ACELYRIN

Izokibep

Psoriatic Arthritis

Global Phase 2b/3 Topline Results

April 16, 2024

Forward Looking Statements And 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 the therapeutic potential of our product candidate izokibep, including with respect to the potential for longer-term treatment with izokibep to provide for continued improvement over time; the long-term safety profile of izokibep; the timing and availability of data from clinical trials; the potential market size and size of the potential patient populations for certain indications we are pursuing, and our product candidates.

These forward-looking statements are based on ACELYRIN's current plans, objectives and projections, and are inherently subject to risks and uncertainties that may cause our actual results to differ materially and adversely from those anticipated in such forward-looking statements. Such risks and uncertainties include, without limitation, those associated with the successful completion of development and regulatory activities with respect to our product candidates; the timing and results of our clinical trials, including the potential that future results could differ adversely from prior results, where applicable; our ability to timely secure adequate supply of our product candidates; sufficient funding; legal proceedings and the outcome thereof; competitive risks; market volatility; macroeconomic conditions and other risks and uncertainties affecting ACELYRIN including those described from time to time under the heading "Risk Factors" and elsewhere in our current and future periodic and other reports filed with the Securities and Exchange Commission ("SEC"), including our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2023. These filings are available on the SEC's website www.sec.gov. In addition, new risks may occur at any time, and we anticipate that subsequent developments could cause our views to change. Forward-looking statements herein are made of the date of this presentation, and ACELYRIN undertakes no duty to update them in the event of new information, future developments, or otherwise, except as required under applicable law. Any reader of this presentation is cautioned not to place undue reliance on these forward-looking statements.

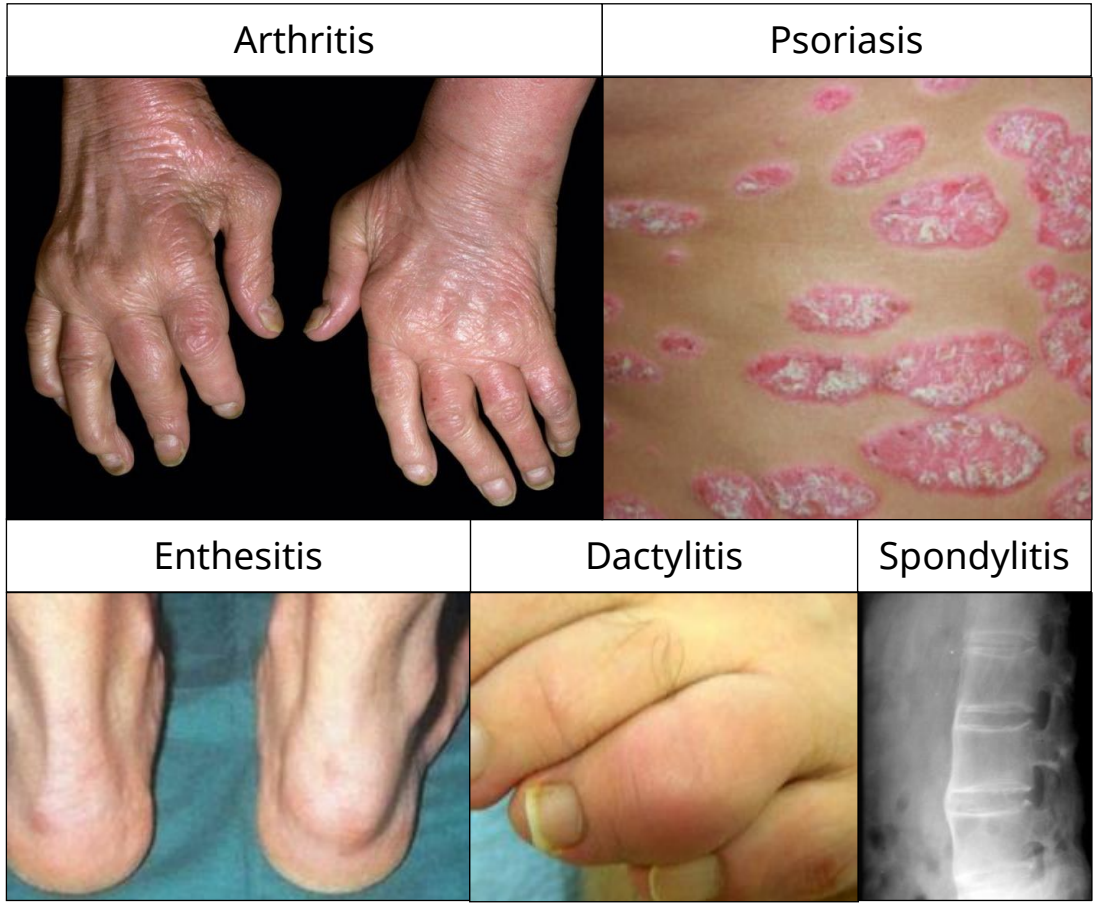
Izokibep is currently under clinical investigation, and no representation is made as of the safety or efficacy of our product candidates.

In addition to our own internal research, this presentation contains information related to or based on studies and other data obtained from third-party sources. 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 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.

The information in this presentation is as of the date of this presentation, and is subject to change without notice.

