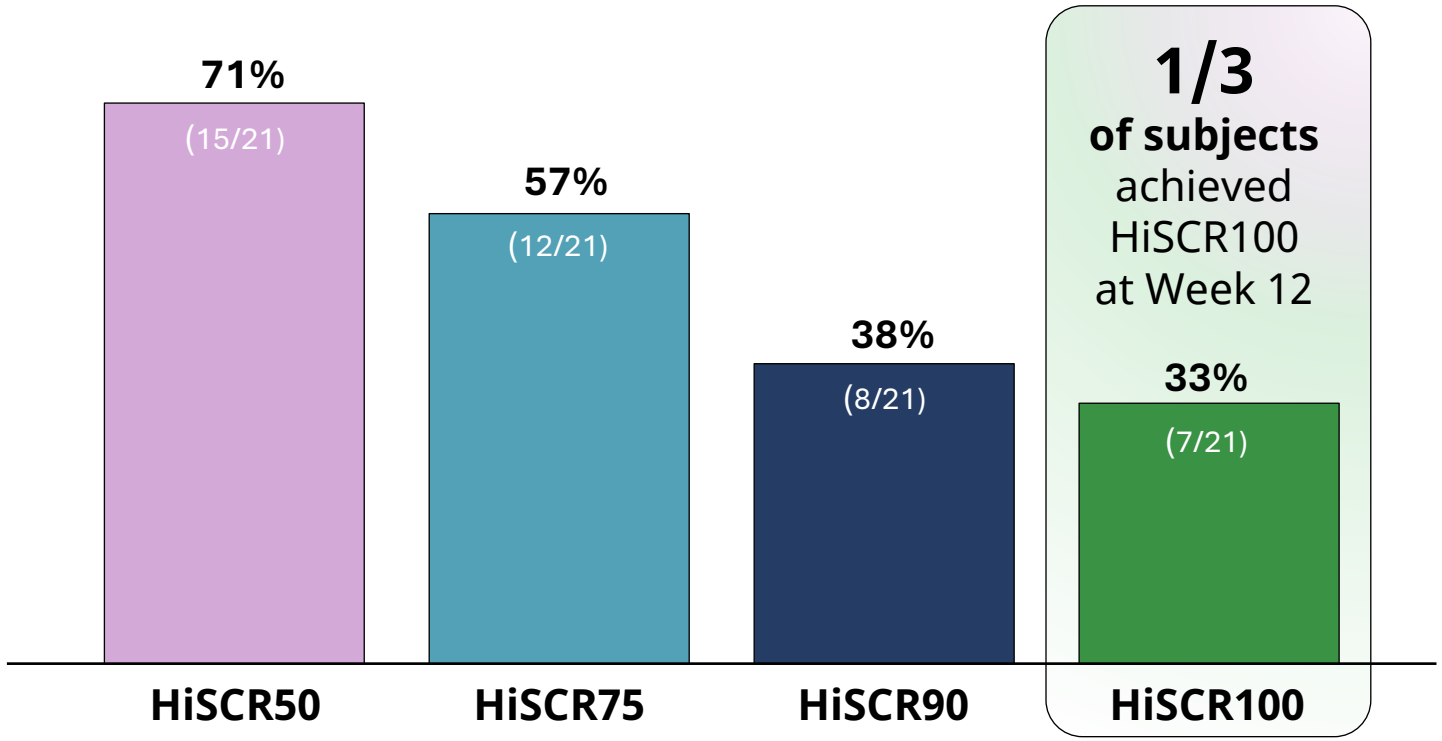
- Hidradenitis Suppurativa is characterized by Hurley Staging:
  - **Stage I:** Abscesses are present without skin tunnels or scarring
  - **Stage II:** Characterized by recurrent abscesses with tunnels and scarring
  - **Stage III:** There are multiple interconnected skin tunnels extending across a large area

- Hurley Stages are used to describe disease severity, as a higher abscess and nodule count can be associated with mild disease in the absence of more complex tunnels and scarring and extent of area affected.

AN, total abscess and inflammatory nodule count; **HS,** hidradenitis suppurativa.

Part A: Izokibep Demonstrated HiSCR100 Responses

All subjects treated with izokibep 160mg QW, reported as observed for the 21/30 subjects who completed through week 12*



HiSCR response

HiSCR50/75/90 is a percent reduction from baseline in the total abscess and inflammatory nodule (AN) count, with no increase from baseline in abscess or draining tunnels (DT)

- HiSCR100 stringent measure of disease control requiring both AN resolution and no new DT

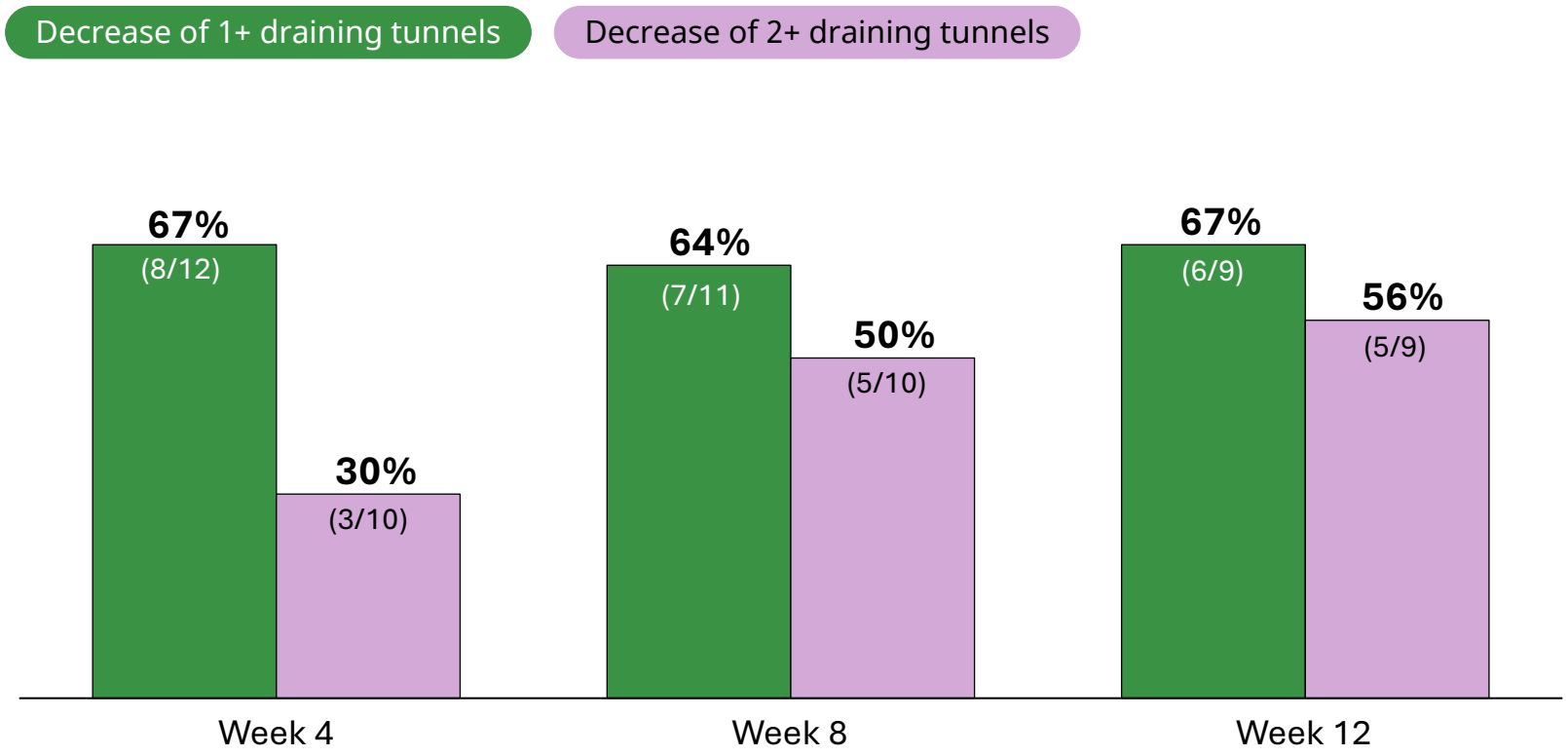
November 7, 2022 data-cut.
AN, total abscess and inflammatory nodule count; **HiSCR**, Hidradenitis Suppurativa Clinical Response; **QW**, once every week.

*Of the 30 subjects enrolled in Part A, 9 discontinued for various reasons including physical relocation and lost to follow up (4), injection site reactions (3), and SAEs relating to GI symptoms (2)

Izokibep HS

Part A: Improvement In Number Of Draining Tunnels Begins As Early As The First Month Of Treatment

Decrease in Number of Draining Tunnels Over Time as Observed in Subjects with Draining Tunnels at Baseline



15 of 30 subjects had 1+ draining tunnels at baseline; denominator affected over time by study discontinuations and baseline number of tunnels

Mean/Median draining tunnel count among these subjects were 3.3/2.0 at baseline with range of 1-7

Interpretation of these results are limited by small sample size. Part B will continue to inform our understanding of these effects

Izokibep HS

Safety Generally Consistent With Previous Experience

Most Common AEs (>5%)

Preferred Term	160 mg QW (N = 30)	
	n (%)	No. Events
All AEs	24 (80.0)	111
Injection site reaction[1]	12 (40.0)	23
Abdominal pain	2 (6.7)	2
COVID-19	2 (6.7)	2
Diarrhea	2 (6.7)	2
Nausea	2 (6.7)	2

AE, adverse event; **ISR**, injection site reaction; **QW**, once every week; **SAE**, serious adverse event; **W12**, Week 12.
1 Injection site reactions could include incidences of injection site pruritis, injection site erythema and/or injection site swelling.

Adverse Events

Common

Mild to moderate injection site reactions (ISRs) were the most common AEs

- Not systemic, and decrease in severity and frequency over time
- 3/30 subjects (10%) discontinued due to ISRs (2 mild, 1 moderate)
  - 2/3 discontinuations from mild ISRs suggests education challenge versus risk/benefit issue

Serious

3 serious adverse events were observed in 2 subjects, who discontinued treatment

- Inflammatory bowel disease, determined by principal investigator to be possibly drug related, reported in 1 subject. We concluded subject had pre-existing symptoms and should have been excluded from trial.
- Peri-colonic abscess/sepsis in another subject with pre-existing symptoms and known diverticulosis

IL-17 AE of Interest

Infections

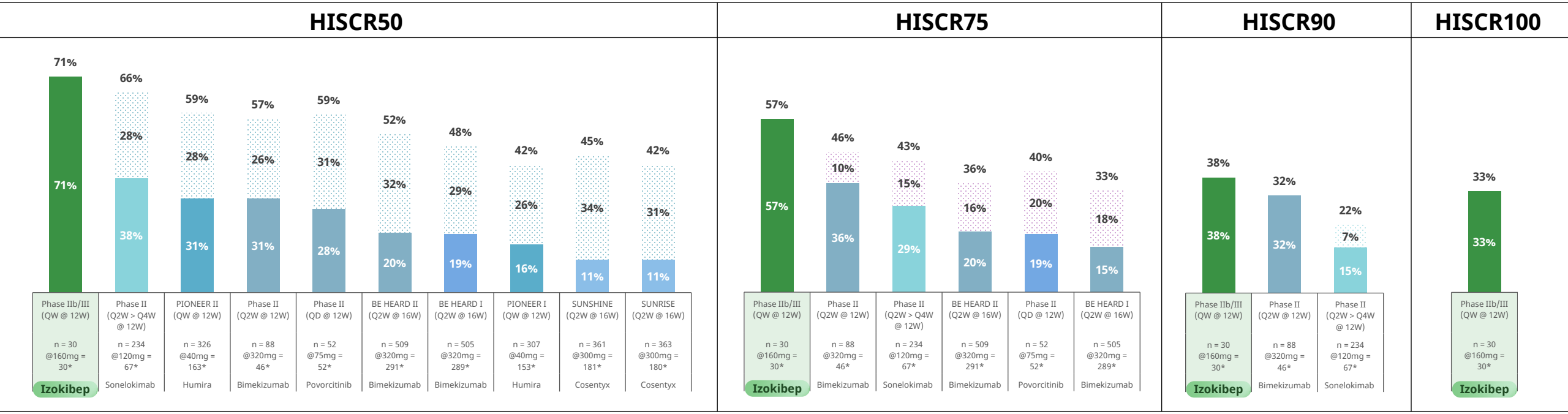
- No candida infections reported through W12
- No evidence of dose responsive infection risk with IL-17A inhibition observed

Izokibep HS

Higher Efficacy Hurdle Yields Fewer Successful Agents

12-16 Week Results From Historical Trials

Placebo-Adj. | Placebo



Field is Moving To Greater Resolution of Disease

- Adalimumab was only approved biologic for HS until recent EU approval of secukinumab (2023).
- Both used HiSCR50 as the primary endpoint
- Similar to PsO moving toward PASI100, HS is seeing shift to more rigorous efficacy goals of HiSCR75, HiSCR90 and ideally HiSCR100

