PARADIGM BIOPHARMA

NWR Healthcare Conference2024

Disclaimer

This document, together with any information communicated by Paradigm Biopharmaceuticals Ltd ASX:PAR (known as “Paradigm”, “Paradigm Biopharma” or “the Company”), in any presentation or discussion relating to this document (collectively, “Information”) is confidential, and has been prepared by the Company on the condition that it is for the exclusive information and use of the recipient. The Information is proprietary to Paradigm and may not be disclosed to any third party or used for any other purpose without the prior written consent of the Company.

The Information is based upon management forecasts and reflects prevailing conditions, which are accordingly subject to change. In preparing the Information, the Company has relied upon and assumed, without independent verification, the accuracy and completeness of all information available from public sources, or which was otherwise reviewed by it. In addition, the analyses are not and do not purport to be appraisals of the assets, stock or business of the Company. Even when the Information contains a kind of appraisal, it should be considered preliminary, suitable only for the purpose described herein and should not be disclosed or otherwise used without the prior written consent of Paradigm. The Information is provided on the understanding that unanticipated events and circumstances may occur which may have significant valuation and other effects.

This Company presentation contains forward-looking statements, including statements regarding anticipated commencement dates or completions dates of preclinical or clinical trials, regulatory developments and regulatory approval.

These forward-looking statements are not guarantees or predictions of future performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this presentation. Readers are cautioned not to put undue reliance on forward-looking statements. The rate and timing of enrolment of our clinical trials and the timing of top-line results of our clinical trials should be regarded as forward-looking statements and the actual dates could differ materially from the expectations and projections set forth in Company presentations or statements especially during a pandemic.

Blockbuster market opportunity

Zilosul® aims to meet a significant unmet need in osteoarthritis.

FDA Fast Track Designation

People affected by OA in 2020[2]

150m+

People affected by OA by 2030

250m+

In the US alone, OA is predicted to increase by 86% to 67 million by 2030.[5]

Knee and Hip[3] (Global)

76%
of all OA

OA patients dissatisfied with current treatments[1]

81%

Target uptake: 10% dissatisfied market[1]

Zilosul® indicative price: US$2500 per year[4]

1. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September
2. OA Official Guidebook and 7th National Census 2020
3. Long H, Liu Q, Yin H, et al. Prevalence trends of site-specific osteoarthritis from 1990 to 2019: findings from the Global Burden of Disease Study 2019. Arthritis & Rheumatology. 2022.
4. Global Pricing Research conducted by Paradigm. EU5: Germany, UK, Spain, France, Italy
5. OARSI. Osteoarthritis: A Serious Disease, Submitted to the U.S. Food and Drug Administration December 1, 2016

Executive Summary

Paradigm Biopharmaceuticals Ltd. (PAR.ASX)

SAS – Special Access Scheme
EAP – Expanded Access Program

Established Molecule

Opportunity

Extensive Market Protection

Pentosan polysulfate sodium for subcutaneous use (PPS, iPPS,Zilosul®)

- PPS is a **non-opioid** with a 60-year track record treating pain, inflammation, and thrombosis in humans.

Osteoarthritis (OA) ZILOSUL®, high unmet need with blockbuster potential

- Extensive clinical data and Real-world evidence of iPPS effect in OA:
  - Phase 2 PARA_OA_005 (121 patients)
  - Phase 2 PARA_OA_008 (61 patients)
  - TGA special access scheme (over 600 patients)
  - US FDA approved EAP (10 ex-NFL Players).
- FDA Fast Tracked phase 3 OA program. Stage 1 completed, randomising over 600 patients across 120 sites in 7 countries.
- Opportunity for expedited approval in Australia through TGA Provisional Approval prior to the completion of the global phase 3 program.
- Recent results indicate treatment effect on OA beyond just the relief of symptoms supports iPPS as a blockbuster opportunity.
- Commercial scale manufacturing capabilities completed.

Exclusivity & market protection

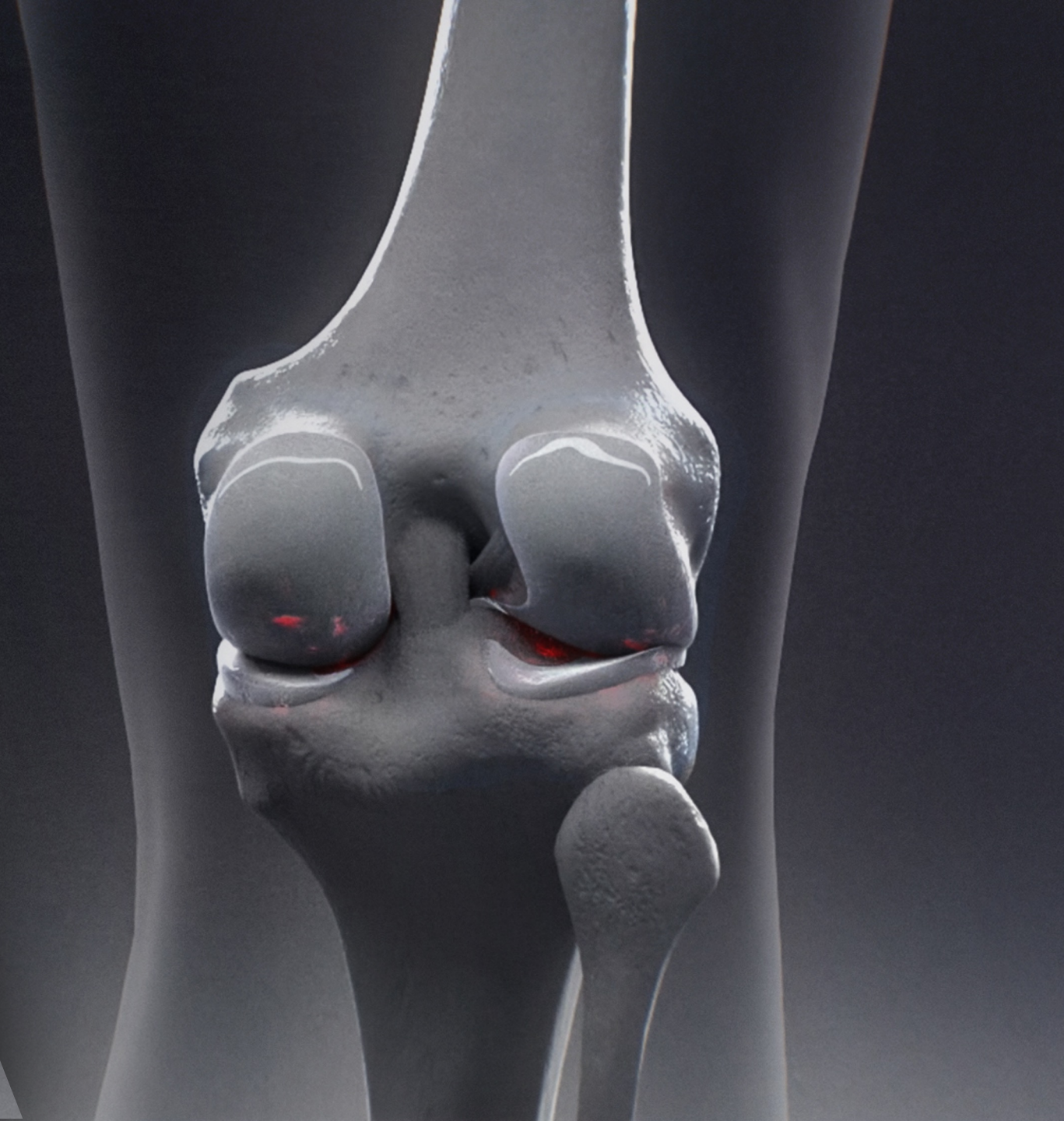
- 25-year post-marketing exclusivity with bene pharmaChem FDA-approved API manufacturer of PPS for human use.
- Complex molecular structure of iPPS provides high barrier of competitive entry.
- Additional global protection via several method of use patents.