PsA 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

Positive Results For Izokibep Global Phase 2b/3 In PsA

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
- Expected to be the first of two registrational trials in psoriatic arthritis; 160mg Q2W appears to be optimal dose

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

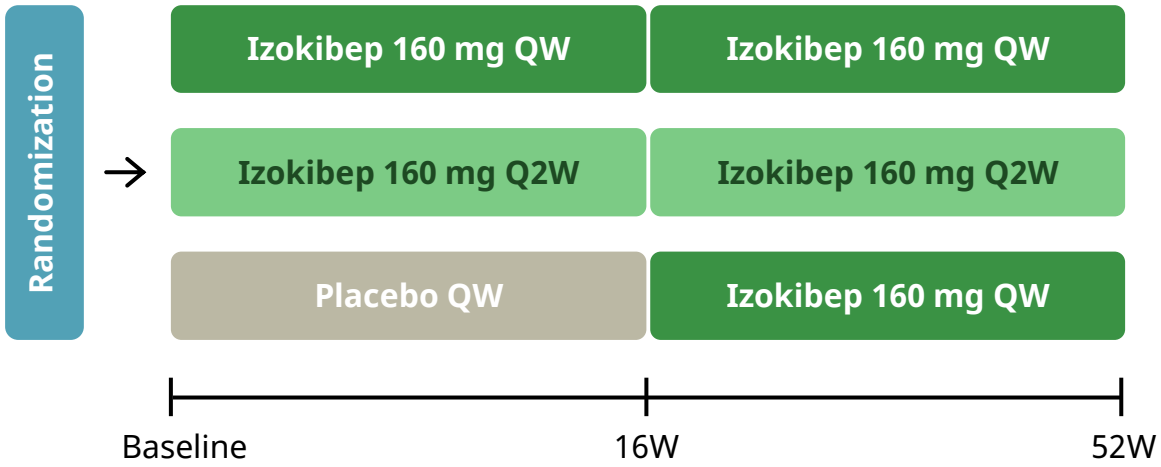
Izokibep PsA

Phase 2b/3 Evaluating Izokibep In PsA

Global Study Across 40 U.S. & 31 International Sites

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

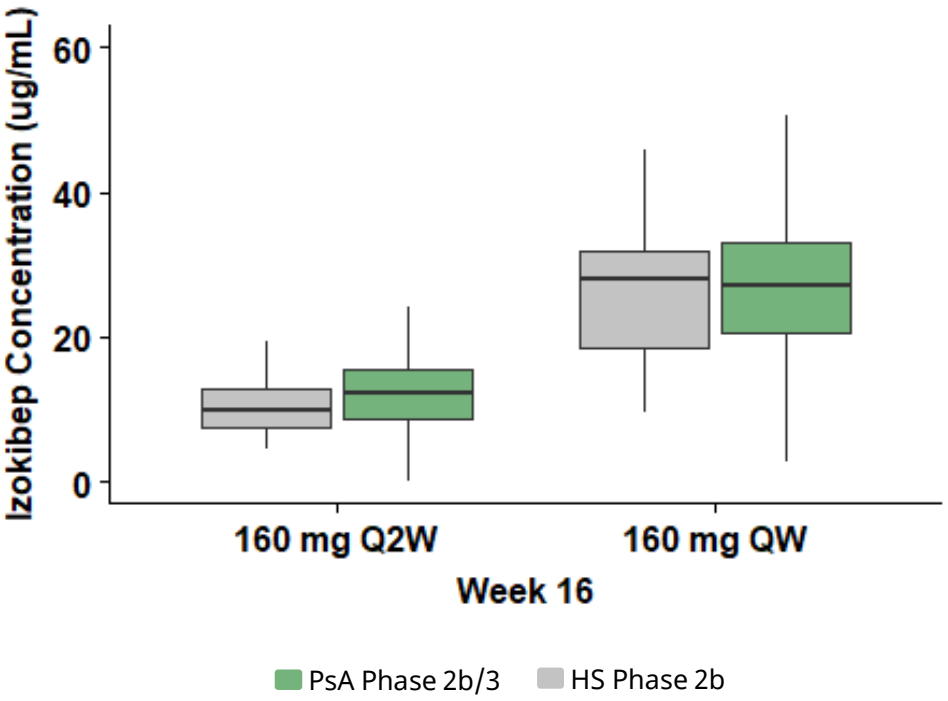
- TEAEs, events of interest, and SAEs
- Laboratory values and vital signs at collected timepoints
- Treatment-emergent ADAs

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

160mg Q2W PsA PK Exposure Comparable To 160mg Q2W HS PK

Similar PK Exposures
For PsA Ph 2b/3 Q2W and HS Ph 2b Q2W



- All patients received correct aggregate amount of drug and placebo
- PK samples collected at every visit demonstrated:
  - 160mg Q2W PsA PK Exposure Comparable to 160mg Q2W HS PK
  - 160 mg Q2W PK is much lower than 160 mg QW as expected per dose level
  - Low overlap provides confidence in interpretability