Exposure Could Be Key

- Adalimumab and secukinumab reported lower drug exposure in HS versus PsO subjects
- Higher exposures are important as weight, disease severity (Hurley Stage II vs III) and CRP (level of inflammatory burden) all impact exposures in HS

Maximizing Efficacy Without Infection Liability

- We believe improved efficacy can come from higher exposures, high potency against IL-17 (i.e., hitting 17A harder or hitting A and F) and smaller size to penetrate hard-to-reach tissues
- Top HiSCR75 data to date have been reported by IL-17 A/F inhibitors but with corresponding dose-related increase in infection (~10-15%)

*At their highest dose level of 75mg, povorcitinib identified approximately 20% HiSCR100 response rates at week 16 from the subjects who had HiSCR100s at Week 52 in their OLE

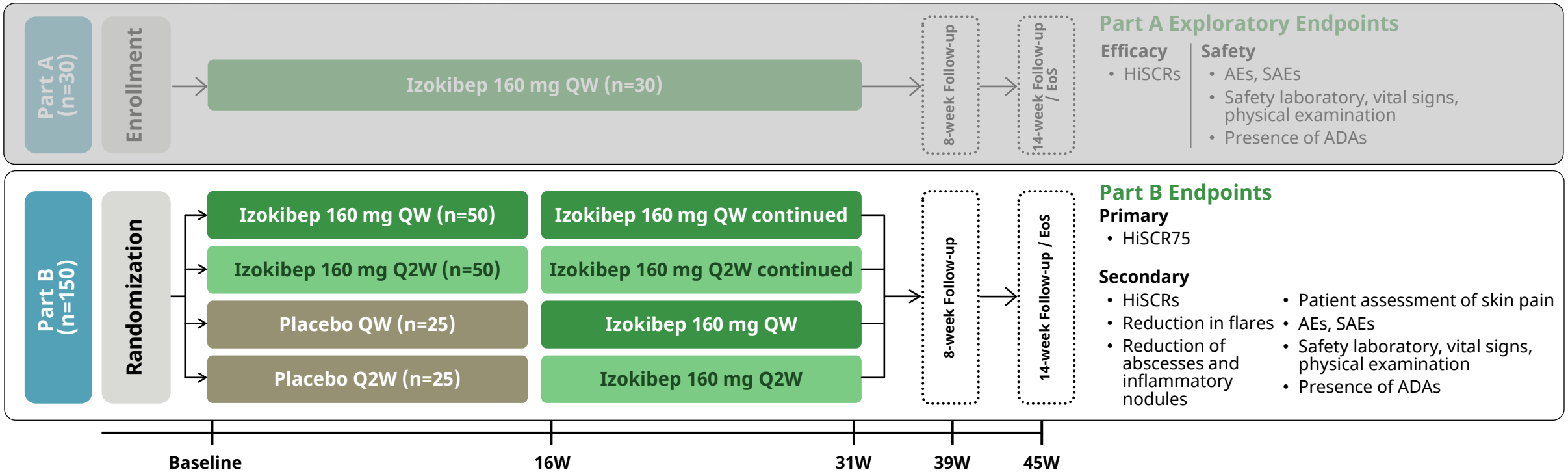
Izokibep HS

Izokibep Phase 2b/3 Hidradenitis Suppurativa Trial

Part B Randomized, Double-blind, Placebo-controlled Top-Line Data Accelerated To 3Q23 From End 2023

Screening/ Eligibility

- Moderate-to-severe HS
- Diagnosis of HS for ≥ 1 year prior to first dose
- HS lesions present in ≥ 2 distinct anatomic areas, one of which is Hurley Stage II or III
- Minimum abscess/ nodule (AN) count of 3 (Part A) or 5 (Part B)
- Inadequate response, intolerance or contraindication to oral antibiotics



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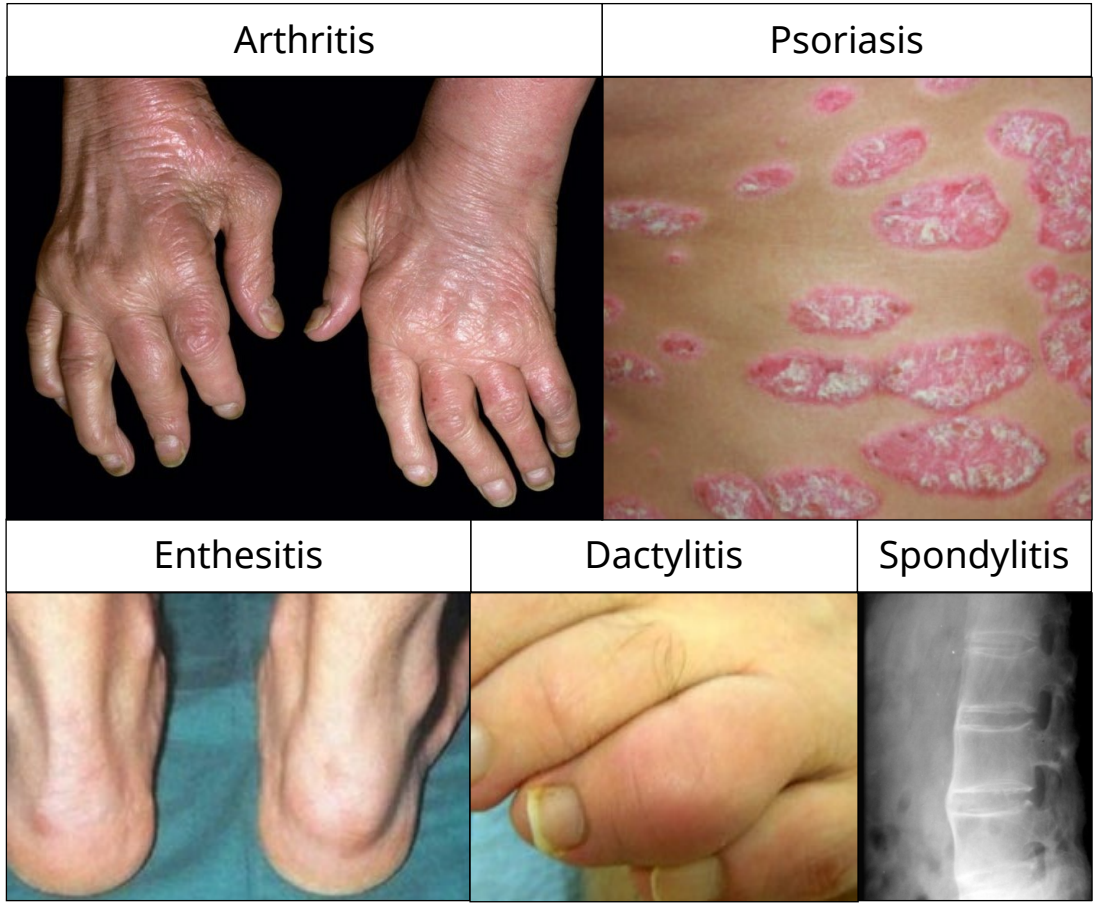
Izokibep

Psoriatic Arthritis

PsA Is A Disease With Multiple Manifestations

Addressing Totality Of Manifestations Remains Unmet Need For Patients



- 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.**; ~10% are moderate-to-severe
- 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

Izokibep PsA

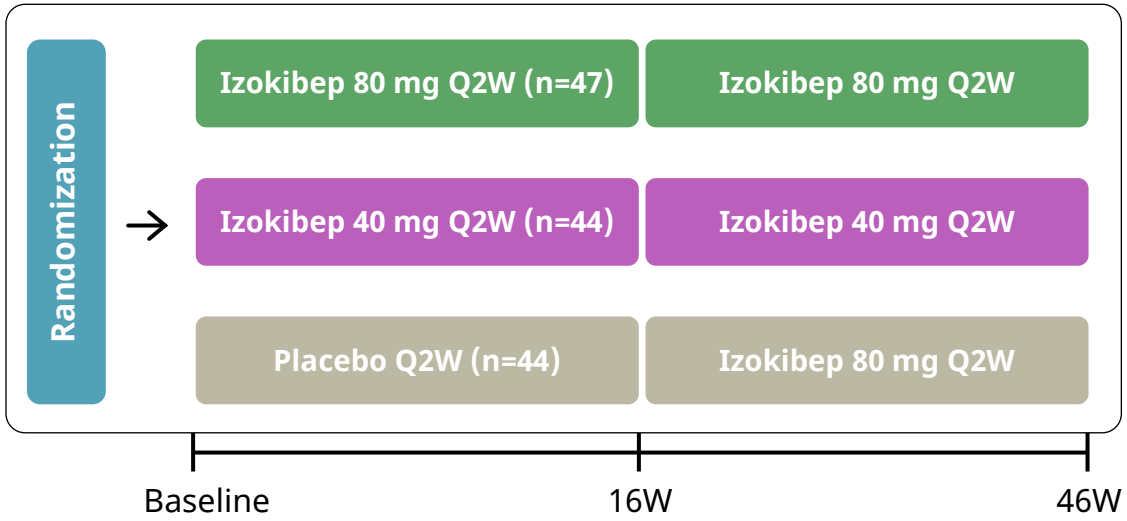
Izokibep Phase 2 Psoriatic Arthritis Trial

Randomized, Double-blind, Placebo-controlled

...

Screening/ Eligibility

- Moderate-Active PsA (CASPAR criteria)
- > 3 TJC68 and > 3 SJC66
- Previous failure to NSAID or csDMARD or TNFi
- One concomitant csDMARD allowed
- Prior anti-IL-17 exposure excluded



Key Efficacy Endpoints

- ACR50 at Week 16 (primary)
- Enthesitis (Leeds Index)
- PASI75/90/100 (if PSO-BSA ≥ 3%)
- Quality of Life (PsAID)

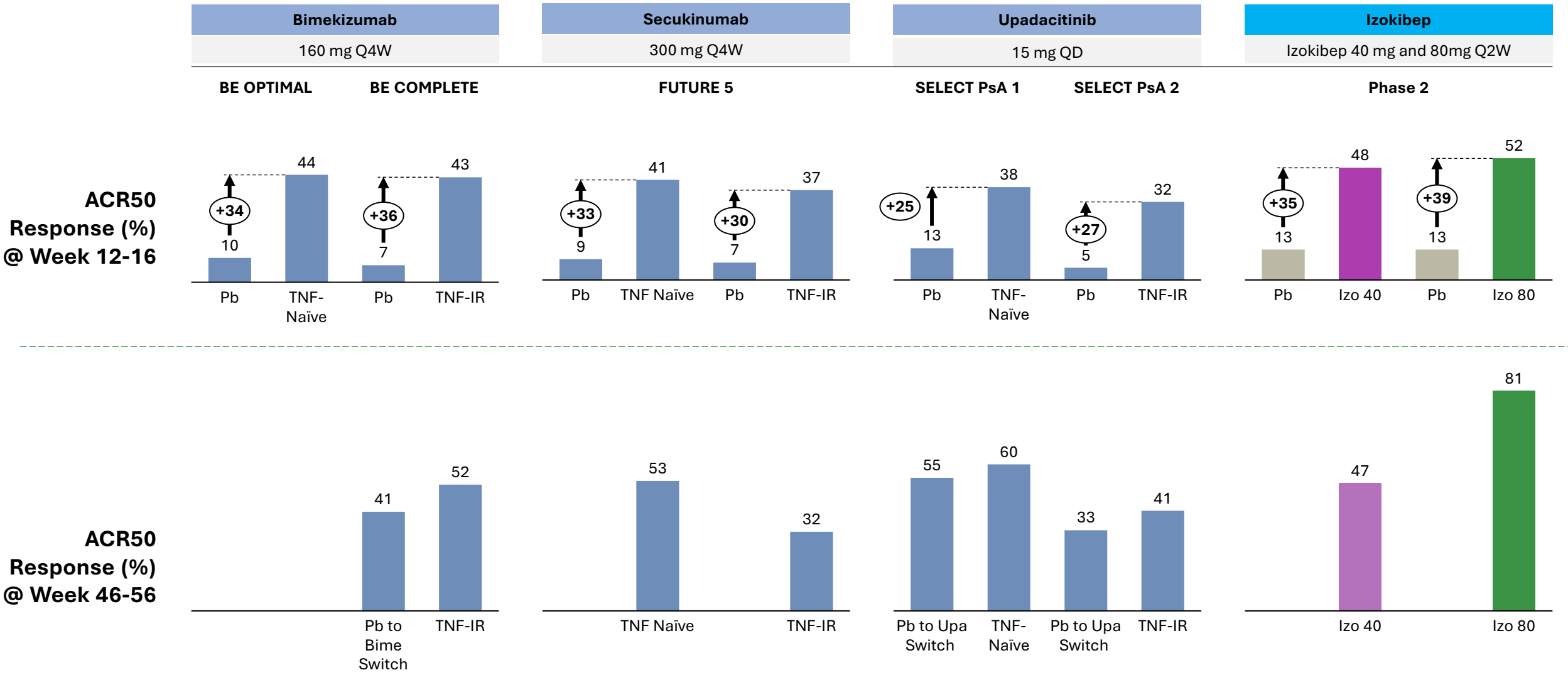
Safety Endpoints

- AEs, SAEs
- AE of Special Interest (candida, IBD, staphylococcal skin infection, moderate to severe ISRs)
- Safety laboratory, vital signs, physical examination