PARADIGM

Phase 2

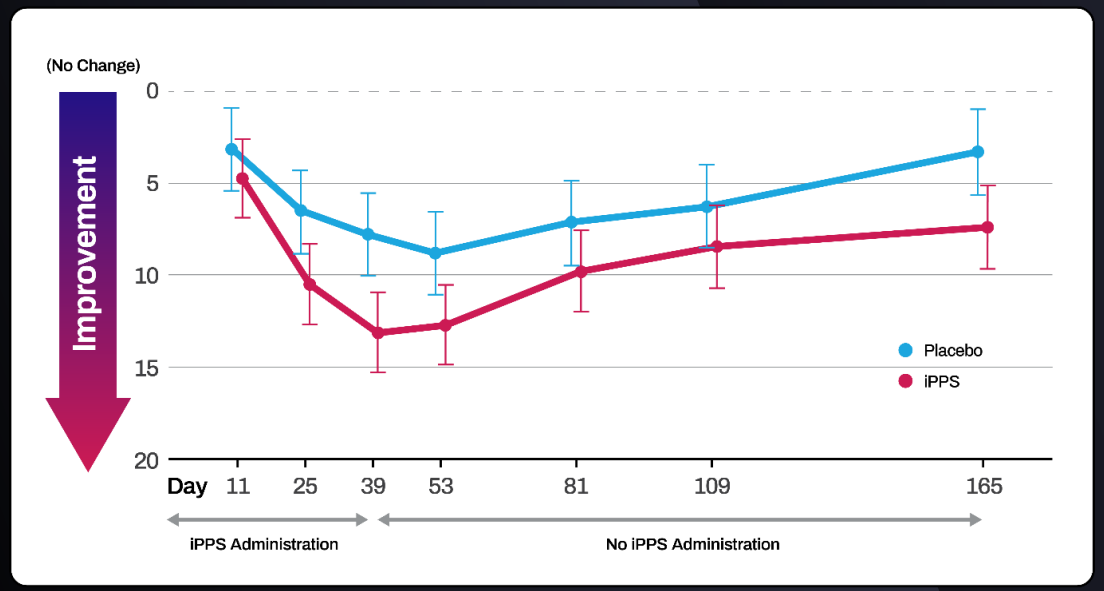
Clinical Outcome Data

OA

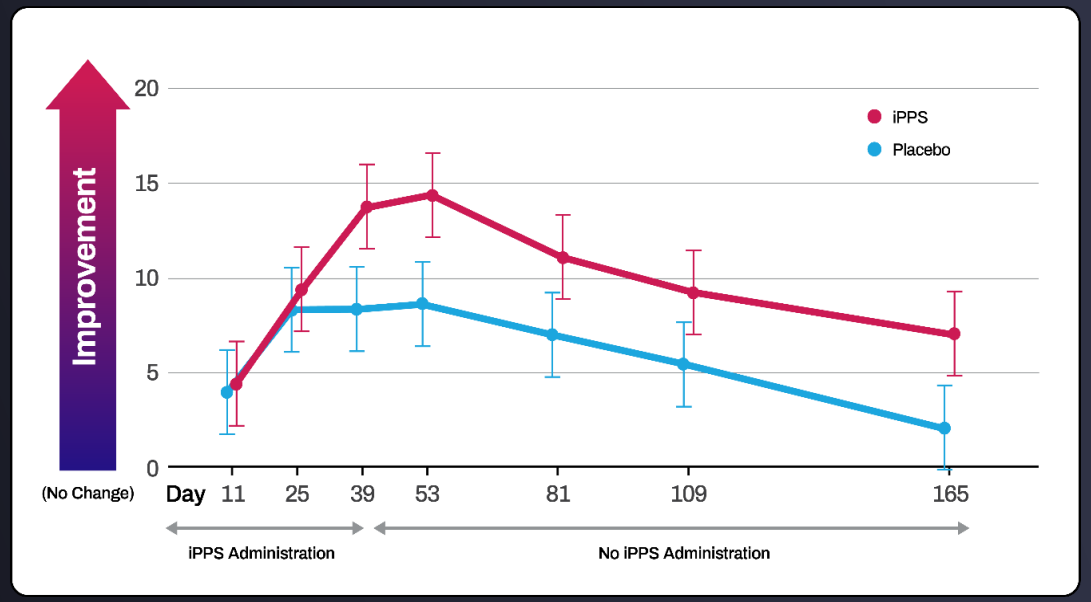


Phase 2: PARA_005 | 2 mg/kg SC twice weekly v placebo for 6 weeks, followed up for 6 months

Pain Reduction | KOOS adjusted least squares mean change from baseline. FAS.



Function ADL | KOOS adjusted least squares mean change from baseline. FAS.



LS Mean Change +/- Standard Error
FAS: Full Analysis Set
KOOS: Knee Injury and Osteoarthritis Outcome Score