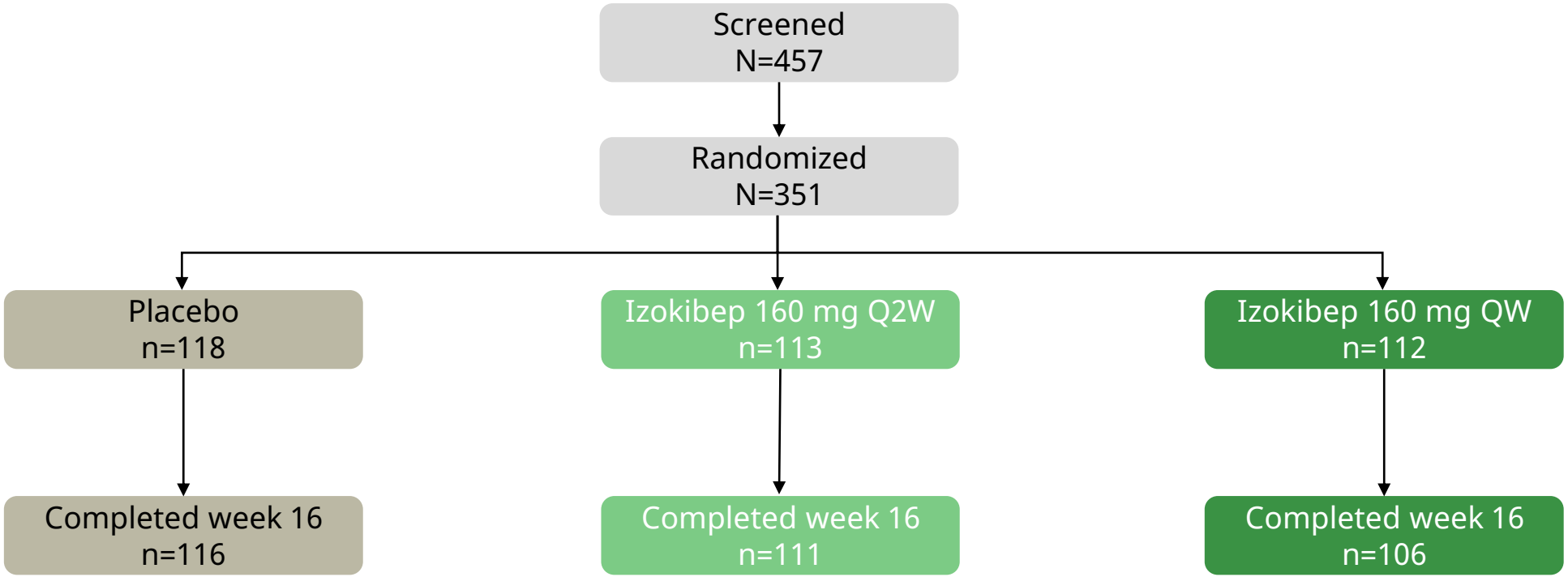
PK, pharmacokinetic; **HS**, Hidradenitis Suppurativa

Patient Demographics And Baseline Characteristics

	Placebo n=118	Izokibep 160 mg Q2W n=113	Izokibep 160 mg QW n=112
Age, mean (SD), years	52.6 (11.7)	49.5 (13.3)	51.8 (12.2)
Male, n (%)	51 (43.2)	67 (59.3)	64 (57.1)
White, n (%)	110 (93.2)	108 (95.6)	109 (97.3)
BMI, mean (SD), kg/m^2	29.7 (6.0)	30.5 (6.6)	29.1 (5.9)
PsO, n (%)	106 (89.8)	105 (92.9)	103 (92.0)
PsA duration, mean (SD), years	7.3 (7.0)	6.5 (7.0)	7.2 (8.2)
Any csDMARD, %	45.8	48.7	52.7
Prior TNFi, %	23.7	21.2	24.1
TJC/68, mean (SD)	16.4 (12.4)	16.4 (13.0)	16.8 (13.0)
SJC/66, mean (SD)	9.3 (6.9)	8.1 (5.8)	9.3 (6.9)
DAPSA, mean (SD)[b]	38.3 (18.2)	37.3 (18.1)	39.4 (17.8)
LEI enthesitis, %/LEI, mean[a] (SD)	63.6 / 2.9 (1.6)	60.2 / 2.8 (1.7)	58.9 / 2.9 (1.6)
SPARCC enthesitis, %/SPARCC, mean[a] (SD)	66.9 / 5.5 (3.7)	70.8 / 5.0 (3.9)	66.1 / 5.0 (3.9)
PsO BSA ≥3%, %/PASI, mean[a] (SD)	50.8 / 6.7 (5.6)	56.6 / 6.9 (6.5)	52.7 / 8.4 (8.8)
PsAID, mean (SD)	5.2 (2.1)	5.5 (2.0)	5.6 (1.9)
HAQ-DI, mean (SD)	1.0 (0.6)	0.9 (0.6)	1.0 (0.6)

Full analysis set. [a]Mean (SD) of subpopulation (LEI >0, SPARCC >0, PsO-BSA ≥3% at baseline).
SD, standard deviation; **BMI**, body mass index; **PsO**, psoriasis; **BSA,** body surface area; **csDMARD**, conventional synthetic disease-modifying anti-rheumatic drug; **DAPSA**, Disease Activity in PsA; **SPARCC**, Spondyloarthritis Research Consortium of Canada; PASI, **PASI90**,Psoriasis Area and Severity Index; **PsAID**, PsA Impact of Disease