Treatment stratified by concomitant csDMARD, previous TNFi exposure, country.
NSAID, non-steroidal anti-inflammatory drugs; **csDMARD,** conventional synthetic disease modifying anti-rheumatic drug; **Q2W,** every two weeks; **ACR50,** American College of Rheumatology Criteria for ≥50% improvement; **PASI,** psoriasis area and severity index; **IBD,** irritable bowel disease; **ISR,** injection site reaction

PsA Treatment Landscape – ACR50 Responses

Izokibep 80 mg Q2W Demonstrates Top-Of-Range Responses For ACR50, Registrational Endpoint



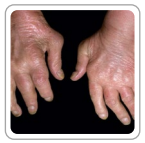
Note: This is a comparison across trials and has inherent limitations

Izokibep PsA

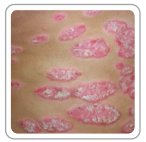
Meaningful Responses Seen Across Manifestations Beyond ACR50

Izokibep Phase 2 Psoriatic Arthritis Trial

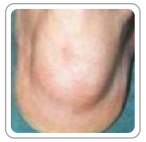
Izokibep 80 mg | Izokibep 40 mg | Placebo



ACR50
at 16 weeks



PASI75
at 16 weeks



LEI
at 16 weeks

Dactylitis, Nail Psoriasis and Enthesitis (SPARCC) Also Demonstrated Improvements By Week 16

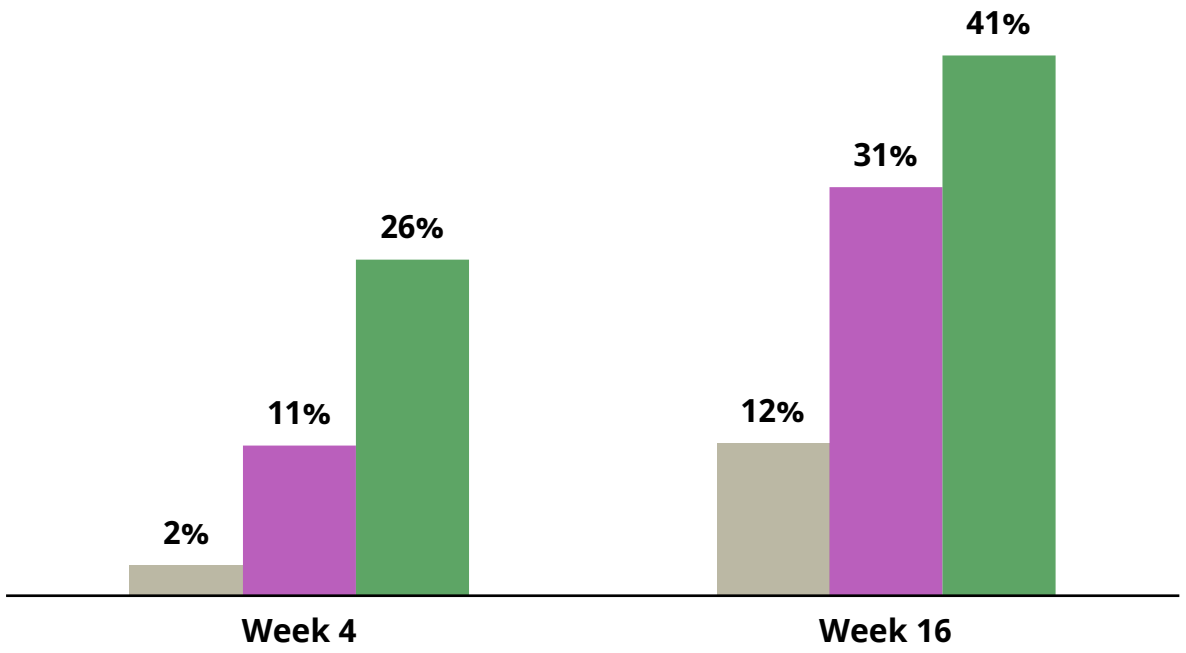
Enthesitis present in 77% of patients when measured by SPARCC, which has **16 sites, 12 unique from LEI.** Enthesitis correlates with severity of disease as well as residual pain and dysfunction

Dose-dependent Responses Were Seen Across All QoL Domains

PsAID-9 MCID (≥3) Responder in %

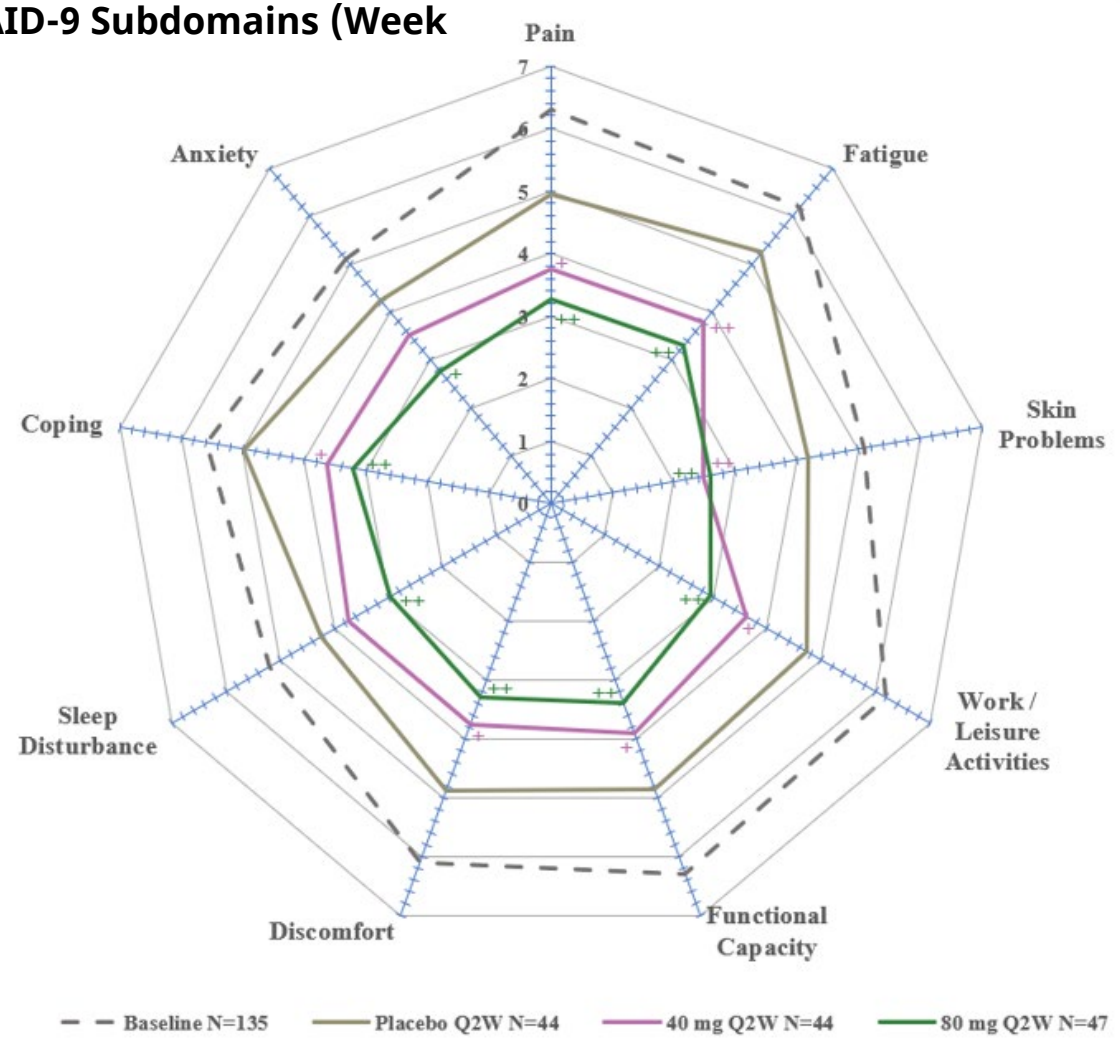
Full analysis set, post-hoc analysis, observed data

Izokibep 80 mg | Izokibep 40 mg | Placebo



Taylor et al. 2022 (ACR P0199)

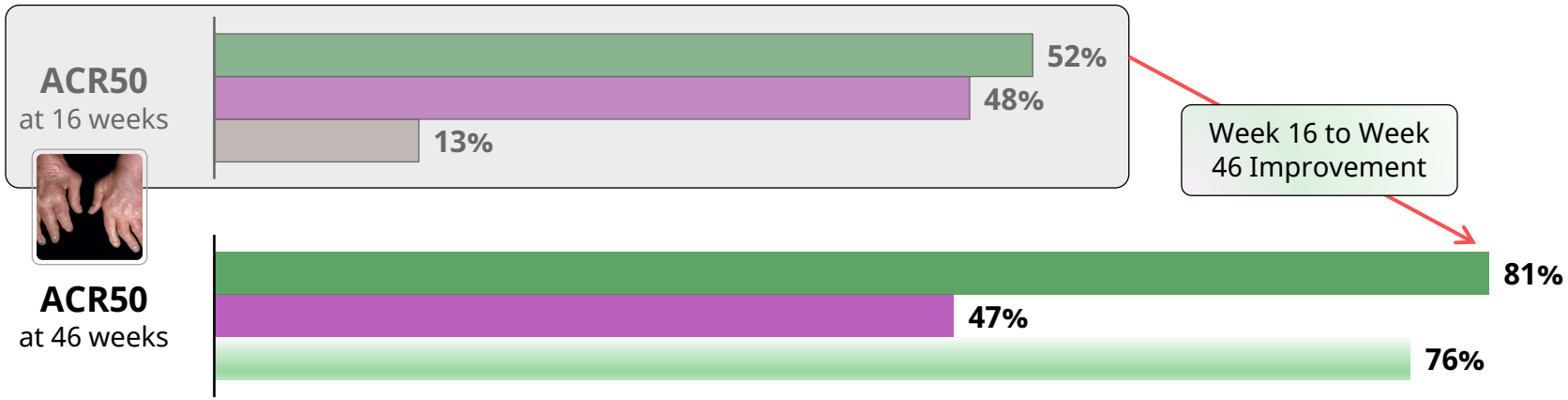
PsAID-9 Subdomains (Week 16)



Izokibep PsA

Magnitude Of Clinical Response Continued To Increase At Week 46

Izokibep Phase 2 Psoriatic Arthritis Trial

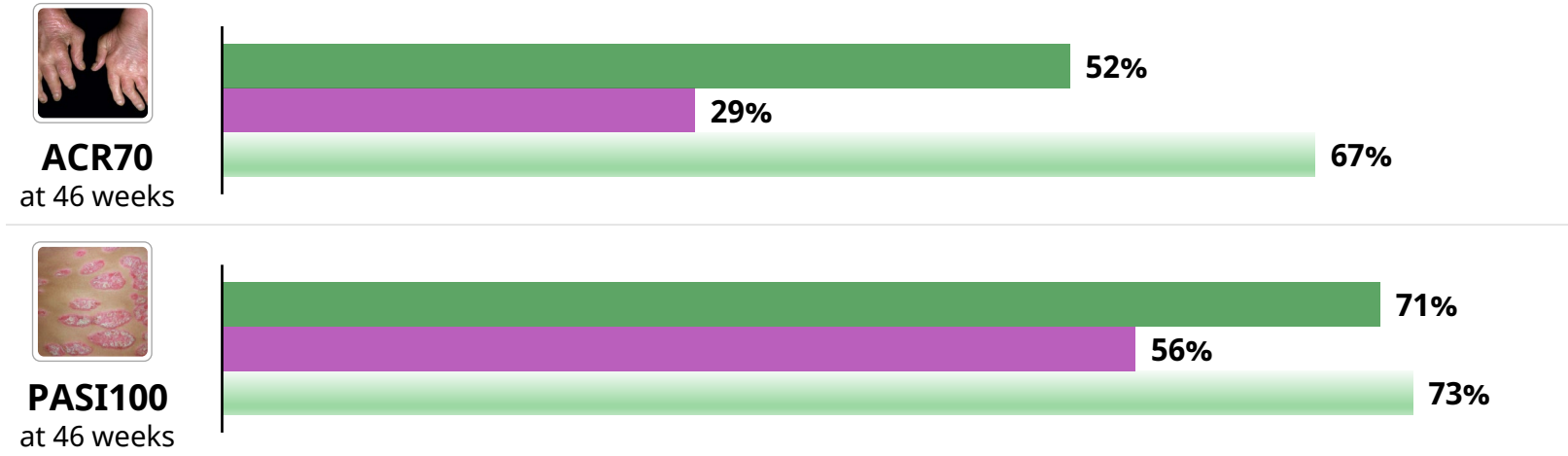


Izokibep 80 mg

Izokibep 40 mg

PbO Switched to 80 mg[1]