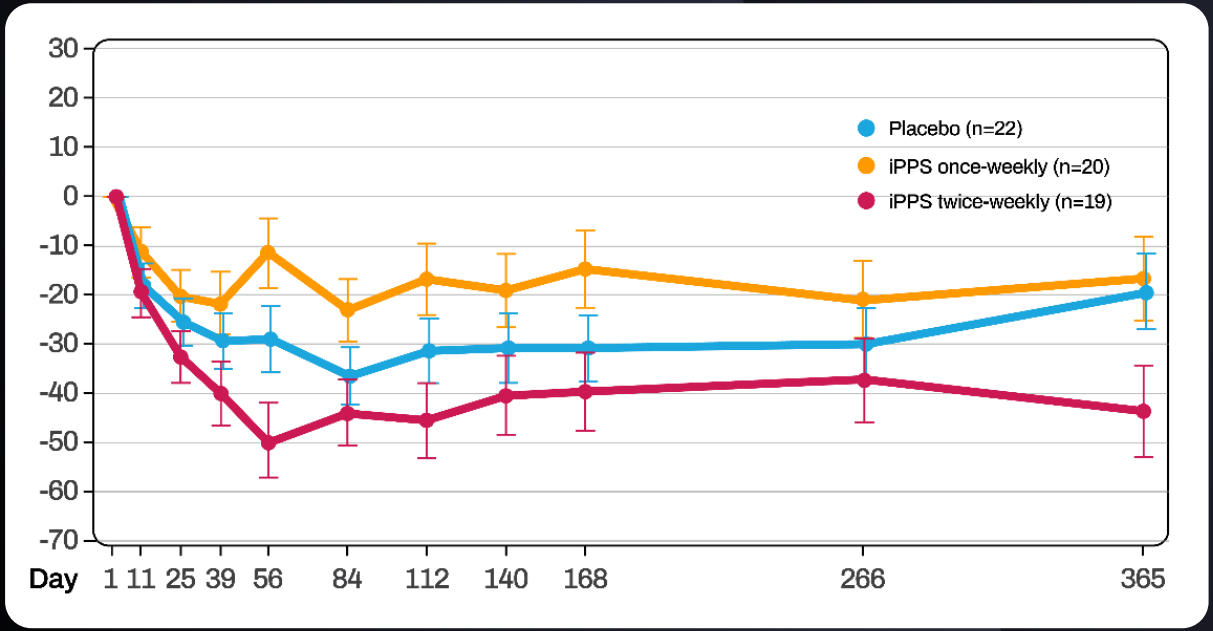
Patient Global Impression of Change (PGIC)

- PGIC significantly higher in the PPS group than placebo group at Day 56 (4.42 mean versus 3.42, respectively; mean difference between PPS and placebo 1.0 [95% CI 0.24, 1.8]; p=0.0106).

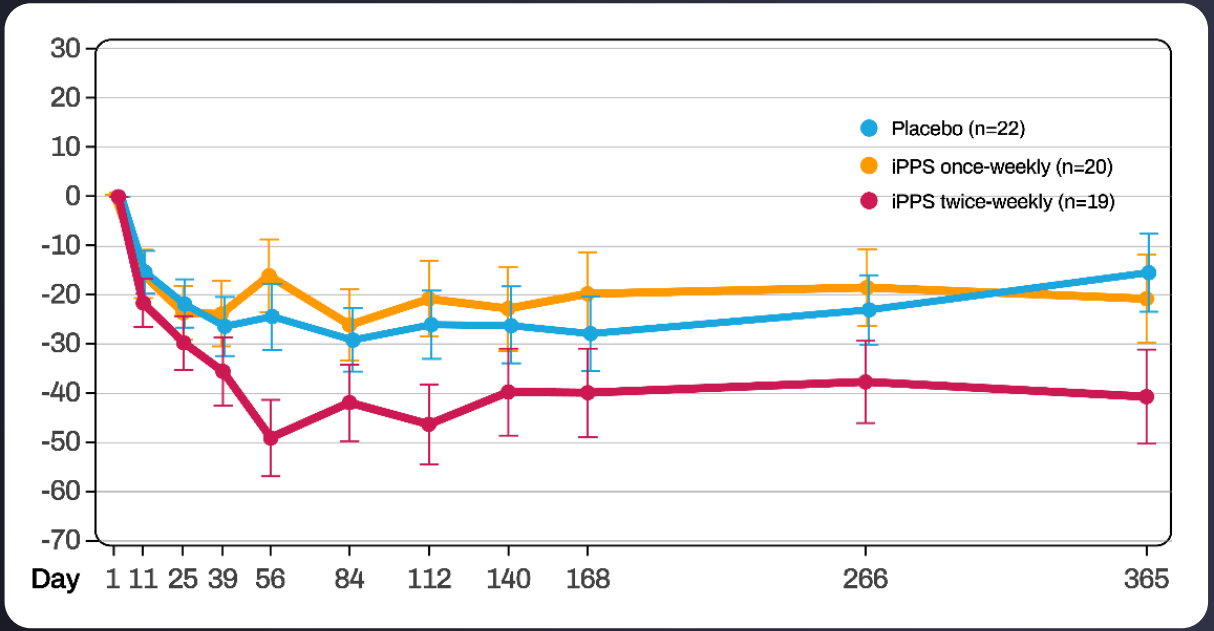
Phase 2: PARA_OA_008 | 2 mg/kg IBW SC twice weekly v placebo for 6 weeks, followed up for 12 months

A single 6-week course of twice-weekly iPPS demonstrates durable clinical outcomes out to 12 months

Pain Reduction | WOMAC least squares adjusted mean change from baseline. FAS.



Function | WOMAC least squares adjusted mean change from baseline. FAS.



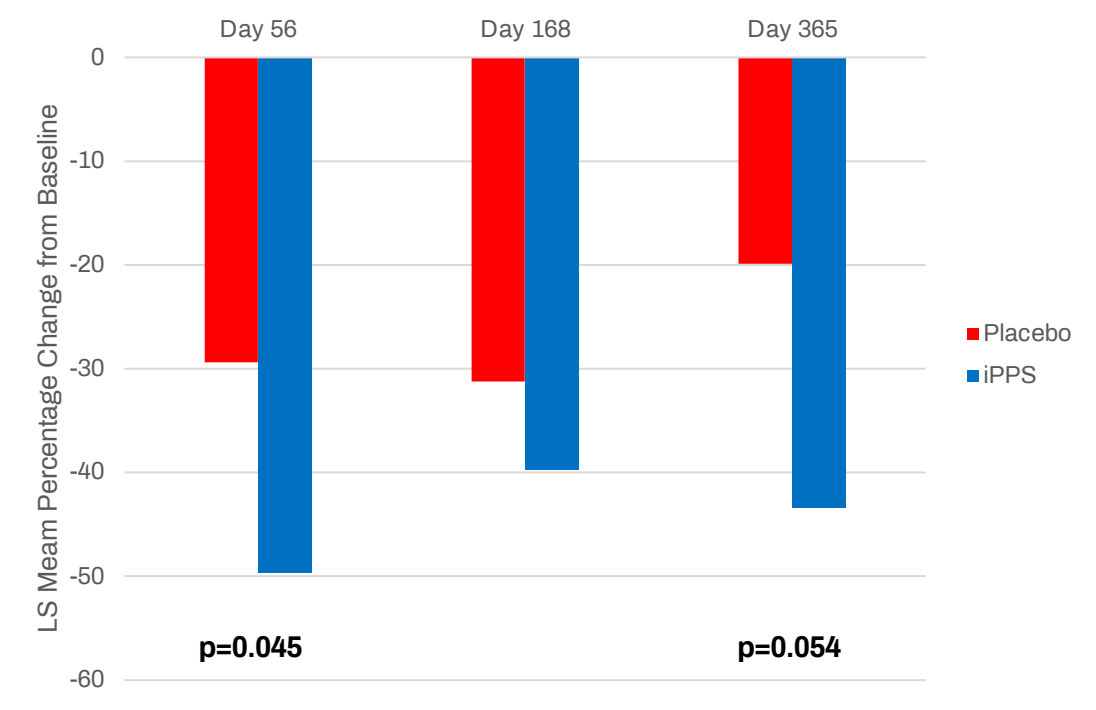
LS Mean Change +/- Standard Error
FAS: Full Analysis Set
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Rescue medication use