Patient Disposition Through Week 16



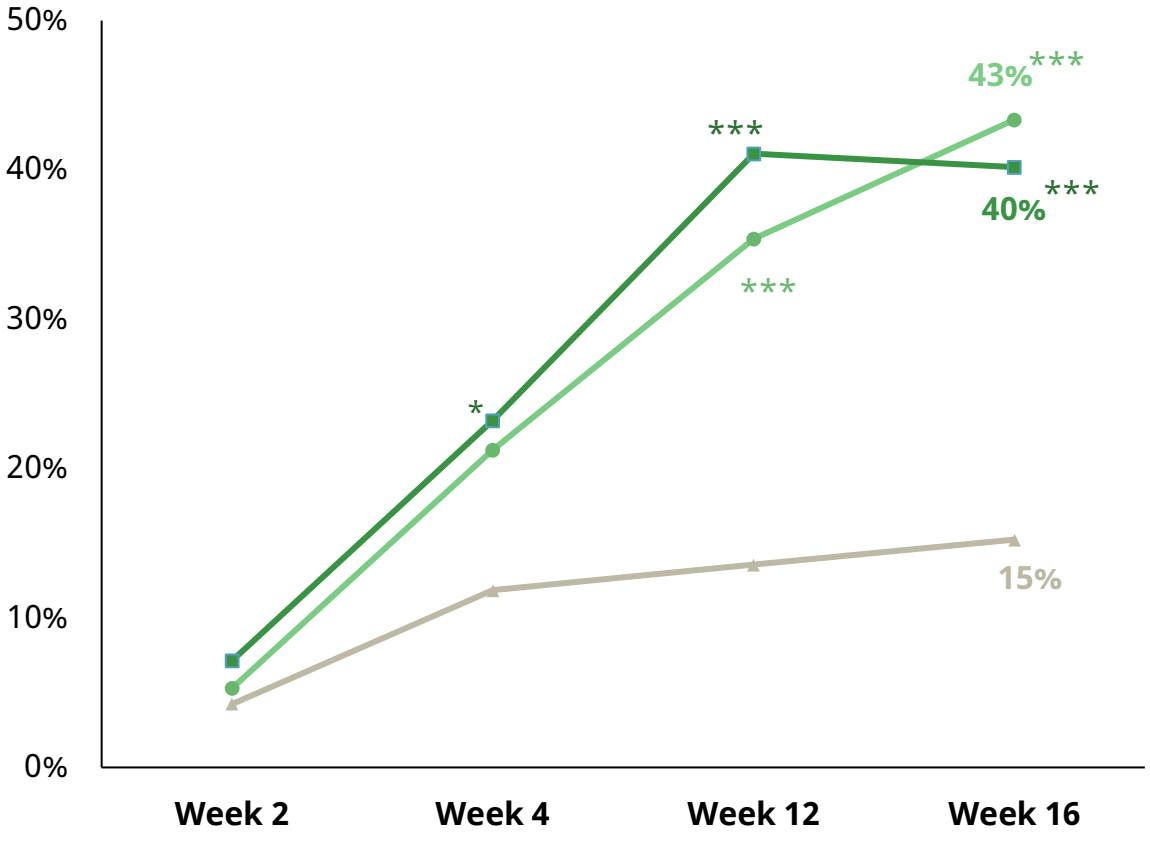
Note: A fourth trial arm evaluating izokibep at 80 mg Q4W (equivalent to ~20 mg Q2W) was also included in study design to enable dose modeling but not shown here due to small sample size, n = 8
There were two patients that discontinued treatment on the Placebo arm, two patients that discontinued treatment on the IZO 160mg Q2W arm, and six patients that discontinued treatment on the IZO 160mg QW arm.