Higher Measures of Response Also Improved Over Time



Enthesitis resolution as measured by both LEI and SPARCC also continued to increase through Week 46

ACELYRIN

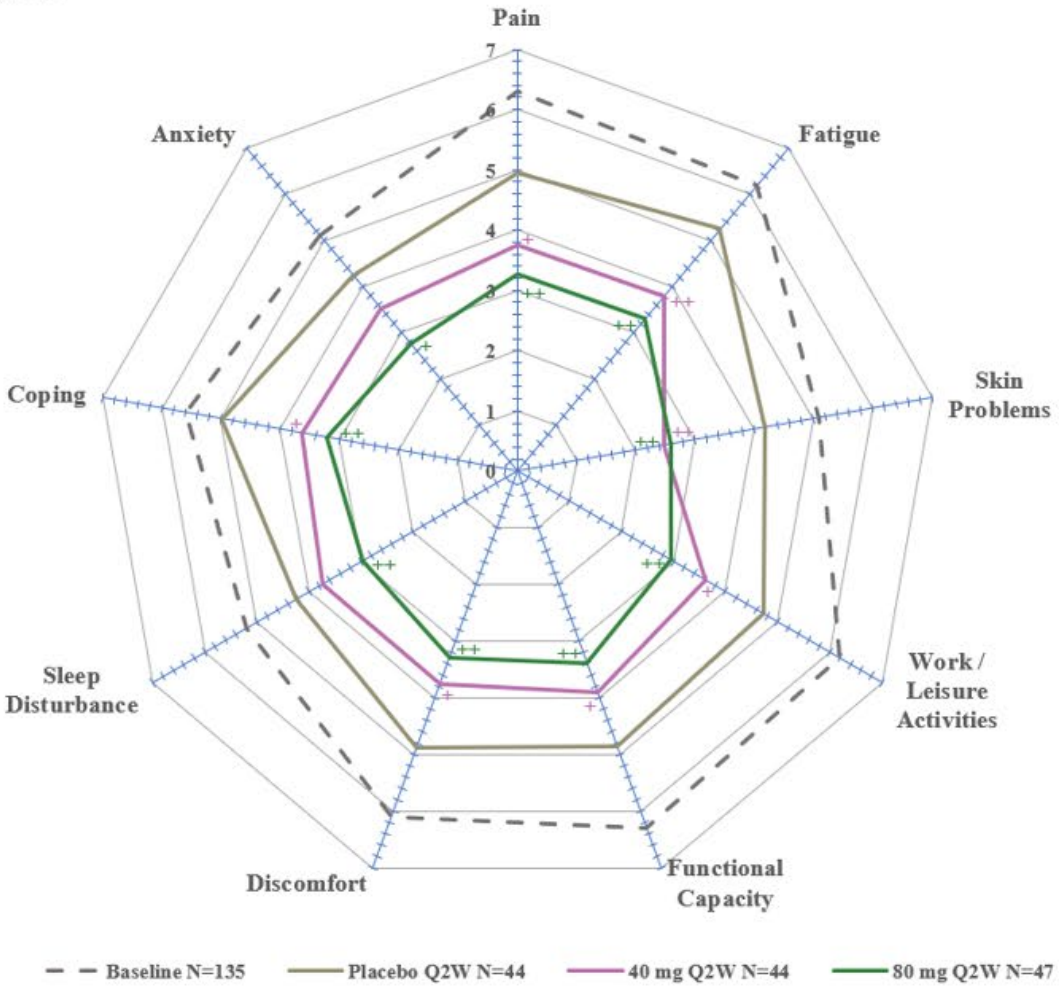
1 After week 16, all patients originally assigned to placebo were switched to izokibep 80 mg Q2W

***** Week 16 analyses are non-responder imputation (NRI); beyond 16 weeks are as observed

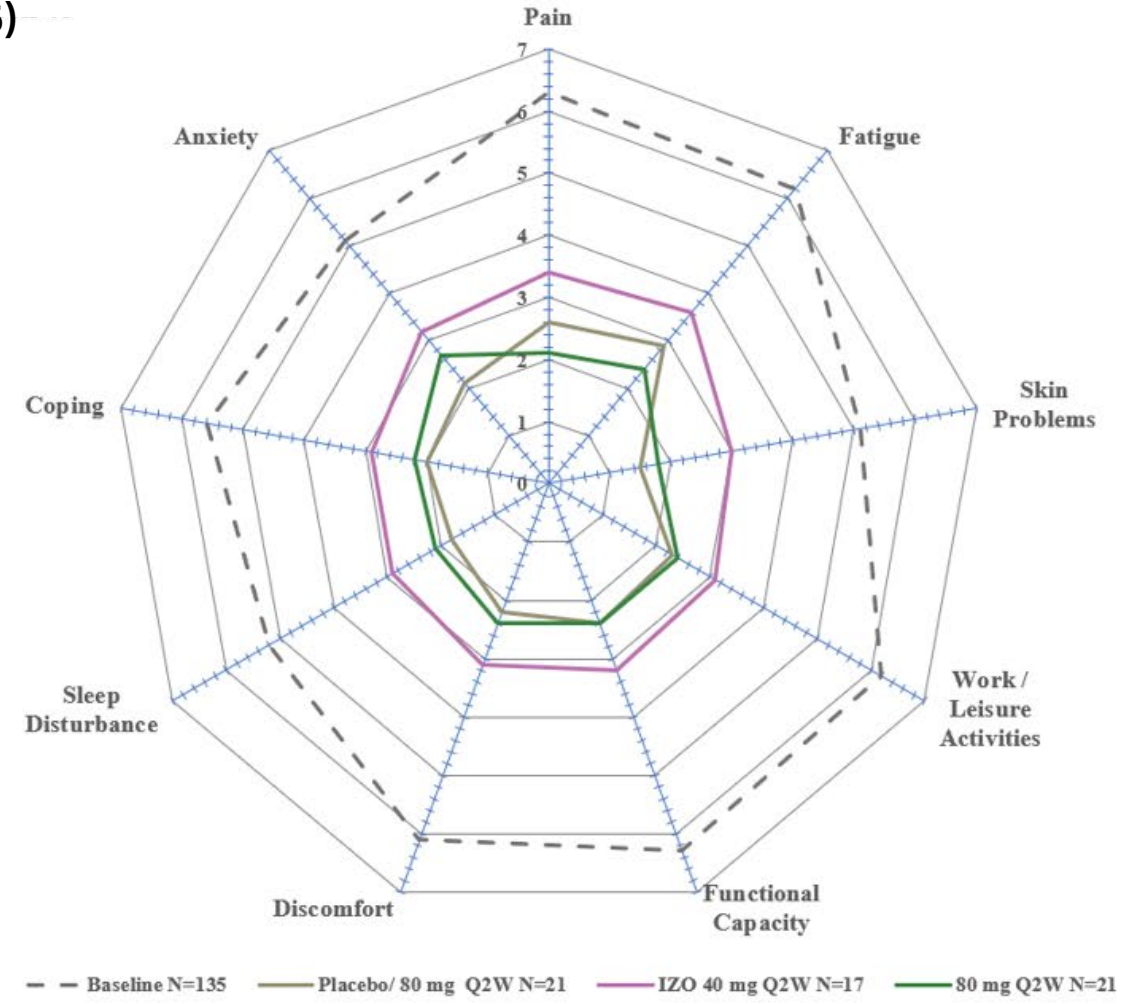
Further Improvements In Quality of Life Seen At Week 46

Izokibep Phase 2 Psoriatic Arthritis Study – 16 to 46 Weeks

PsAID-9 Subdomains (Week 16)



PsAID-9 Subdomains (Week 46)



Izokibep was Generally Well-tolerated With Consistent Safety Profile

Izokibep Phase 2 Psoriatic Arthritis Trial

	Week 16 Placebo Controlled			Post Pbo-Controlled Period to Week 46		
Adverse Events (AEs)	Placebo (N=44) n (%)[1]	Izokibep 40 mg (N=44) n (%)[1]	Izokibep 80 mg (N=47) n (%)[1]	Placebo switched to Izokibep 80 mg Q2W (N=43) n (%)[1]	Izokibep 40 mg (N=42) n (%)[1]	Izokibep 80 mg (N=46) n (%)[1]
Serious AEs	0	0	0	3 (7.0%)	1 (2.4%)	3 (6.5%)
Preferred Term (≥5%)[3]						
Injection site reaction	0	12 (27.3%)	12 (25.5%)[4]	7 (16.3%)	5 (11.9%)	7 (15.2%)
Upper respiratory tract infection	1 (2.3%)	2 (4.5%)	3 (6.4%)	0	3 (7.1%)	1 (2.2%)
Hyperkalaemia	2 (4.5%)	3 (6.8%)	2 (4.3%)	0	4 (9.5%)	1 (2.2%)
Nasopharyngitis	0	1 (2.3%)	2 (4.3%)	2 (4.7%)	3 (7.1%)	4 (8.7%)
Back pain	0	0	0	2 (4.7%)	3 (7.1%)	2 (4.3%)
Headache	4 (9.1%)	0	4 (8.5%)	2 (4.7%)	1 (2.4%)	4 (8.7%)
COVID-19 infection	2 (4.5%)	1 (2.3%)	1 (2.1%)	2 (4.7%)	2 (4.8%)	3 (6.5%)
Other AEs of Interest						
Candidiasis	0	1[5] (2.3%)	0	0	0	0

1 Number (%) of patients with at least one Adverse Event (AE)
2 Two treatment discontinuations: 1 for ISR, 1 for injection site erythema
3 Most commonly reported AEs occurring in ≥ 5% of patients in any group
4 Mild or moderate AE only
5 Mild vulvovaginal candidiasis
6 7 SAEs not related to treatment occurred in 6 participants
*Vulvar cancer reported ~4 months into treatment in patient with extensive previous exposure to methotrexate

Week 16, no deaths and no SAEs were reported

Week 46, no deaths, 1 SAE of vulvar cancer reported as potentially related to treatment (see footnote), 7 SAEs reported as not related to treatment[6]

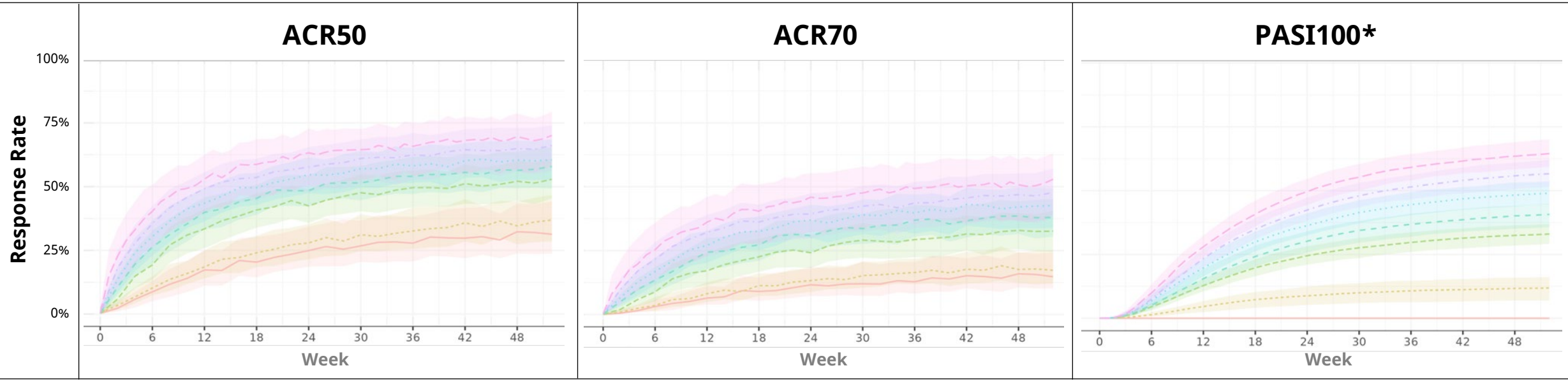
AEs leading to withdrawal were uncommon, and <2% overall

No evidence of a dose relationship in AEs moving from 40 mg to 80 mg observed

Safety profile remains consistent during longer-term follow-up

Izokibep PsA

PsA Phase 2 Modeling Data Predicted Further Improvement Beyond 16 Weeks And Predicts Improvement With Higher Dosing



* PASI100 underpredicted due to numerical complexity around PASI = 0; relative change is well-estimated