- 5x higher cumulative doses of rescue medication
- 4x more days rescue medication

used in the placebo cohort compared to iPPS twice weekly cohort at Day 365

PARA_OA_008 | Top-Line Clinical Endpoints at Day 365

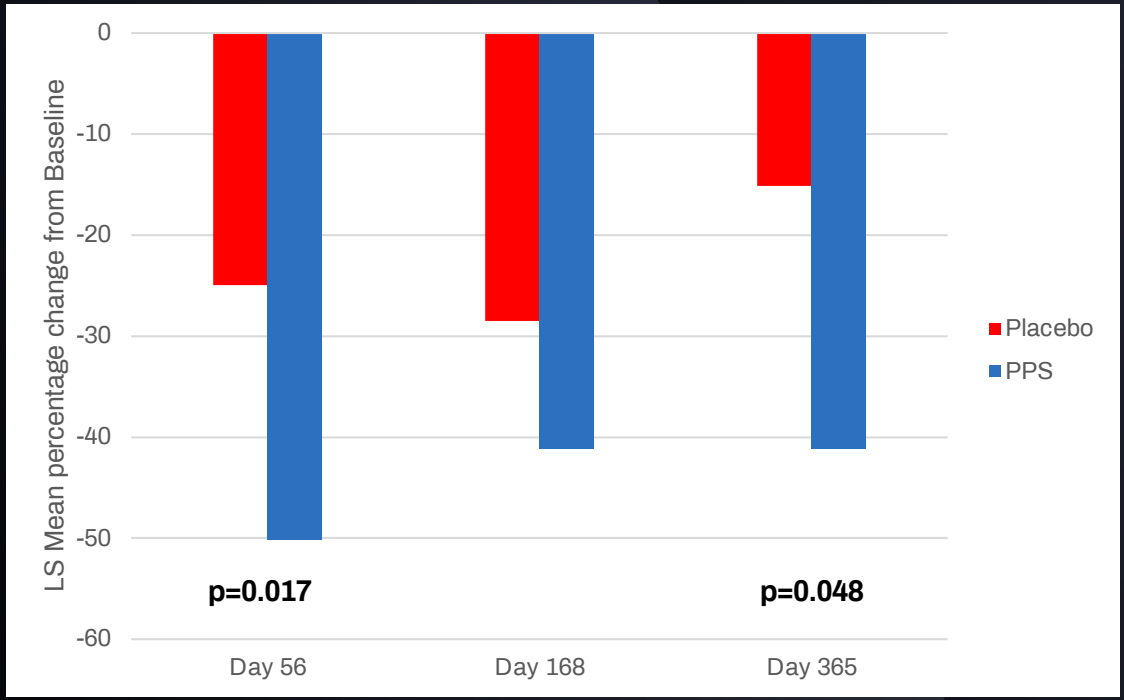


Adjusted LS mean % change in WOMAC pain from baseline at Day 56, 168, and 365 in participants treated with twice-weekly iPPS versus placebo .

Changes in WOMAC pain from baseline

- Twice-weekly iPPS treatment showed significant improvement at Day 56 (p=0.045) and Day 365 (p=0.054) in WOMAC pain compared to the placebo arm.
- iPPS treatment demonstrated clinically meaningful response to pain.
- The proportions achieving ≥30% improvement in pain in the twice-weekly group were 54.5% compared to 33.3% in the placebo group

PARA_OA_008 | Top-Line Clinical Endpoints at Day 365



Adjusted LS mean % change in WOMAC function from baseline at each visit in participants treated with twice-weekly iPPS versus placebo.

Changes in WOMAC function from baseline

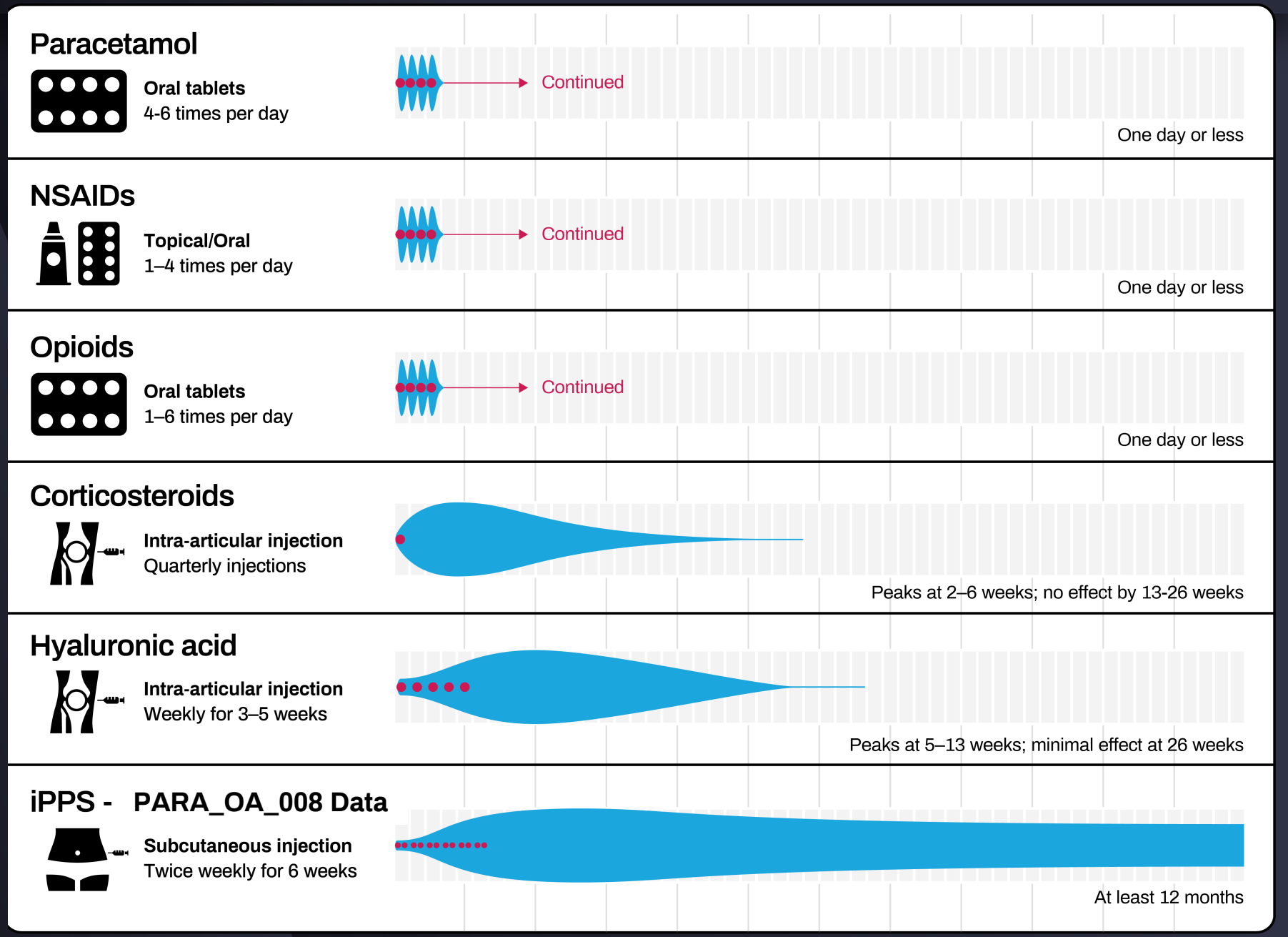
- Significant improvements in function at Day 56 (p=0.017) and Day 365 (p=0.048) in iPPS twice-weekly compared to placebo.
- iPPS treatment demonstrated clinically meaningful response to WOMAC function.
- 55% of participants receiving iPPS twice-weekly reported >50% improvement in pain compared to 28% in the placebo arm.