Positive Phase 2b/3 Topline Results

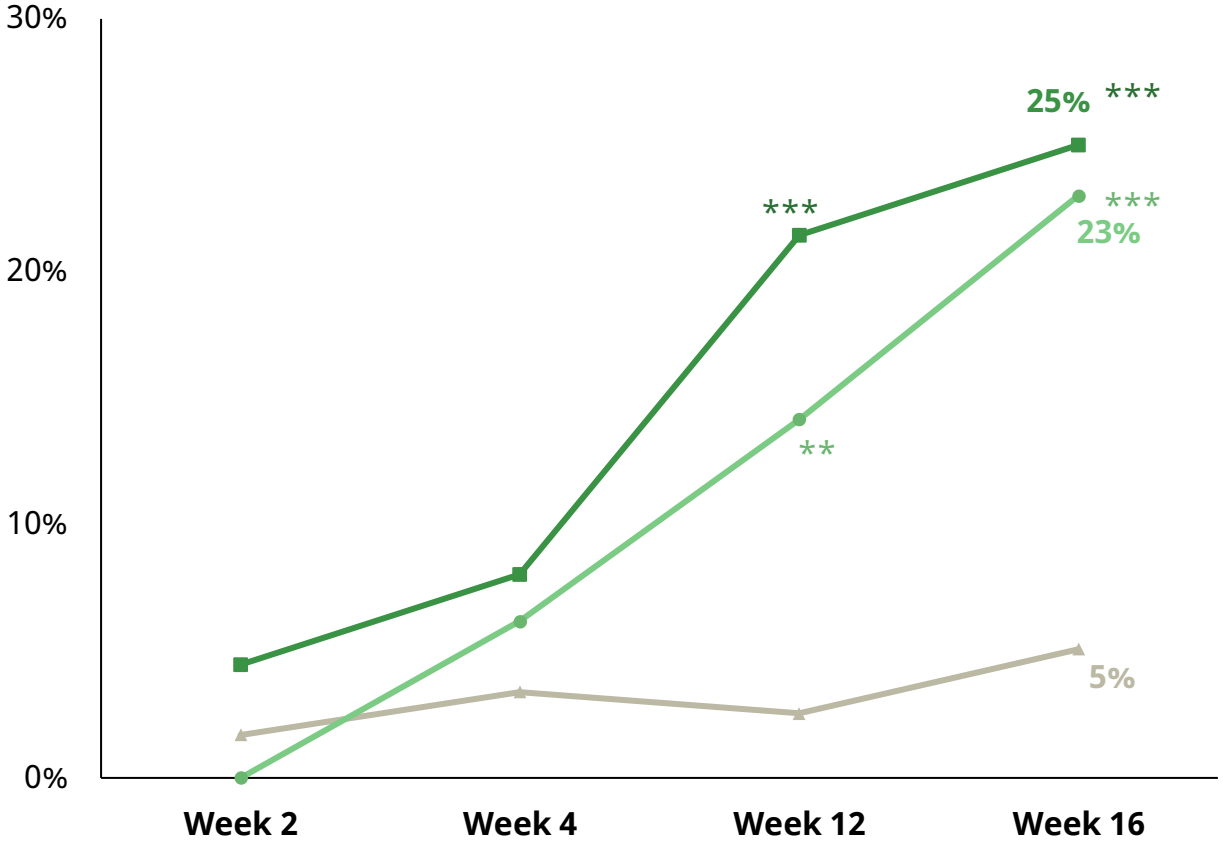
ACR50 and ACR70 at Primary Endpoint

Registrational Endpoint Of ACR50 In Joints Showed Rapid And Robust Improvement; Achievement Of ACR70 Demonstrates Even Deeper Levels Of Response

Improvement in ACR50 through Wk 16 (1)



Improvement in ACR70 through Wk 16 (1)

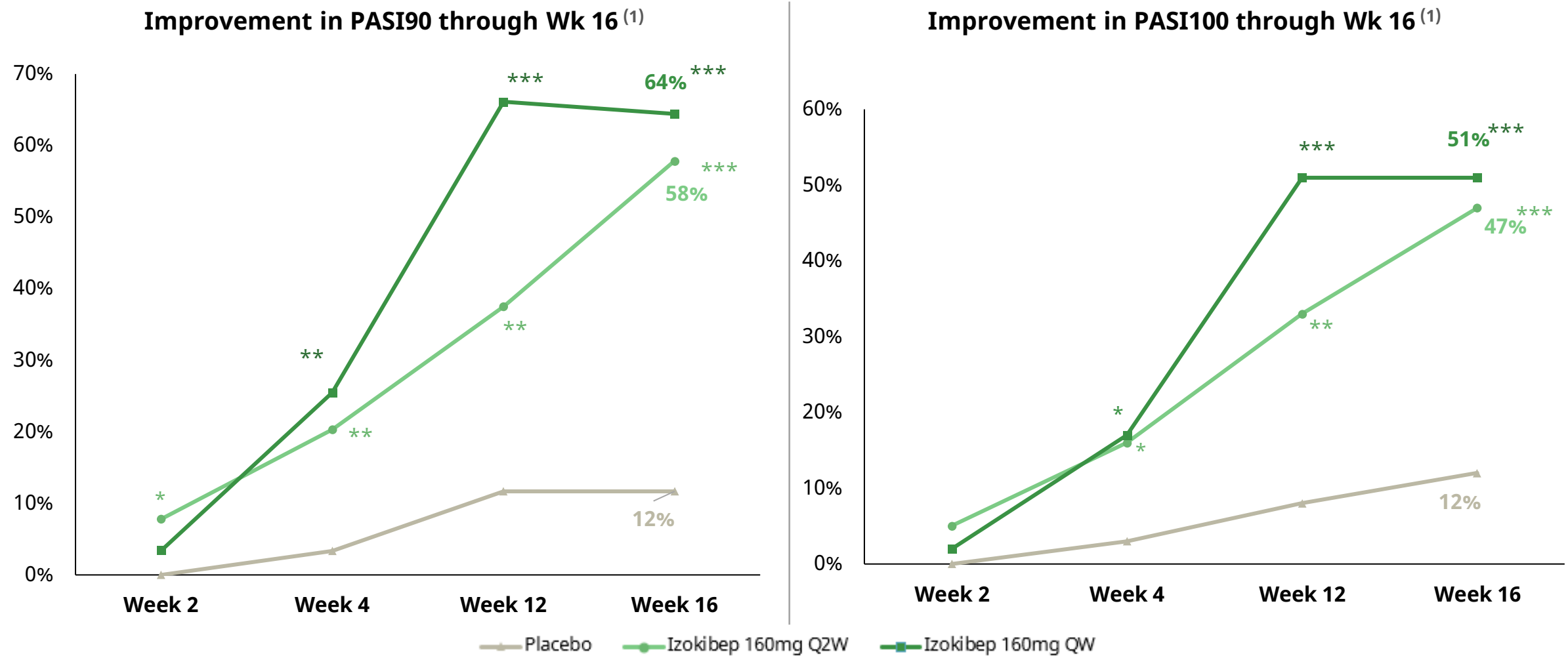


Placebo — Izokibep 160mg Q2W — Izokibep 160mg QW

(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI). *P<0.05; **P<0.01; ***P<0.0001 (stratified test of risk differences)