PopulationPK: IV and SC ph1, 2 data in healthy volunteers, psoriasis (PsO), and psoriatic arthritis (PsA) subjects. ACR: individual PK linked to observed ACR in PsA subjects using a categorial model (likelihood of achieving ACRxx based on PK concentration), including a time-dependent placebo effect. PASI: individual PK linked to observed PASI in PsO and PsA subjects using a continuous model (actual PASI score), with no evidence of a placebo effect. PASI100 calculated from change from baseline. No effect of disease (PsO vs PsA) on PASI response to izokibep. Simulated 300 replicates of 1000 subjects

Izokibep PsA

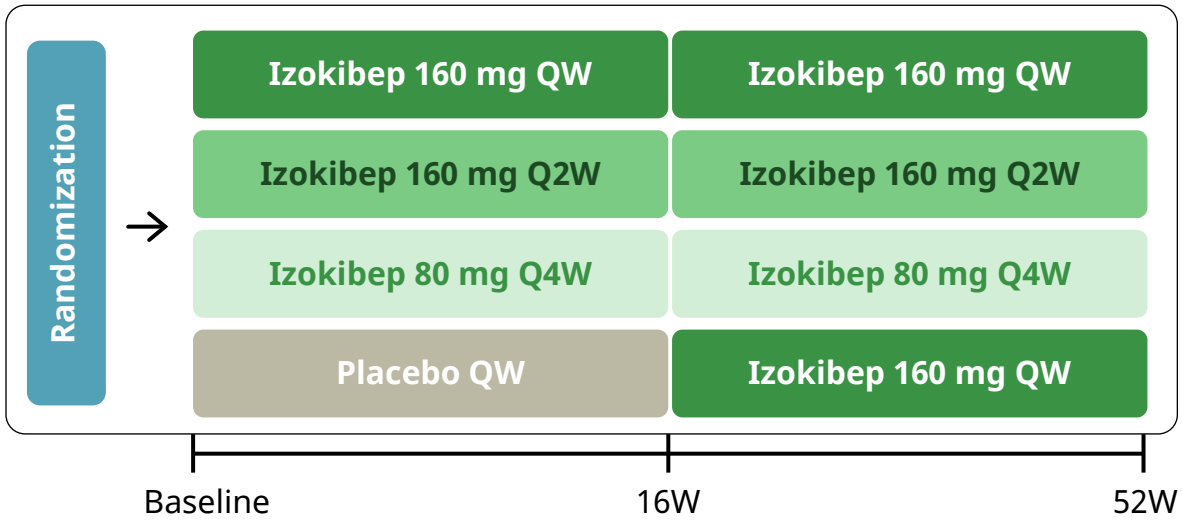
Enrollment Completed Phase 2b/3 Psoriatic Arthritis Study

Top-Line Data Anticipated 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*

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

*Primary and secondary endpoints, all week 16

Safety Endpoints*

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

*All secondary endpoints

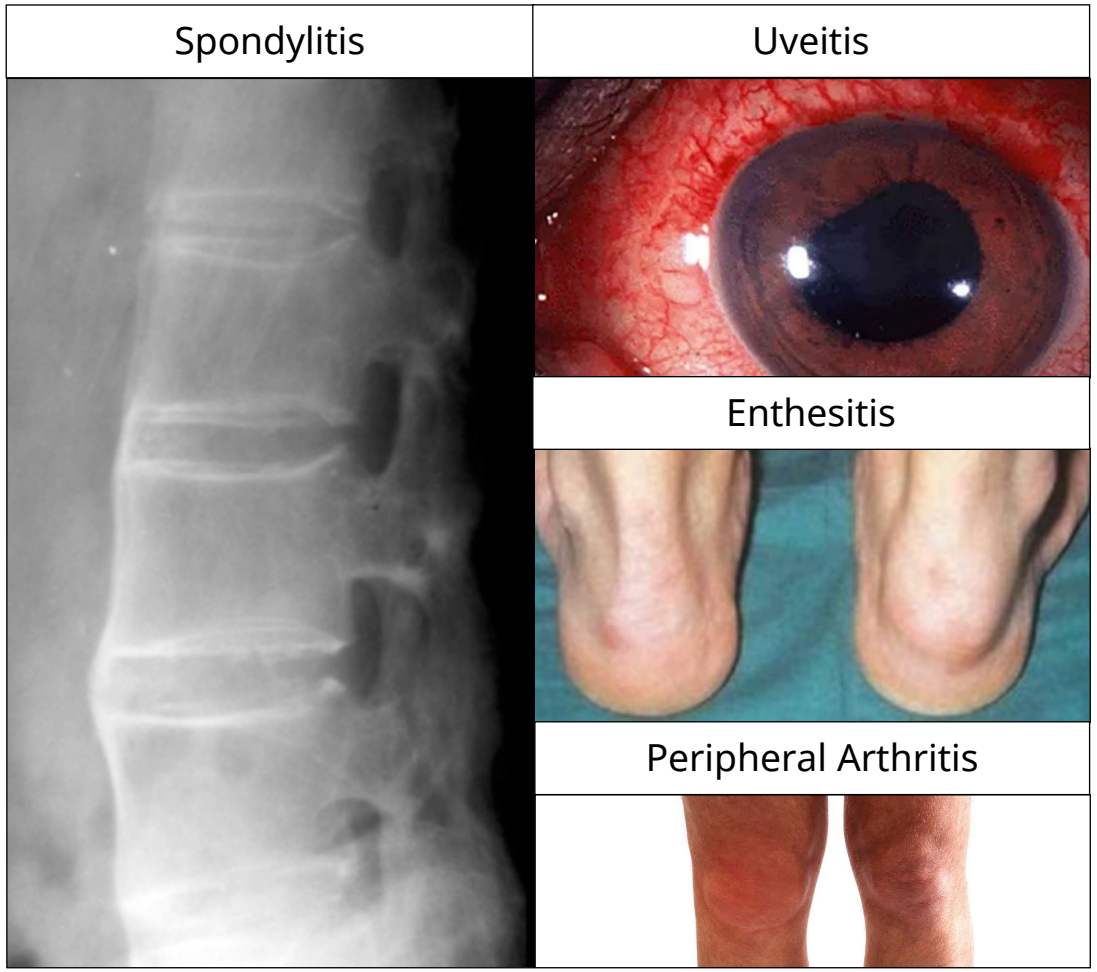
[1]4:4:1:4 160 mg QW, 160 mg Q2W, 80 mg Q4W and placebo
80 mg Q4W equivalent to ~20 mg Q2W and included to enable dose modeling
NSAID, non-steroidal anti-inflammatory drugs; **csDMARD,** conventional synthetic disease modifying anti-rheumatic drug; **TNFi,** TNF inhibitor; **QW,** Every Week; **Q2W,** Every Two Weeks

Izokibep

Axial Spondyloarthritis

AxSpA Response Rates With SoC Are Inadequate

Historically, Dose-Related Response Is Similar In AxSpA And PsA

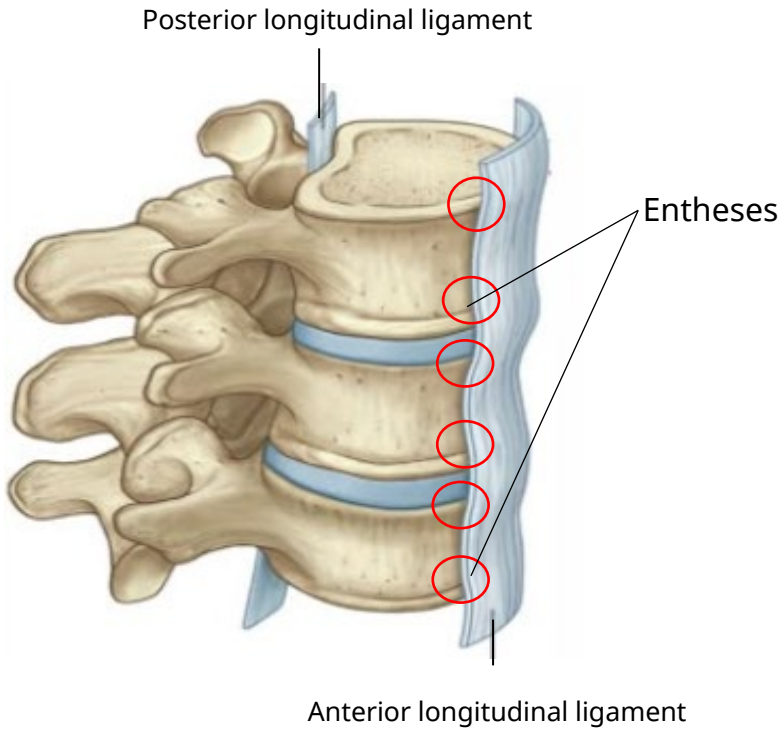


- AxSpA **comprises ankylosing spondylitis (AS) and nonradiographic Axial SpA**
- **Predominantly affects the spine and may also have enthesitis,** peripheral arthritis and uveitis
- **~2.6M AxSpA patients in the U.S.**; up to 10% are moderate-to-severe
- **~40% fail** available therapies
- Like PsA, **more complete and faster resolution of disease symptoms** manifesting in dense tissues (e.g., enthesitis) remain an unmet need

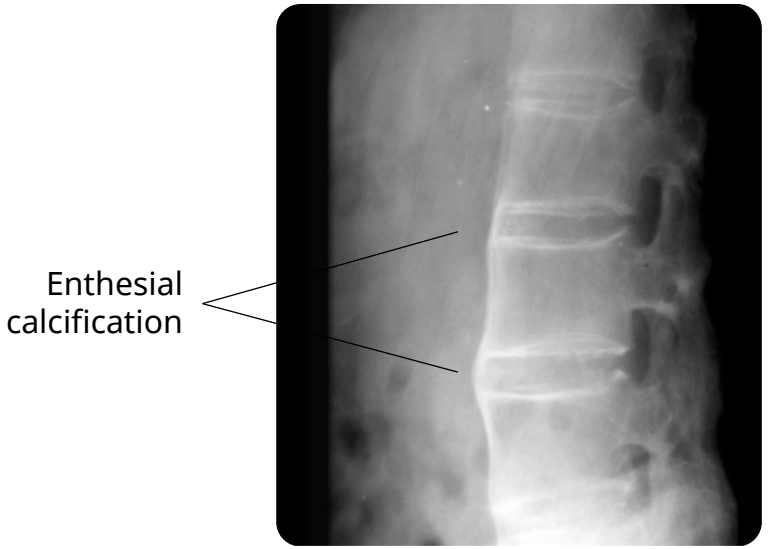
Enthesitis Is First Site Of Inflammation In AxSpA

Izokibep Has Shown Profound Effects On Enthesitis

Posterior & Anterior Longitudinal Ligament attaches to boney spine through entheses

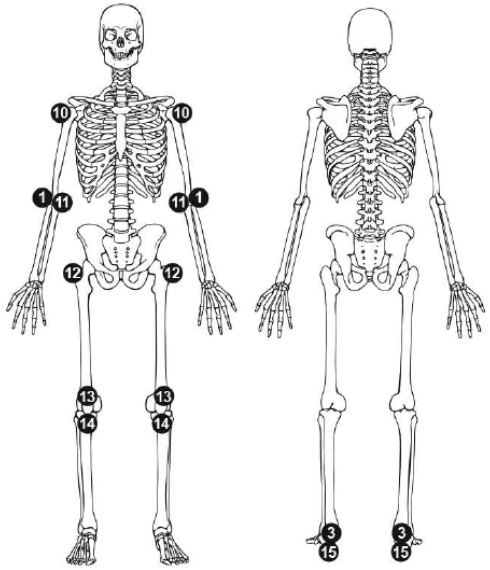


Lateral Spine X-Ray shows calcification along entheses. New bone is AxSpA hallmark



Calcification of anterior Longitudinal ligament at Enthesis locations

Enthesitis commonly occurs beyond the spine as well, leading to pain and disability



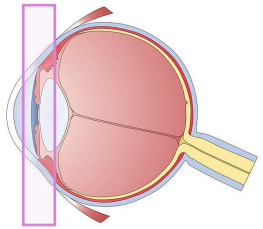
SPARCC Enthesitis Index for AxSpA assesses 16 sites, for use in trials

Entheses join ligaments and tendons to bone throughout the body.
Enthesitis is Central to AxSpA pathogenesis

Izokibep

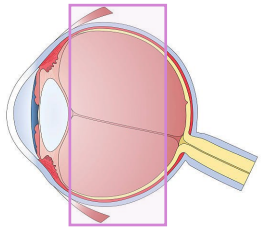
Uveitis

Uveitis Is inflammation In The Eye - Often Associated With Other Inflammatory Conditions – With High Unmet Need



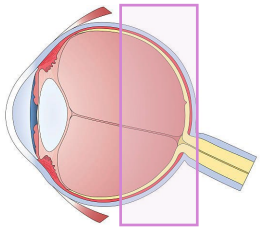
Anterior Uveitis

Anterior chamber (iris, ciliary body)