Current Therapies

Effect Duration

- 1 week
- Treatment
- Approximate timing & duration of peak effect

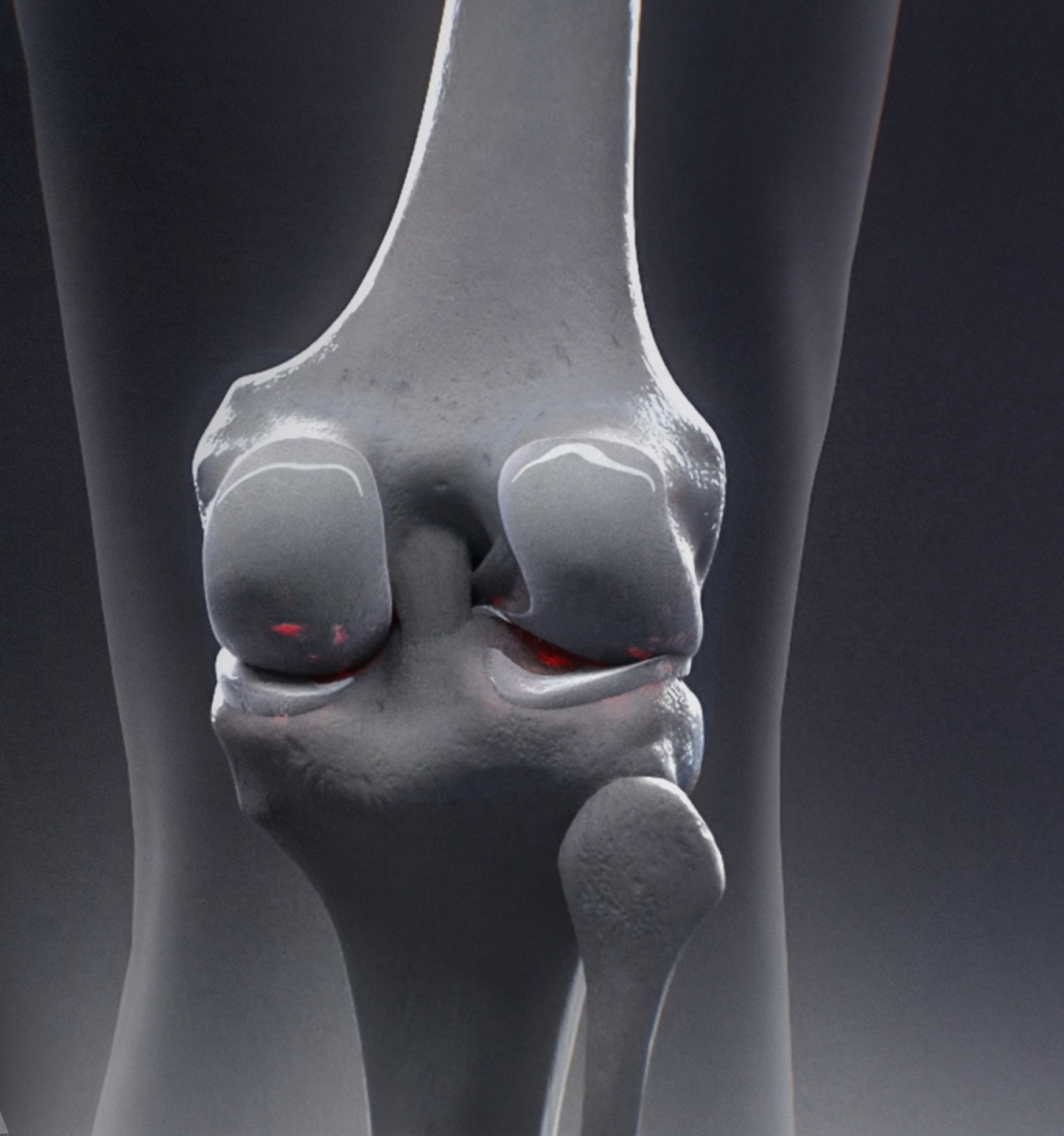
Current OA medication effect duration. Representative infographic reflecting current literature on the timing of the peak and estimated duration of treatment effect of currently available OA medications* and iPPS data from the PARA_OA_008 clinical trial. *References in Day 365 ASX release.