PASI90 and PASI100 at Primary Endpoint

Rapid and Robust Achievement of All-Clear Skin

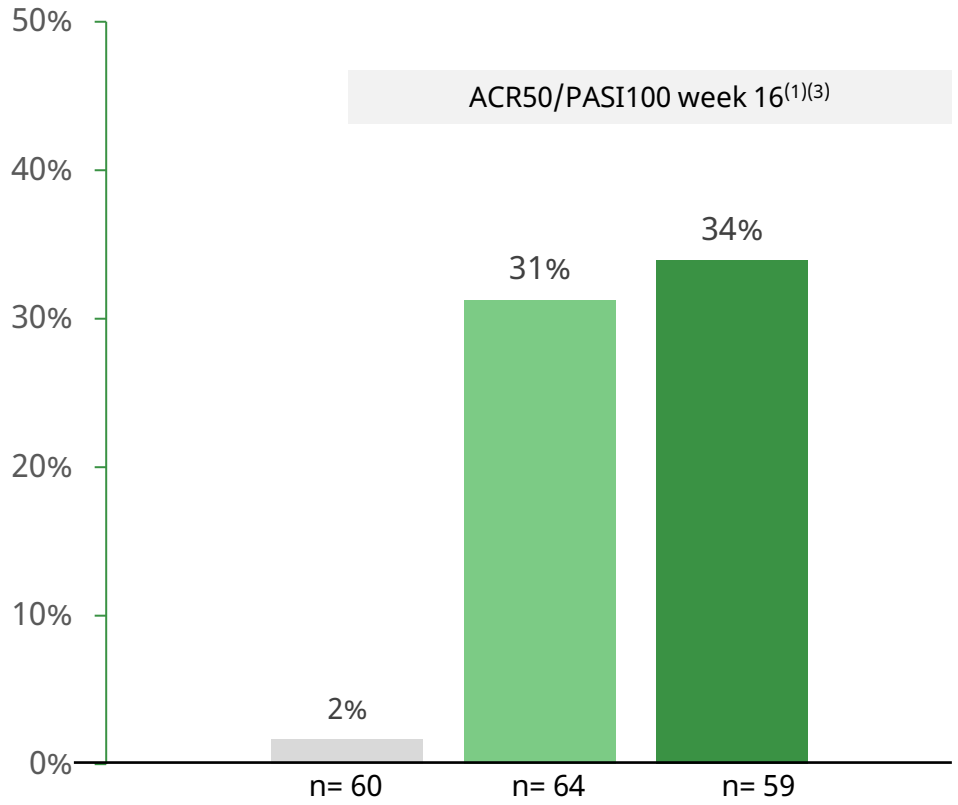


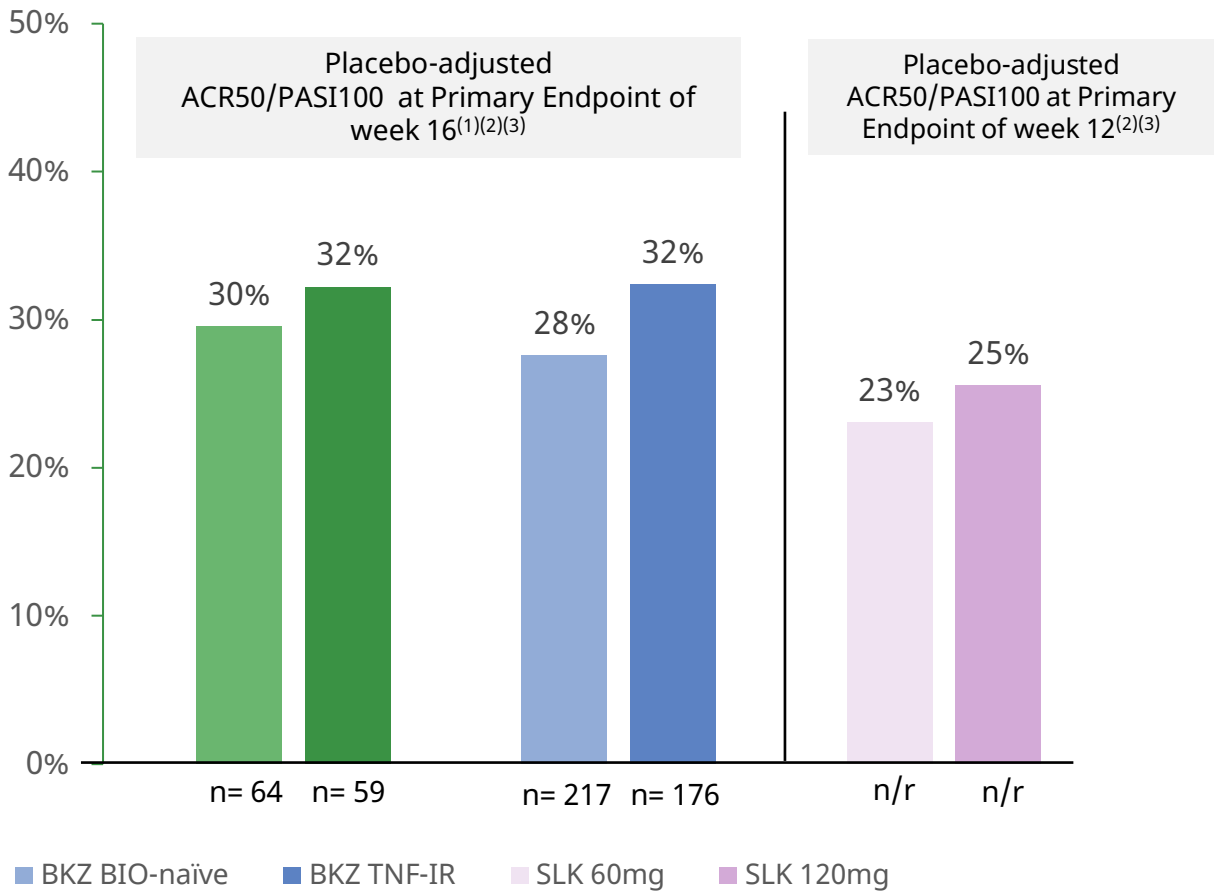
(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI). *P<0.05; **P<0.01; ***P<0.0001 (stratified test of risk differences)