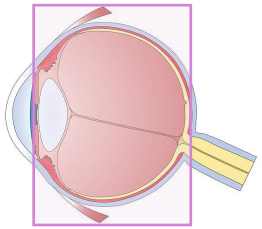
Intermediate Uveitis

Vitreous Chamber



Posterior Uveitis

Retina or choroid



Panuveitis

Anterior or vitreous chamber, retina or choroid

Limited Therapeutic Approaches

Steroids

Corticosteroids are effective first line therapy in ~60% of patients

Immunomodulators

Added for patients who do not respond (or relapse) during corticosteroid therapy

Biologics

Adalimumab: only approved biologic

- Relapse/failure is observed in 39% to 55% of patients within one year

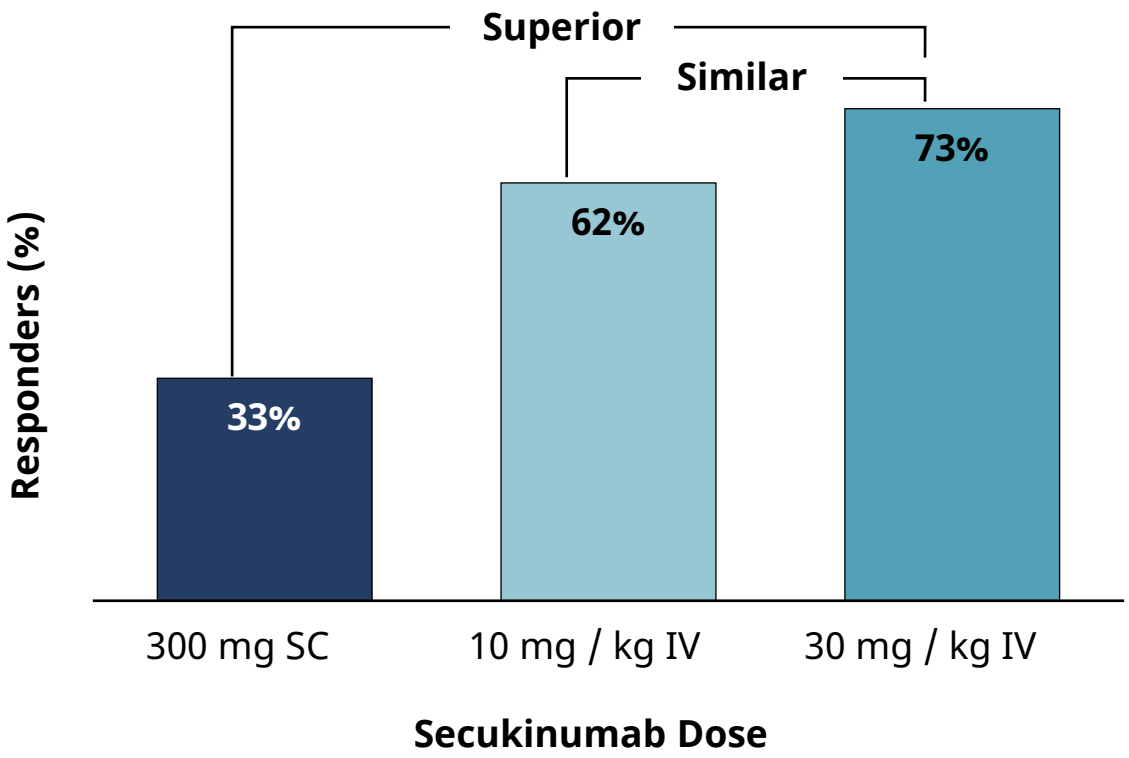
- Inflammation **can lead to vision loss;** demands more efficacious therapies/persistent responses
- More than **90% of uveitis cases have been reported to be non-infectious, chronic and recurrent** in nature
- **~300K uveitis patients in the U.S;** nearly a third are treated with biologics today
- Only approved treatments are corticosteroids and adalimumab; **~40% fail available biologics**
- More complete **reduction in vitreous haze without increased steroid use and without disease worsening remain an unmet need**

Secukinumab Demonstrated Response In Uveitis With IV Dosing

Unable To Achieve Satisfactory SC Response Beyond Placebo, Development Discontinued

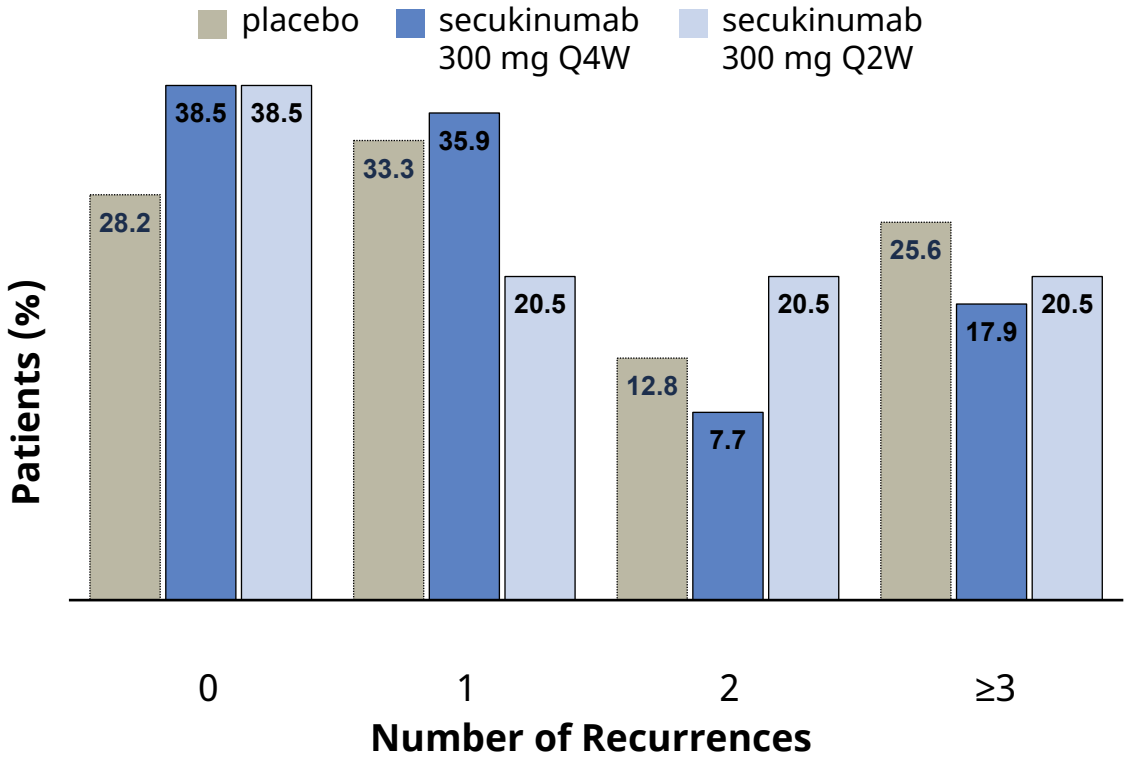
Dose Response Shows Superior Efficacy Advantage with Secukinumab IV

SC vs IV Dosing[1]



Secukinumab SC Administration Does Not Separate from Placebo

SC vs Placebo[2]



Izokibep Achieves Secukinumab IV Exposures With A Single SC Injection[3]

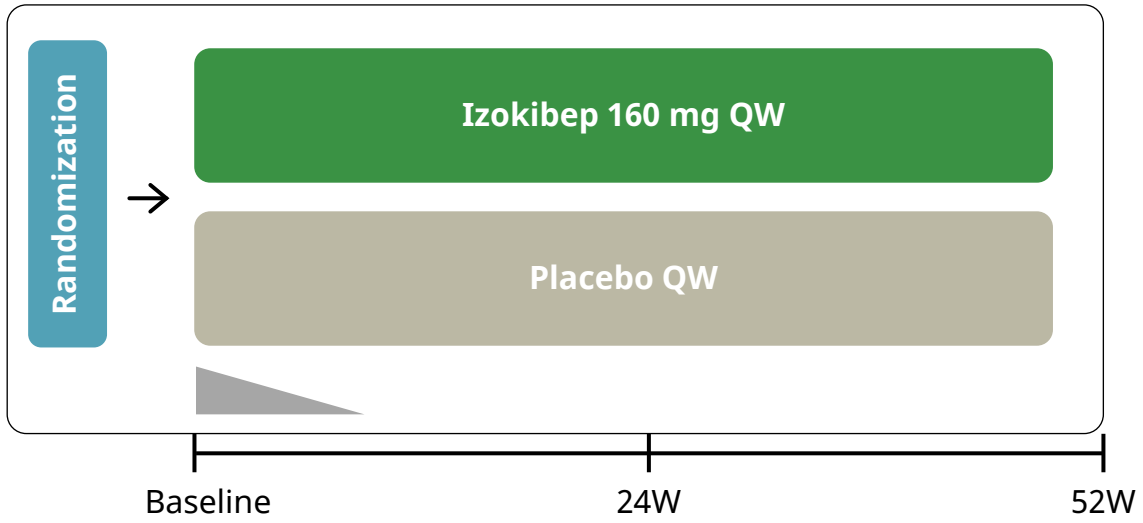
1. Letko, et al. *Ophthalmology,* 2015.. 2. Dick, et al. *Ophthalmology,* 2013. 3. Cetara modeling demonstrating izokibep exposures up to 160 mg SC QW can match secukinumab 10-30mg/kg IV Q2W; Confirmed with observed data in Phase 2 PsO Trial 4. Secukinumab is marketed by Novartis AG

Izokibep UV

Actively Enrolling Phase 2b/3 Non-Infectious Uveitis Study

Screening/ Eligibility

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



Efficacy Endpoints*

- Time to treatment failure (Primary)
- Quiescence
- BCVA
- NEI VFQ-25 score
- Central retinal thickness

*Primary and secondary endpoints

Safety Endpoints*

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

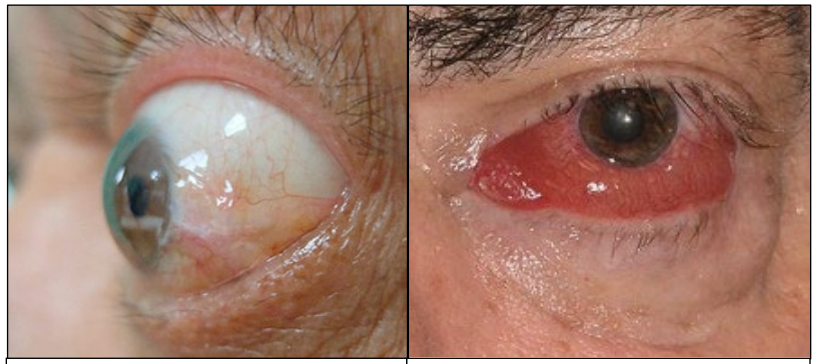
*Secondary endpoints

Lonigutamab

(anti-IGF-1R)

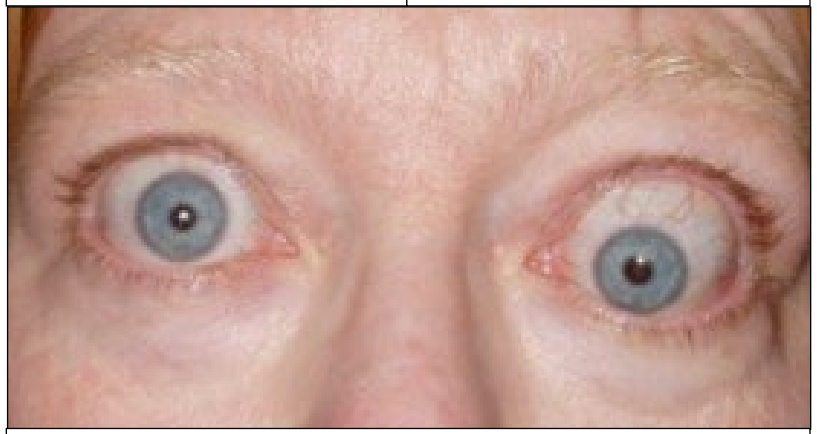
Lonigutamab TED

Thyroid Eye Disease (TED) Is A Vision-Threatening Autoimmune Disease



Proptosis

Redness



Diplopia

- **TED is characterized by progressive inflammation** that can lead to irreversible damage to tissues around the eye, threatening vision.
- **Understanding of TED as a chronic inflammatory condition has continued to evolve,** especially with recent studies demonstrating efficacy in subjects considered chronic vs. acute.
- **Greater depth and durability of response is needed;** standard of care (SoC) has a fixed treatment duration and IV administration.
- **Recent safety updates to SoC label highlight hearing impairment as serious,** potentially permanent.
- **~100,000 TED patients in the U.S.;** 35% are characterized as having moderate-to-severe disease

Lonigutamab TED

Ideal TED Treatment Will Offer Potential For Improved Depth & Durability of Response, Minimized Safety Liability Via SC Dosing

Optimize Clinical Response

Maintain C_{min} at levels to achieve improved depth and durability of response.