PARADIGM

Phase 3

OA

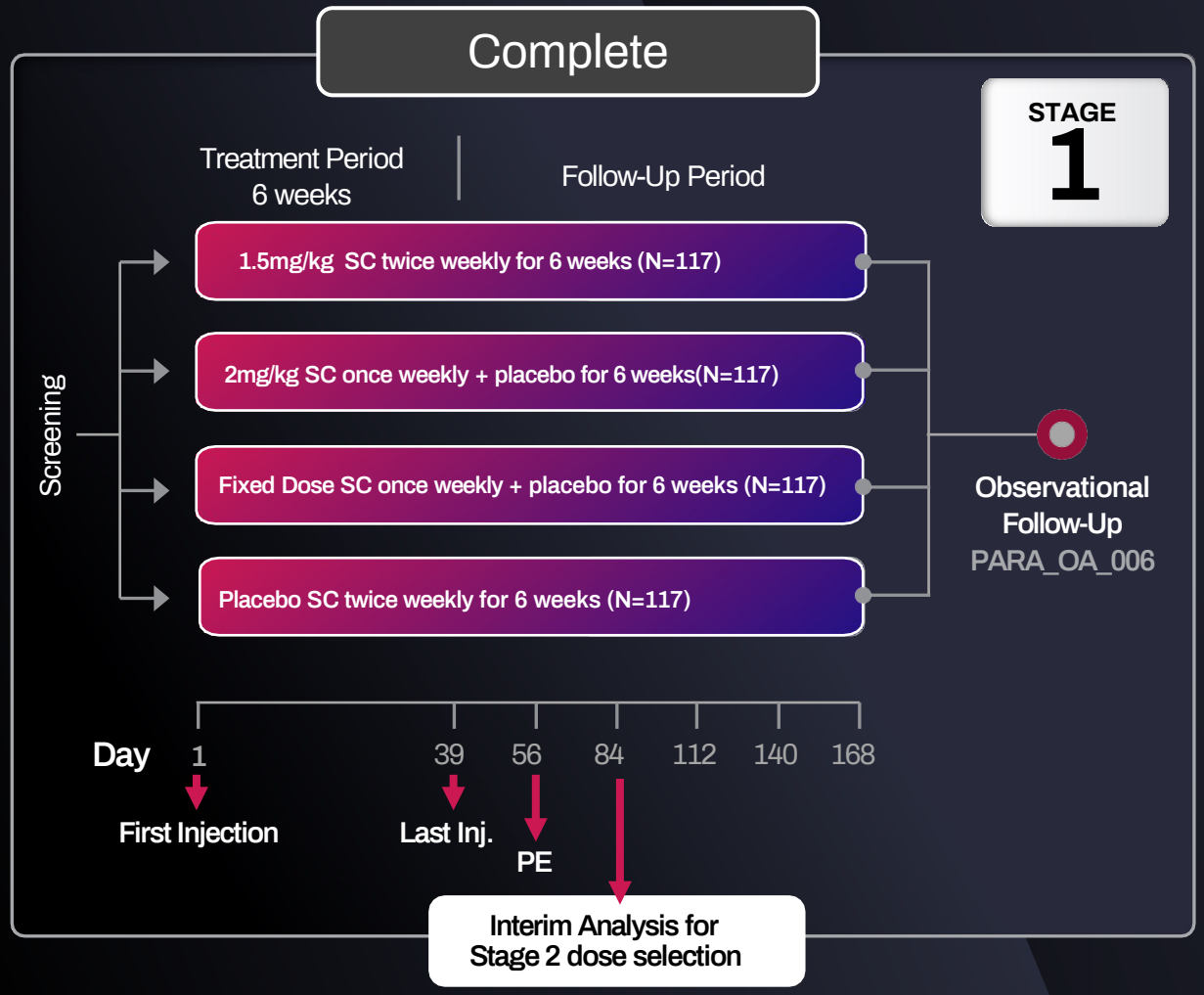


Osteoarthritis - Global Phase 3 | Harmonised clinical protocol to achieve simultaneous registration in key jurisdictions

PARA_OA_002 Global Progress

- 120+ sites across the US, EU, UK, Canada, and Australia.
- Stage 1 completed recruitment in October 2023.
- Confirmation of dose for progression to next stage of phase 3.
- Protocol for next stage of phase 3 being finalised for submission to the US FDA.

PARA_OA_002 | Phase 3 Clinical Trial Design



STAGE 2

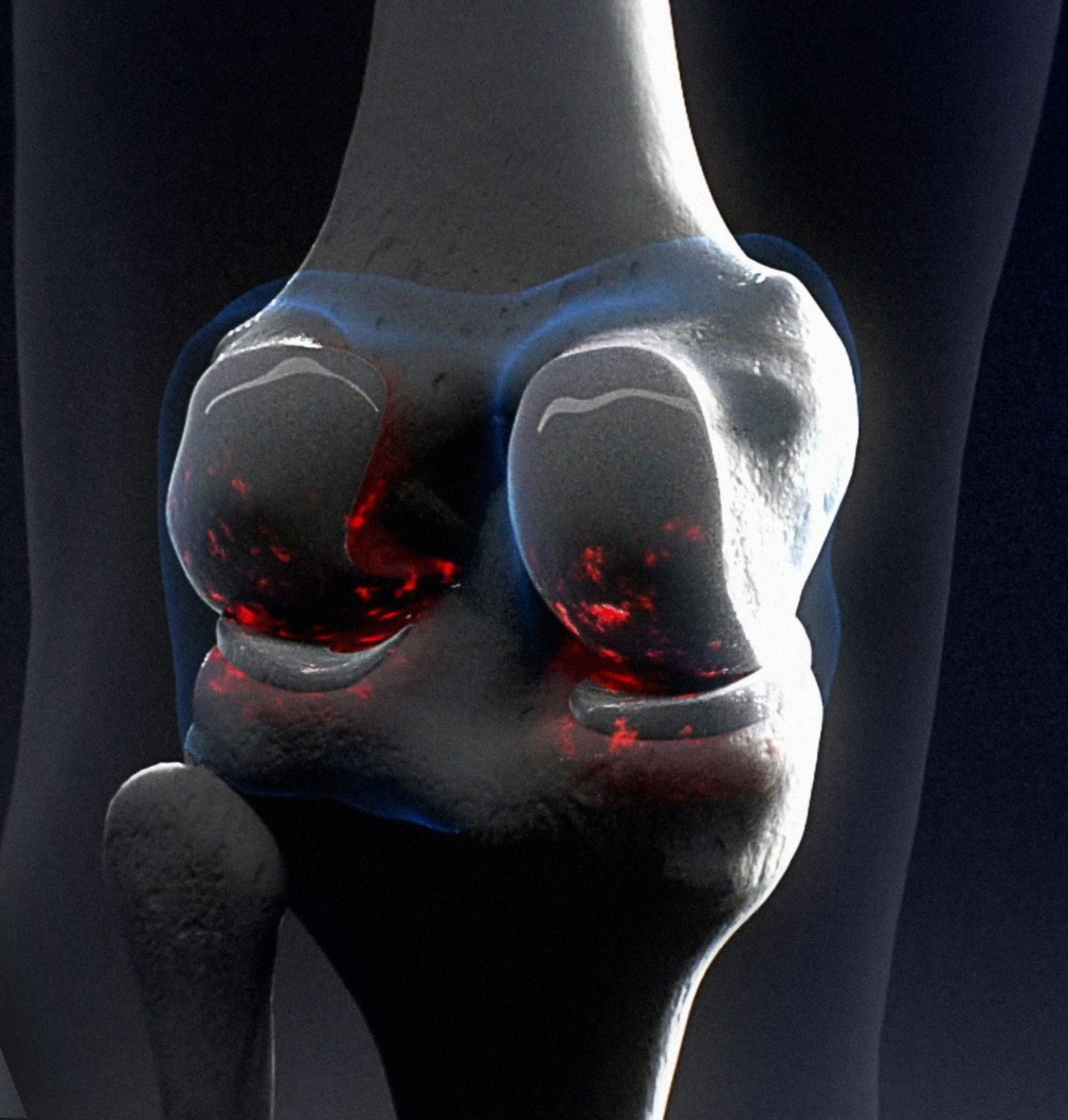
Stage 2 Clinical Protocol being finalised for submission to US FDA.