Izokibep PsA

ACR50 and PASI100 Composite at Primary Endpoint

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

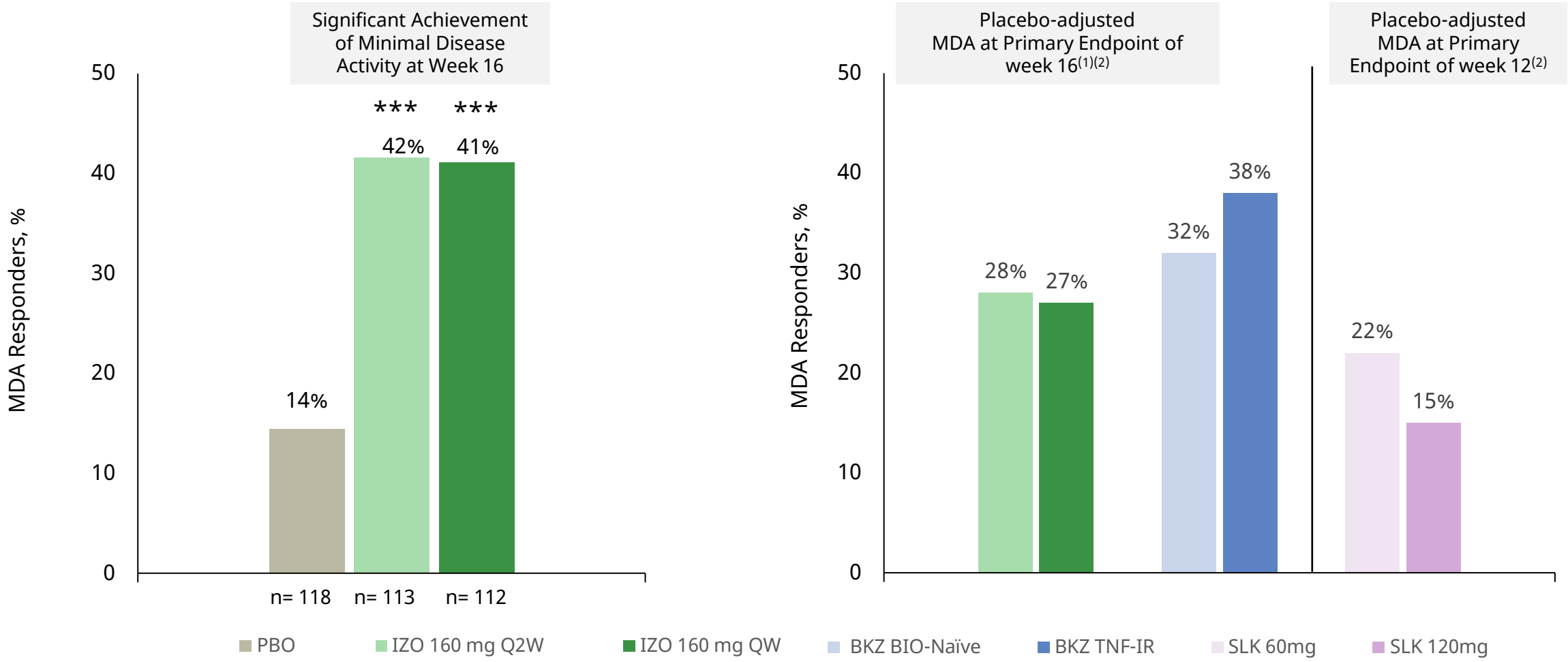




(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI).
(2) Comparisons across trials, with inherent limitations. Not head-to-head trials. Bimekizumab and Sonelokimab data from public source: Ritchlin CT, Coates LC, McInnes IB, et al. Ann Rheum Dis 2023;82:1404–1414 BE OPTIMAL; Merola et al Lancet 2023 401: 38–48 BE COMPLETE. Moonlake R&D day November 6, 2023 ARGO Part A week 12.
(3) In patients with psoriasis involving at least 3% body surface area at baseline