Minimize Safety Impact

Minimize C_{max} to reduce risk of hearing impairment.

IGF-1 functions to regenerate cells of the inner ear subsequent to auditory insults. We hypothesize that high C_{max} due to IV dosing of anti-IGF-1R breaches the blood labyrinth barrier and inhibits this normal function leading to hearing impairment.

Maximize Patient Convenience

Patient-delivered, at-home or in-office administration via pre-filled syringe or autoinjector.

Lonigutamab TED

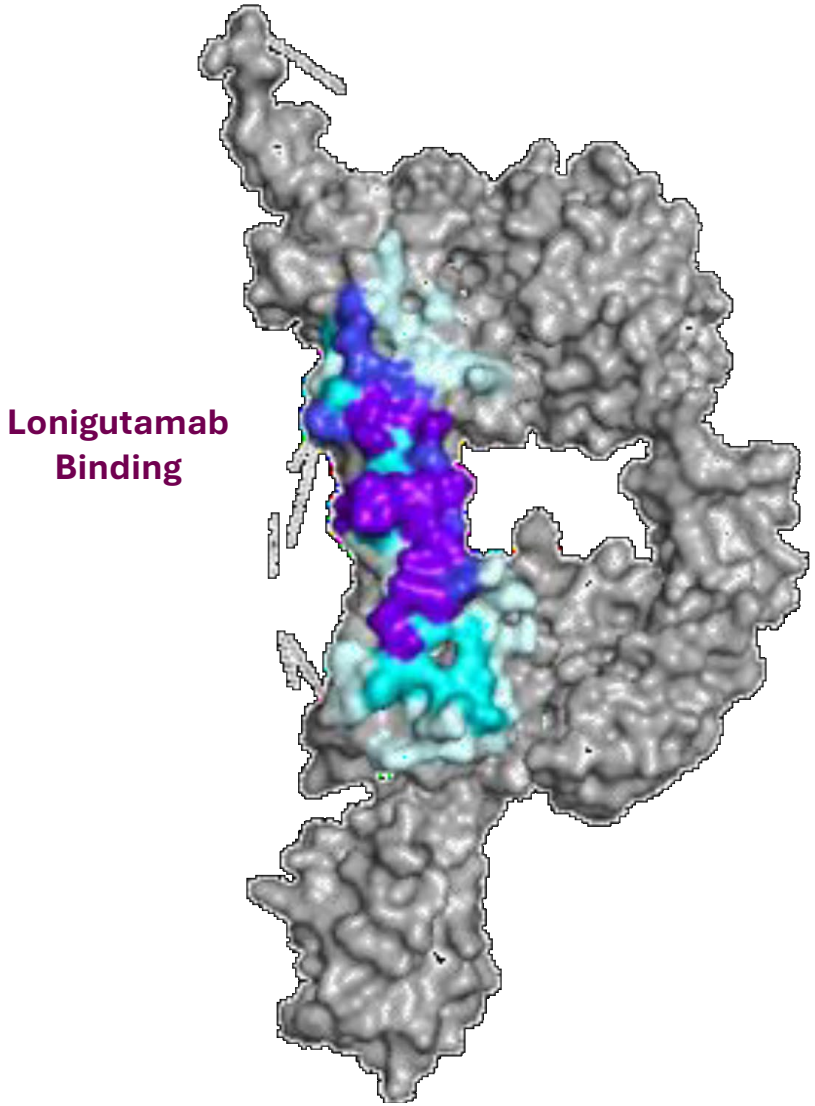
Lonigutamab Has Potential To Deliver On Unmet Need In Depth & Durability Of Disease Control And Safety Liability

- **Highly Potent**
  Consistently ~70 times more potent than teprotumumab across binding and functional assays

- **Subcutaneous Dosing**
  Single Ascending Dose data establishes that the high potency enables clinically relevant exposures to be achievable with low volume (e.g., <2 mL via autoinjector)

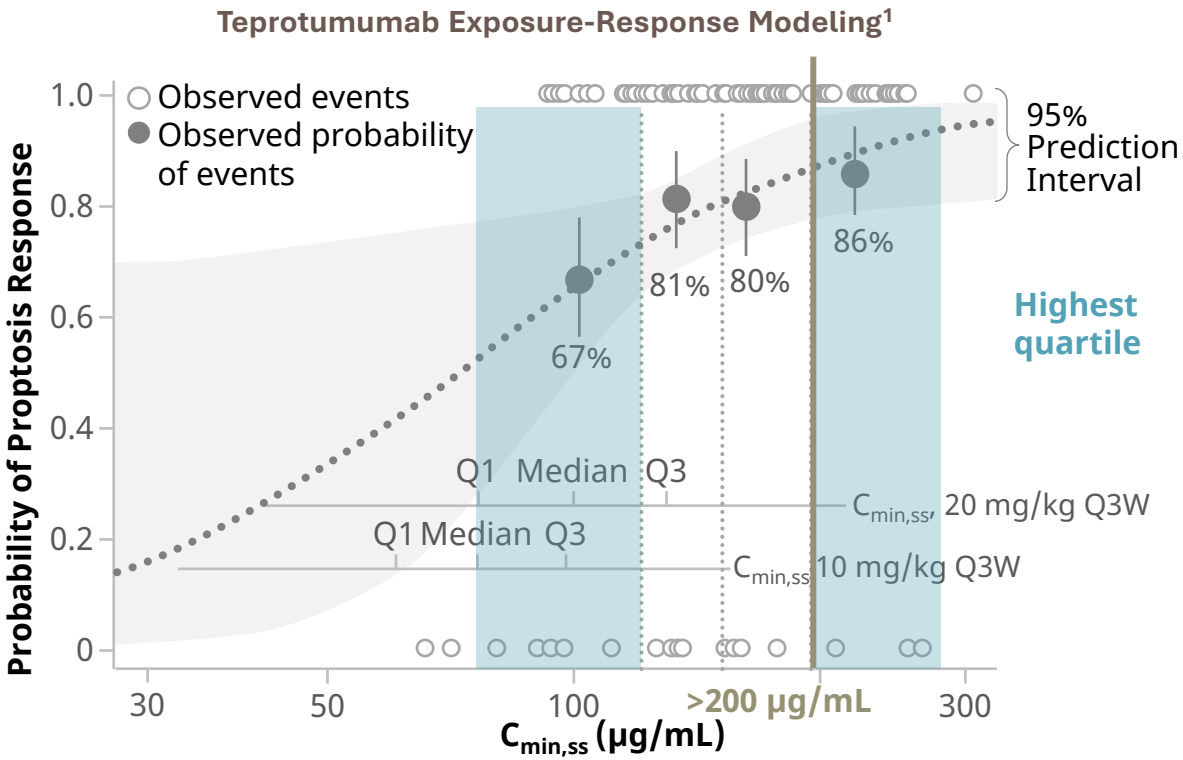
- **Potential for Improved Efficacy**
  Depth and durability of disease control enabled by potential longer term SC dosing

- **Potential for Improved Safety**
  By limiting Cmax, potential to reduce hypothesized Cmax effects (hearing impairment). Further, binding to a unique epitope results in rapid internalization as well as limiting potential for interaction with insulin receptor, potentially reducing hyperglycemia risk



Lonigutamab Is ~70x More Potent Than SoC

SC lonigutamab Can Achieve The Effective Scaled teprotumumab Exposure Target C_{min} Of 2-3 µg/mL



Teprotumumab[4] program showed exposures of C_{min} ≥ 200 µg/mL increase probability of proptosis response

	Binding (K_D)	Internalization Potency (EC_{50})
Lonigutamab	<0.03 nM[2]	<100 pM[2]
Teprotumumab	2.2 nM[3]	>6667pM[3]
Potency Shift	**>75x**	**>66X**

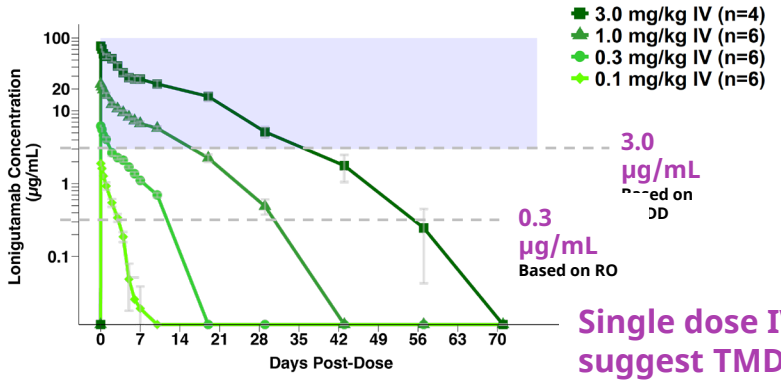
Potency shift calculated via K_D and internalization EC_{50} reflect a similar magnitude

Potency shift for lonigutamab versus teprotumumab supports effective subcutaneous dosing

1. Xin Y, et al. Clin Pharmacokinet. 2021; 2. Akla et al 2020 Mol Cancer Ther; 3. FDA Pharm/Tox Review Application Number 761143 (Link) 4. Teprotumumab is marketed by Horizon Therapeutics plc

Phase 1a SAD Trial Results Presented At 2023 NANOS Meeting Demonstrate SC Achievement Of Target C_{min} At Multiple Doses

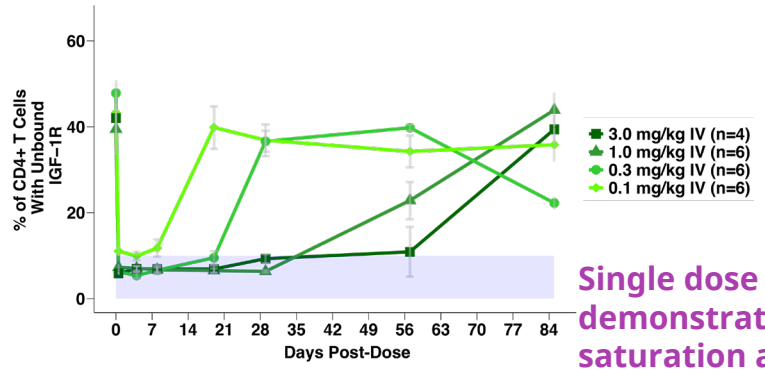
PK



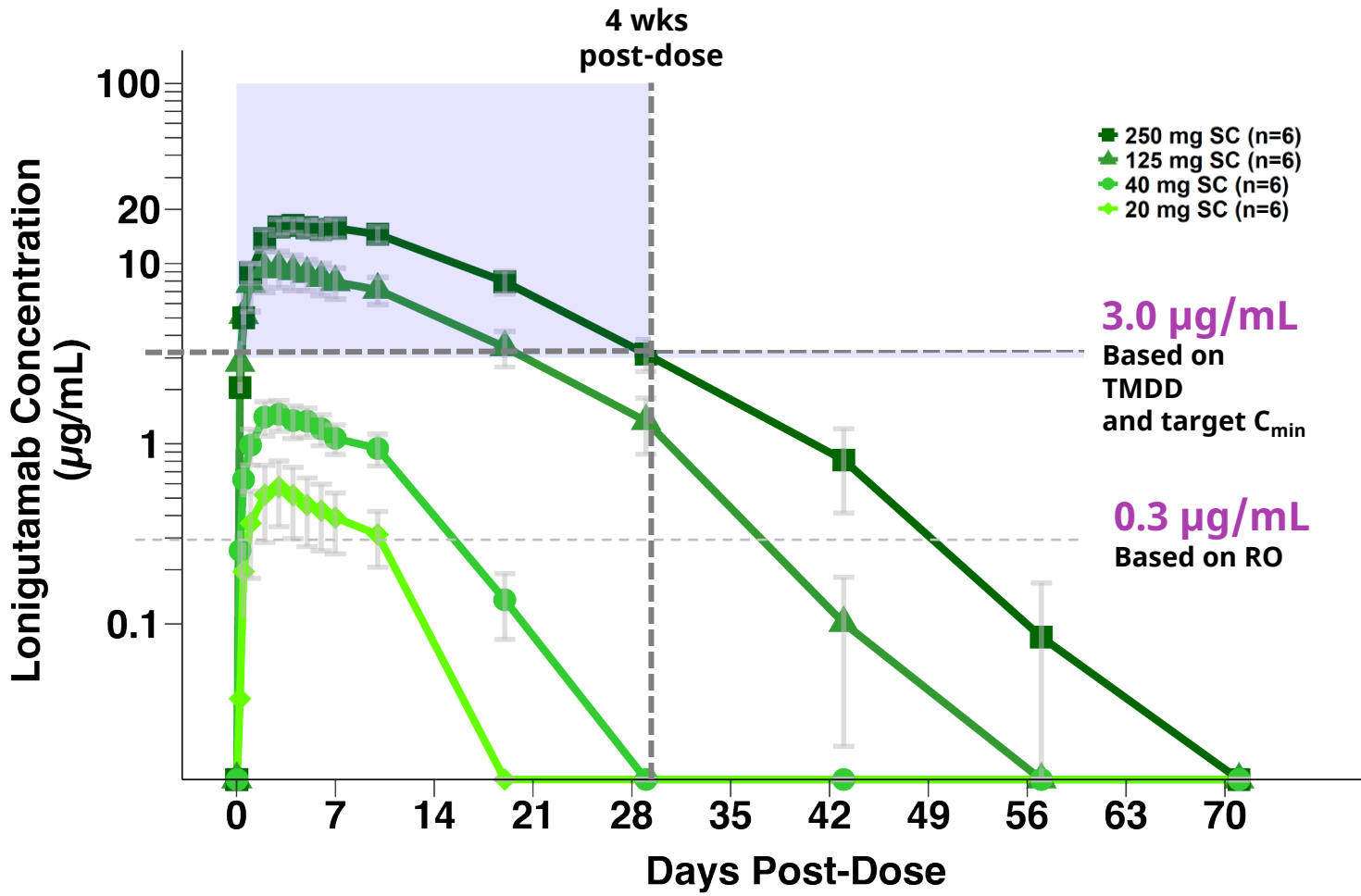
Single dose IV data suggest TMDD saturation at >3.0 ug/mL