- Regulatory authorities requested identifying the minimal effective dose.
- Included a dose finding arm in the two-stage global placebo-controlled, randomised, adaptive PARA_OA_002 phase 3 trial.
- Program to proceed with dose of 2 mg/kg iPPS twice weekly for further development based on prior clinical experience and dose finding results.

NB: Approximate recruitment numbers, may be subject to change.

Top-line Results

PARA_OA_008



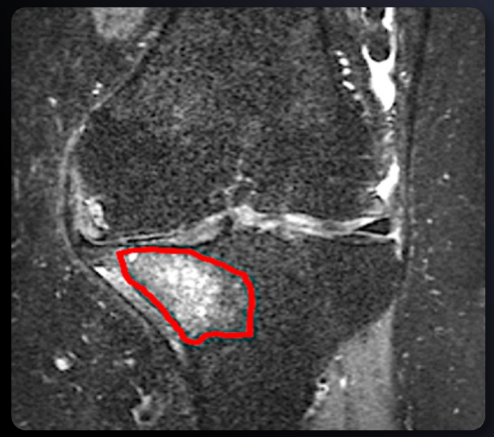
PARA_005

Exploratory Endpoints

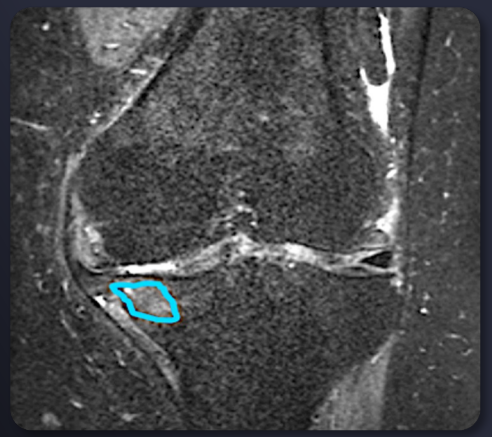
- 2 mg/kg SC twice-weekly v placebo
- PPS showed significantly reduced serum levels of cartilage degradation biomarkers and significant reduction in BML size as compared with placebo controls.

Reduction in size of bone marrow lesions

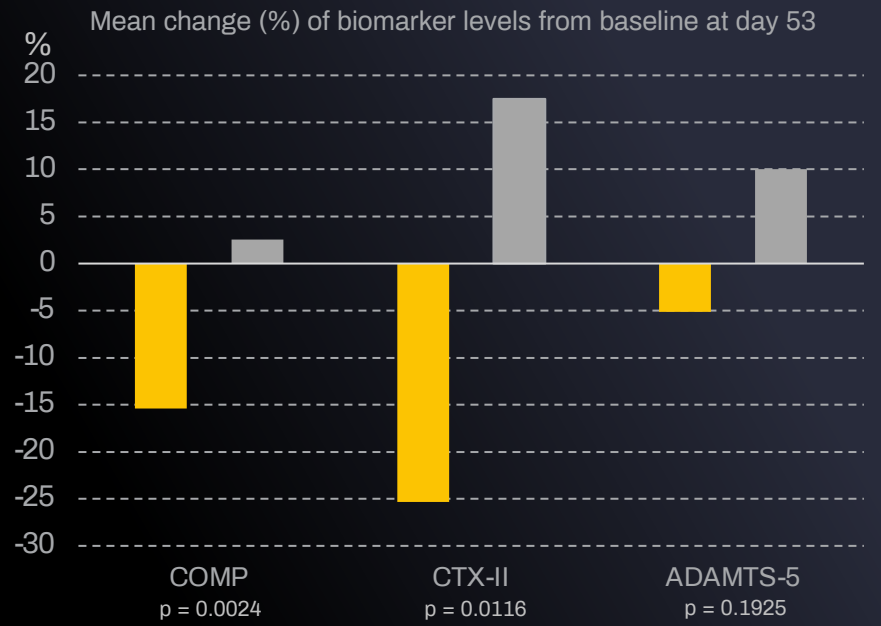
Grade 3
medial tibial BML
at baseline



Grade 2
medial tibial BML
at follow-up day 53



Reduction in serum levels of COMP & CTX-II biomarkers



Among subjects with symptomatic knee OA, **a single measurement of increased COMP predicted subsequent cartilage loss on MRI**[1]

1. Hunter DJ et al. Arthritis Res Ther. 2007;9(5):R108

Summary of Results

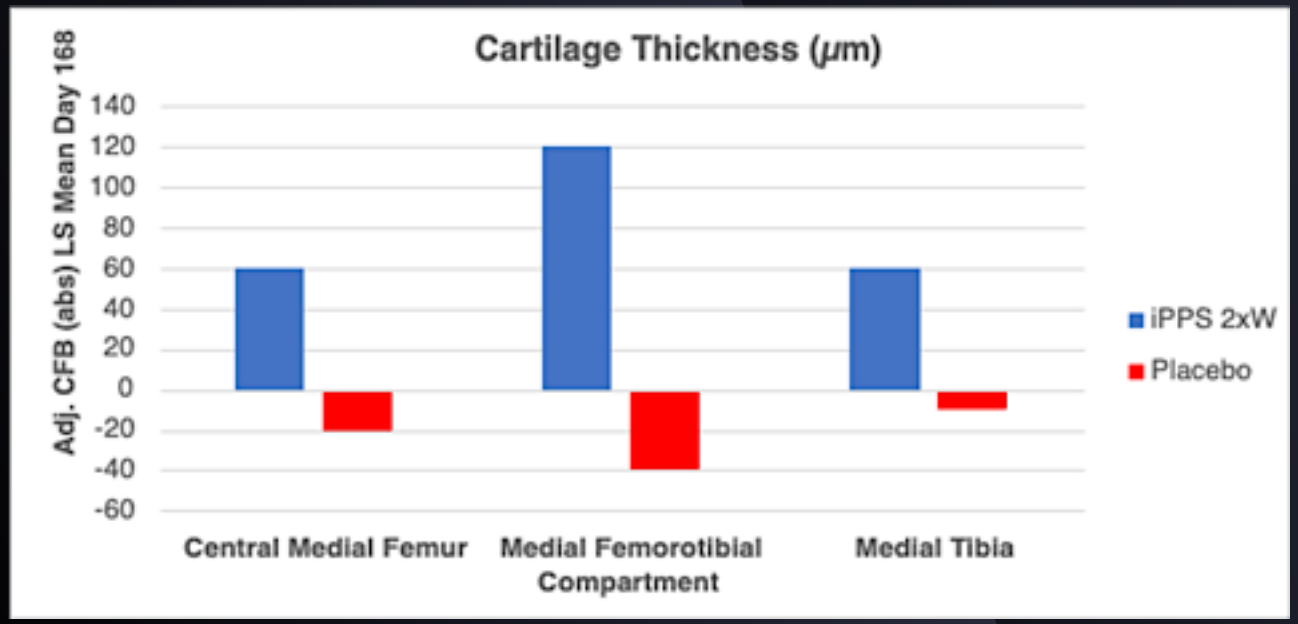
PARA_OA_008

iPPS demonstrated efficacy for both **objective** and **subjective** measures compared to placebo