Minimal Disease Activity at Primary Endpoint

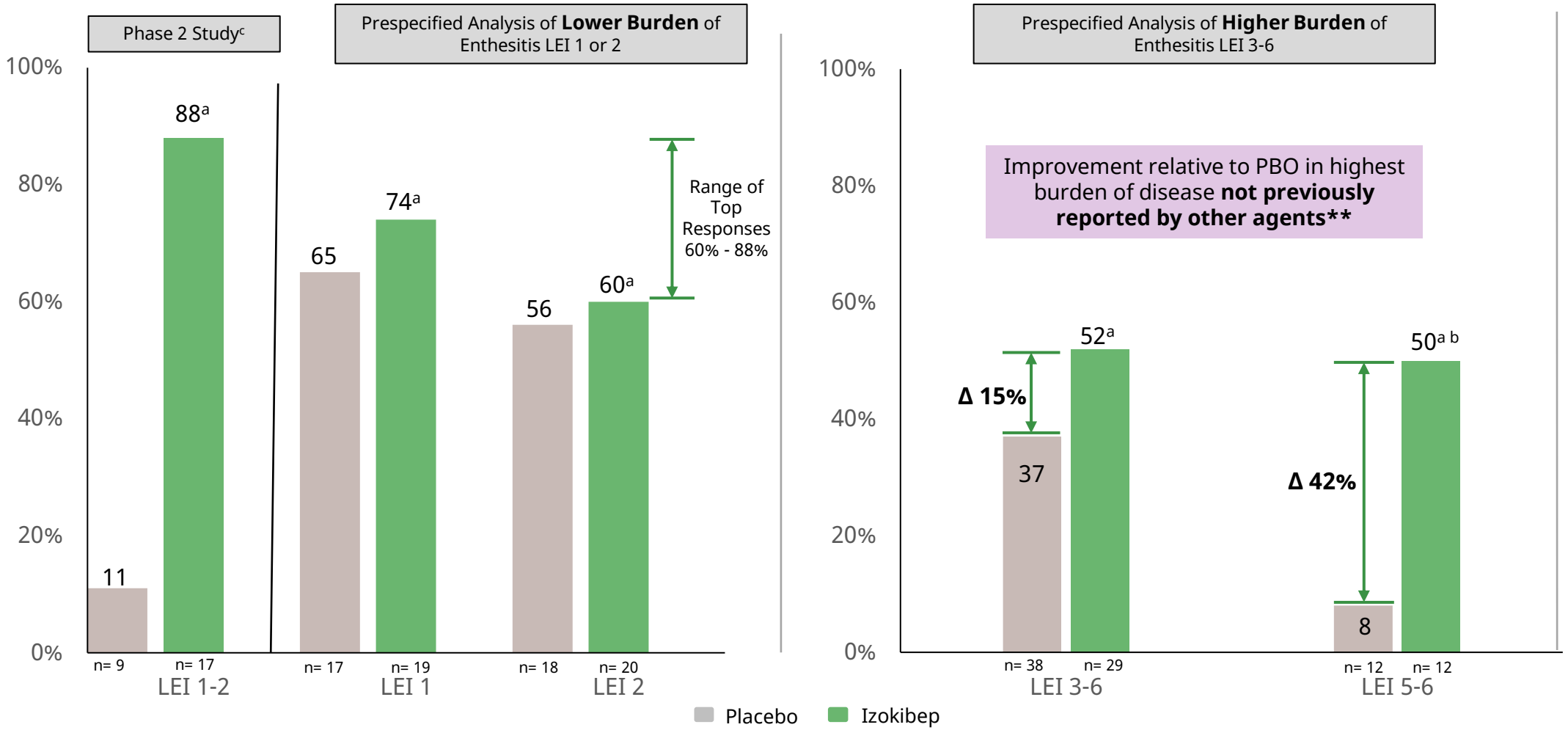
Improving The Totality of Manifestations Is The Goal for Minimizing Disease Activity for Patients



(1) Week 16 data are from the full analysis set using prespecified non-responder imputation (NRI).)***P<0.0001 (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 November 6, 2023 ARGO Part A week 12.

Izokibep Demonstrated Resolution Despite Highest Burden Of Enthesitis*

Consistent High Magnitude Enthesitis Responses In Phase 2-comparable Population Were Observed



*Enthesitis resolution overall in Phase 2b/3 was not statistically significant due to high placebo response: PBO: 47% Q2W: 56% QW: 45%. [a] Represents best responses across doses – observed data. For 2b/3 LEI 1 = 160mg Q2W, LEI 2 = 160mg QW, LEI 3-6 = 160mg Q2W, LEI 5-6 = 160mg Q2W; For 2b LEI = 80mg Q2W; [b] Post Hoc Analysis [c] LEI enthesitis resolution in LEI 1-2 at baseline, post hoc analysis, as observed data. ** 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. Note: slide includes an April 16, 2024 correction to the LEI 3-6 placebo rate.

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.

Positive Results For Izokibep Global Phase 2b/3 In PsA

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
- Expected to be the first of two registrational trials in psoriatic arthritis; 160mg Q2W appears to be optimal dose

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

ACELYRIN

Thank You

Contact

investors@acelyrin.com