PD

- Receptor occupancy (RO) is a measure of unbound IGF-1R on circulating CD4⁺ T-cells
- Receptor saturation occurs when RO reaches ≥90% (i.e., E_{max})



Single dose IV data demonstrate RO saturation at >0.3 µg/mL



PK, Pharmacokinetics; **PD,** Pharmacodynamics; **RO,** Receptor Occupancy; **SC,** Subcutaneous, **IV,** intravenous **TMDD,** Target Mediated Drug Disposition

Lonigutamab TED

Phase 1/2 Trial Of SC Lonigutamab Underway In TED Patients

Proof Of Concept Data Expected End 2023 Or Early 2024

Screening/ Eligibility

- Proptosis defined in the study eye as ≥3 mm above normal
- Clinical Activity Score (CAS) ≥4 (using a 7-item scale) for the most severely affected eye
- Onset of active TED symptoms within 15 months prior to the baseline

12-week treatment duration, open-label, n<~15/cohort

- **Cohort 3 TED**: SC Q4W (planned)
- **Cohort 2 TED**: SC QW (planned)

6-week treatment duration, pbo-controlled, n<~8

- **Cohort 1 TED**: Low Dose Safety (ongoing)

Two-Dose Healthy Cohort

- Multiple Dose Healthy Subjects PK study (complete)

Key Efficacy Endpoints

› Exploratory measures including proptosis (reduction in eye bulging), diplopia (reduction in double vision), and Clinical Activity Score (change in CAS)

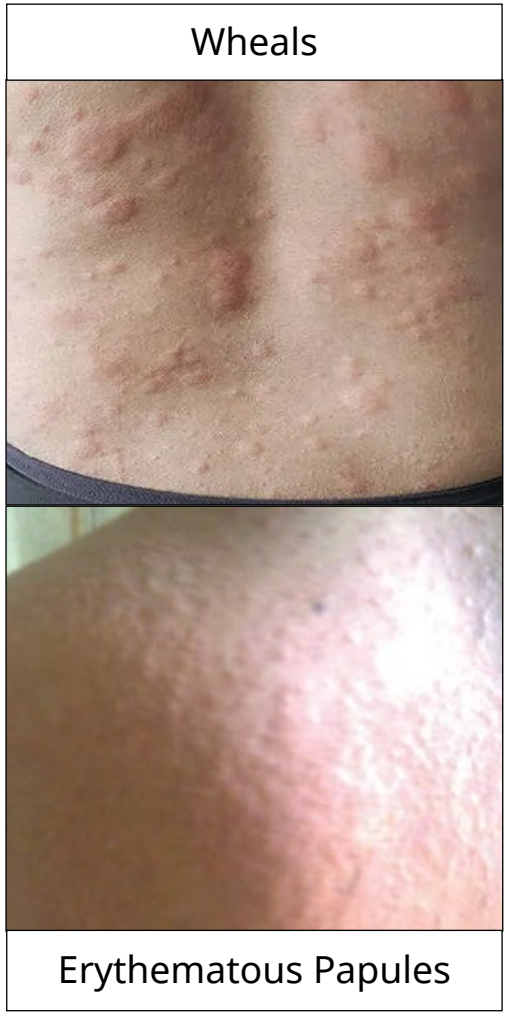
Safety Endpoints

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

SLRN-517

(anti-c-KIT)

Chronic Urticaria (Hives) Is An Inflammatory Disease Driven By Mast Cells



- Chronic Urticaria (CU) results from pathogenic activation of mast cells and basophils, leading to the release of proinflammatory mediators[1]
- CU occurs in the absence of identifiable, provoking factors and persists for more than 6 weeks
- Pathogenesis of CU is not well understood; however, evidence often points toward a potential autoimmune etiology with mast cells at center of pathophysiology

- **One of the most prevalent dermatologic diseases** with more than ~1M U.S. patients.
- **Current therapies provide patients with only modest relief** and do not target the root cause of disease.
- Targeting mast cell activation is hypothesized to **provide more rapid and sustained improvements for patients.**

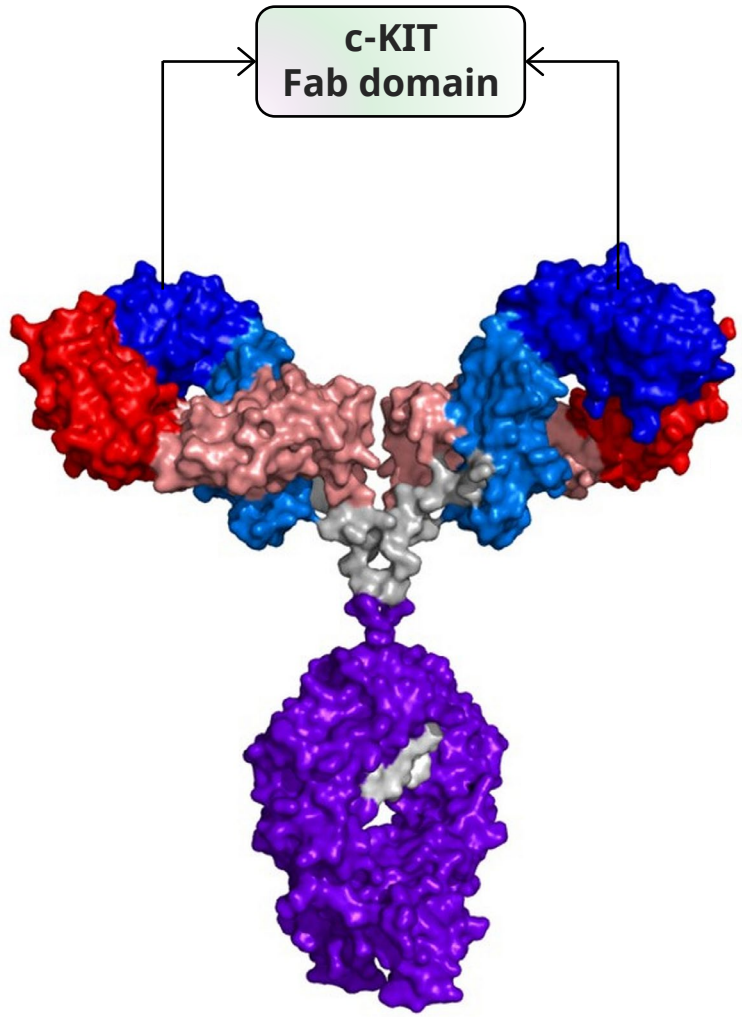
SLRN-517 Urticaria

SLRN-517 Has The Potential To Differentiate In Mast Cell Driven Disease

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
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

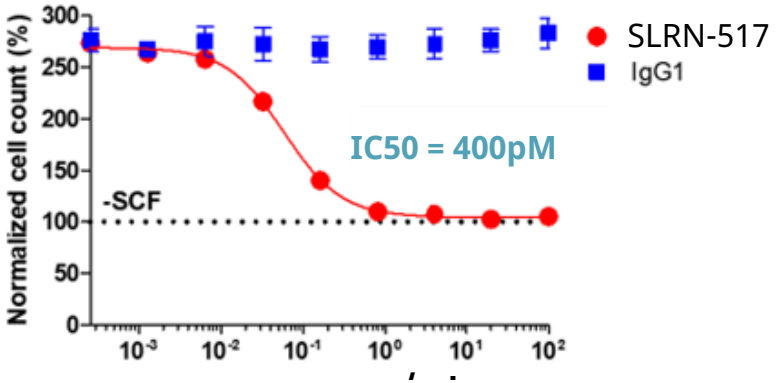
Minimizing On-Target Safety Impact
Combined with high potency, human half-life anticipated to be ~16 days, potentially enabling rapid depletion of mast cells while limiting opportunity for other effects on c-KIT or other sensitive tissues (spermatogenesis, hair color, hematopoietic cells (neutropenia))



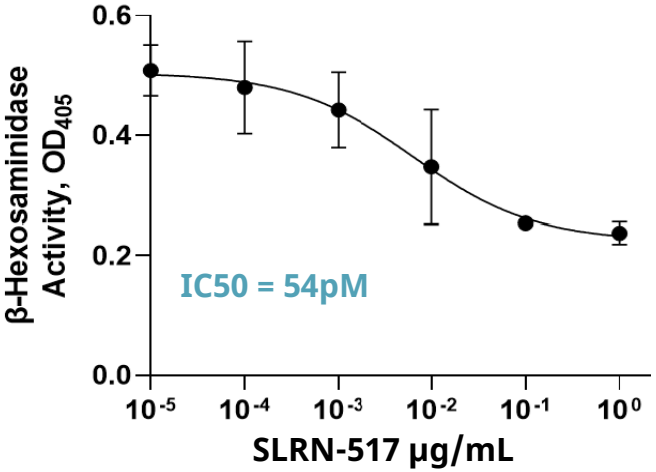
Highly Potent, Fully Human c-KIT Targeting mAb Hypothesized To Enable Clinically Meaningful Differentiation In Allergy / Inflammation

	SLRN-517	CDX-0159
Binding Affinity, SPR (KD)	1.55pM	10pM[1]
Inhibition of SCF Mediated Mast Cell Proliferation (IC_{50})	400pM	1,100pM[1]
Inhibition of IgE Dependent Degranulation (IC_{50})	54pM	165pM[1]
Projected Human Dose	<1mg/kg	3mg/kg[A]

SLRN-517: Mast Cell Proliferation Assay



SLRN-517: Mast Cell Degranulation Assay



[1]Alvarado et al 2022 Allergy; [2]Patent US 10,774,146, B2
[A] Subcutaneous administration in chronic spontaneous urticaria and chronic inducible urticaria at 150mg and 300mg is being evaluated

SLRN-517 Urticaria

SLRN-517 Phase 1/2 Study For Safety And Proof Of Concept

Actively Enrolling Healthy Volunteers In Single Ascending Dose Study With Multiple Dose Evaluation Including In Chronic Spontaneous Urticaria (CSU) Subjects To Follow

Screening/ Eligibility

- Healthy Subjects: 18-65 years
- CSU subjects: 18-75 years
- Males and Females
- No chronic medical conditions or con meds
- CSU: symptoms despite H1-anti-histamines

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)

MAD and CSU

Cohort 5: 2-3 dose SC
Healthy Subjects N=8 (incl 2 placebo)

Cohort 6: 2-3 dose SC
Healthy Subjects N=8 (incl 2 placebo)

Cohort 7: 2-3 dose SC
CSU N=8 (incl 2 placebo)

Efficacy Endpoints

- Tryptase Levels for healthy and chronic urticaria subjects
- Itch and hives scores for urticaria subjects (Urticaria Activity Score – 7)
- Angioedema score

Safety Endpoints

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

ACELYRIN Is A Late-Stage Clinical Biopharma Company Creating An Industry Leading Immunology Portfolio

Focused Strategy and Experience

- Experienced management team
- Identifying, acquiring, and accelerating development and commercialization of potentially transformative therapies

Attractive Pipeline

- Izokibep is a “pipeline-in-a-program” where we hypothesize that high potency and small size could lead to improved outcomes
- Both HS and PsA now have data supporting this hypothesis, which enabled internal program acceleration
- Building a portfolio of programs, including both lonigutamab in TED and SLRN-517 CU in clinical stage PoC studies

Positioned for Growth

- Robust immunology portfolio covers areas of significant unmet need and includes several multi-billion-dollar indications
- Well-capitalized having raised more than $1 billion in private and public equity in 3 years since founding in July 2020
- Continuing to attract leading talent, build capabilities and seek additional partnership opportunities

ACELYRIN

Thank You

Contact

investors@acelyrin.com