Objective Data Measures	Reported At
Improvement in synovial fluid biomarkers associated with OA disease progression	Day 56 & 168
Improvement in structural changes in the knee determined by MRI	Day 168

Subjective Data Measures	Reported At
Significant improvement in mean change from baseline in WOMAC pain, function, and overall scores.	Day 56, 168 & 365
Significant improvement in Patient Global Impression of Change (PGIC)	Day 365

PARA_OA_008 | Top-Line Day 168 Quantitative MRI Results

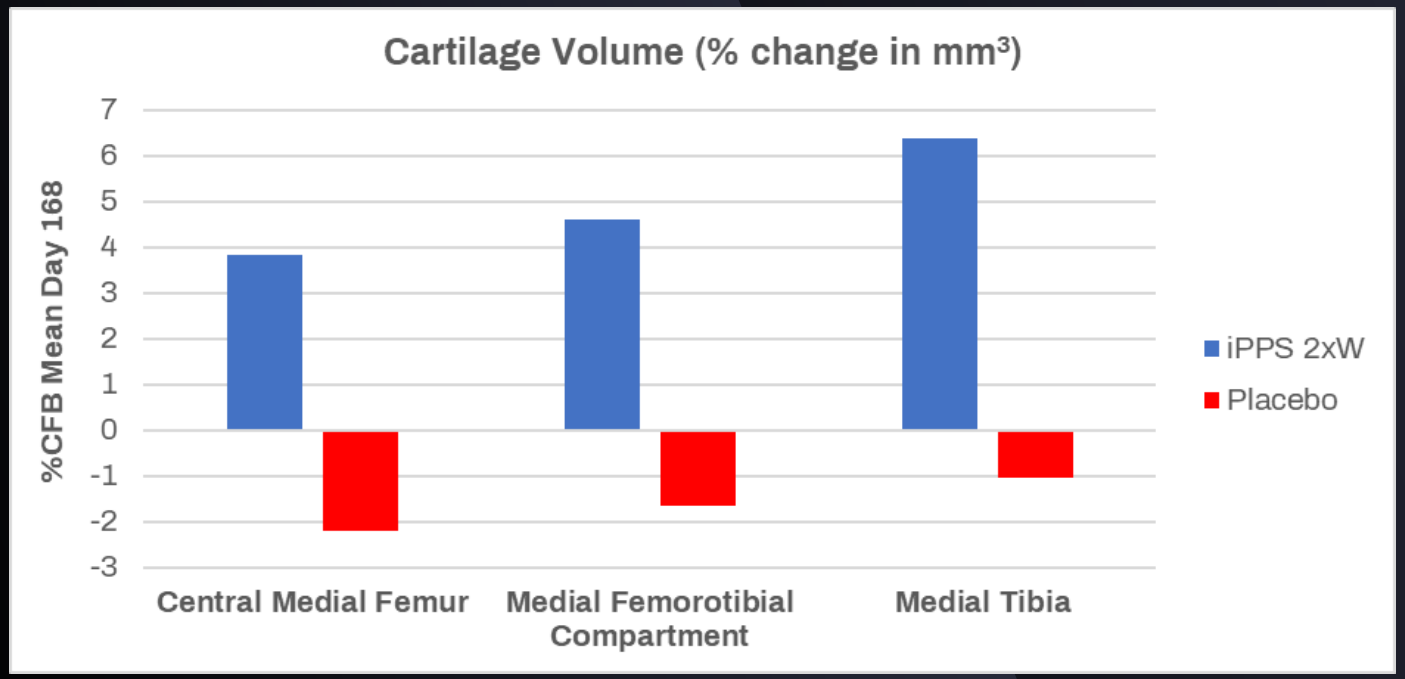


Cartilage Thickness (μm) Adj. CFB (abs.) LSM results by medial region in the knee

Changes in cartilage thickness from baseline

- Twice weekly iPPS arm, demonstrated a consistent pattern across regions of cartilage thickening over 6 months
- Placebo showed a loss in cartilage thickness in all medial compartments at 6 months.
- iPPS increased the cartilage thickness in the central medial femur by 60μm (0.06mm) compared to a reduction of -20μm (-0.02mm) in the placebo group at 6 months.
- Placebo consistent with the naturally occurring cartilage loss rate in knee OA progression (-40μm or 0.04mm per year).

PARA_OA_008 | Top-Line Day 168 Quantitative MRI Results



Average percentage (%) change from baseline (CFB) in cartilage volume (mm3) by medial region in the knee.

Changes in cartilage volume from baseline

- iPPS showed an average increase in cartilage volume of 4.6%, in the medial femorotibial compartment compared to baseline, whereas the placebo arm showed a loss of cartilage volume of -1.7%.
- iPPS is reversing the breakdown of cartilage at 6 months, compared to placebo which is showing further cartilage volume loss from baseline consistent with the natural progression of the disease (4% reduction in cartilage volume per year).

Summary

Paradigm Opportunity

Opportunity

- Extensive clinical data and real-world evidence of iPPS effect in OA.
- FDA Fast-tracked phase 3 OA program. Stage 1 completed randomising 579+ patients across 120 sites globally. Next stage of phase 3 OA program to planned commence in CY2024.
- Opportunity for expedited approval in Australia through TGA Provisional Approval prior to the completion of the global program.
- Recent results indicating a treatment effect on OA beyond the relief of symptoms supports iPPS as a blockbuster opportunity.
- Strong IP and patent protection.
- Commercial scale manufacturing capabilities completed.
- Recent data chosen for podium presentation at the OARSI International conference on OA. Demonstrates the strength and interest of Paradigm's PARA_OA_008 data amongst our peers.

Near-term News flow

Upcoming Catalysts

Event	Target Date
Phase 3 OA program – FDA protocol submission next stage of Phase 3 program.	Q1 CY2024
TGA Provisional Approval OA - submission for next stage determination application.	Q1 CY2024
Phase 3 OA program – Next stage enrollment commencement, subject to regulatory agreement.	H1 CY2024
Regional licensing agreement(s) in OA and MPS	H1 CY2024
TGA Provisional Approval OA - Dossier Submission, pending determination application approval.	Q3 CY2024
PARA_OA_008 – clinical data sets are currently being prepared for peer review and publication.	CY2024

Questions

For more information please visit:
paradigmbiopharma.com

Paul Rennie

Managing Director

Email: prennie@paradigmbiopharma.com

Simon White

Director IR

Email: swhite@paradigmbiopharma.com