PARADIGM BIOPHARMA

BELL POTTER HEALTHCARE CONFERENCE | 2024

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Executive Summary

Paradigm Biopharmaceuticals Ltd. (PAR.ASX)

Established Molecule

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

- A non-opioid with 60 years of success treating pain, inflammation, and thrombosis in humans.
- Strong clinical and real-world evidence of iPPS's effectiveness in treating OA.

Lead Program

Osteoarthritis (OA) ZILOSUL® - High potential for blockbuster treatment:

- FDA fast-tracked Phase 3 OA program.
- Achieved key goals in two Phase 2 studies, consistent with Phase 3 goals.
- 12 months of benefit from one treatment.
- Effects go beyond just OA symptom relief.

TAM

Blockbuster Market Potential:

- Broad label supports premium pricing and market reach.
- 5% market penetration of 72M+ potential customers could generate $5B in revenue.

Extensive Market Protection

Exclusivity & market protection

- 25-year exclusivity from bene pharmaChem, an FDA-approved manufacturer of PPS for human use.
- Commercial-scale manufacturing is ready.
- Global protection secured through multiple patents for use.

Development Program

Knee OA

Significant clinical data generated providing confidence of success

Over 1400 people have received iPPS

- Special Access Scheme in Australia.
- Expanded Access Program in US.
- Phase 2 clinical trials investigating iPPS versus placebo.

Completed Clinical Program

- 2018 Phase 2 PARA_OA_005.
  - AU trial, N=126, investigating pain and function.
  - Confirmed safety profile, target population and informed P3 design.
- 2021 Phase 2 PARA_OA_008.
  - AU trial, N=61, investigating how iPPS might affect OA progression with assessment by knee fluid and blood samples, X-ray & MRI, and durability of pain and functional improvement to 1-year.
- 2021 Phase 2b PARA_OA_002.
  - Global trial, N=602. Dose confirmation, efficacy and safety.
  - Dosing confirmed for continuation to phase 3 PARA_OA_012 study.

Development Program

Knee OA

Consistent data across Phase 2 clinical program.

Objective: Evaluate the efficacy, durability, and minimum effective dose of iPPS for knee osteoarthritis (OA) pain and function improvement.

Phase 2 Clinical Trial Summaries

PARA_005 Trial:

- iPPS demonstrated a 37.2% pain reduction vs. 23.1% in placebo at Day 53 (KOOS score).
- Durable pain and function improvement up to Day 165.

PARA_OA_008 Trial:

- iPPS showed a 50% reduction in WOMAC pain score vs. 30% in placebo at Day 56.
- Statistically significant improvements in pain and function observed up to Day 365.
- Structural improvements observed via MRI at 6-months.

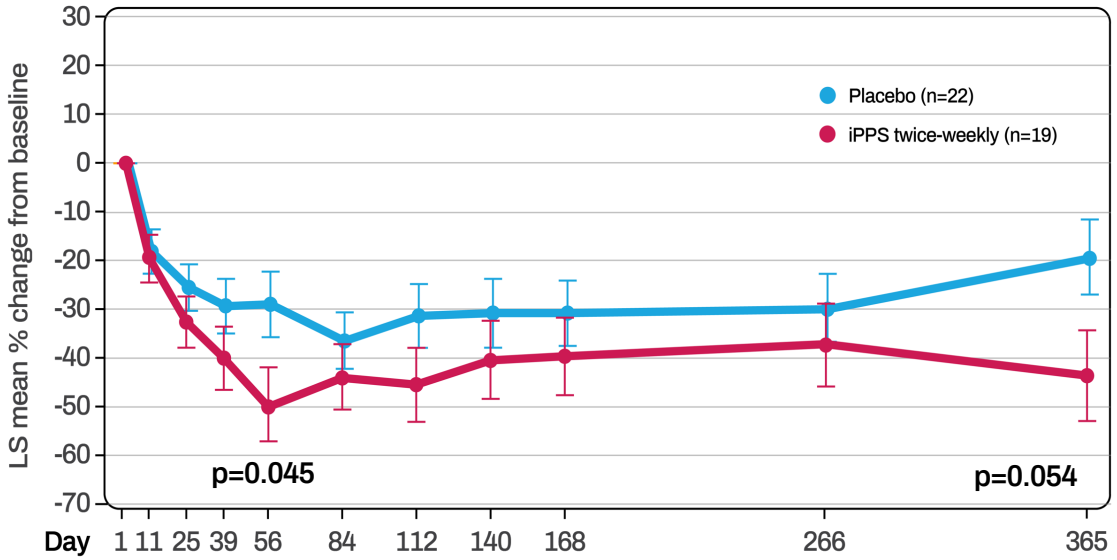
PARA_OA_002 Trial:

- Stage 1 of Phase 3 program evaluating lower doses of iPPS.
- Lower doses did not meet the efficacy of the 2 mg/kg twice-weekly regimen.
- Similar safety profile observed across all dosing levels.

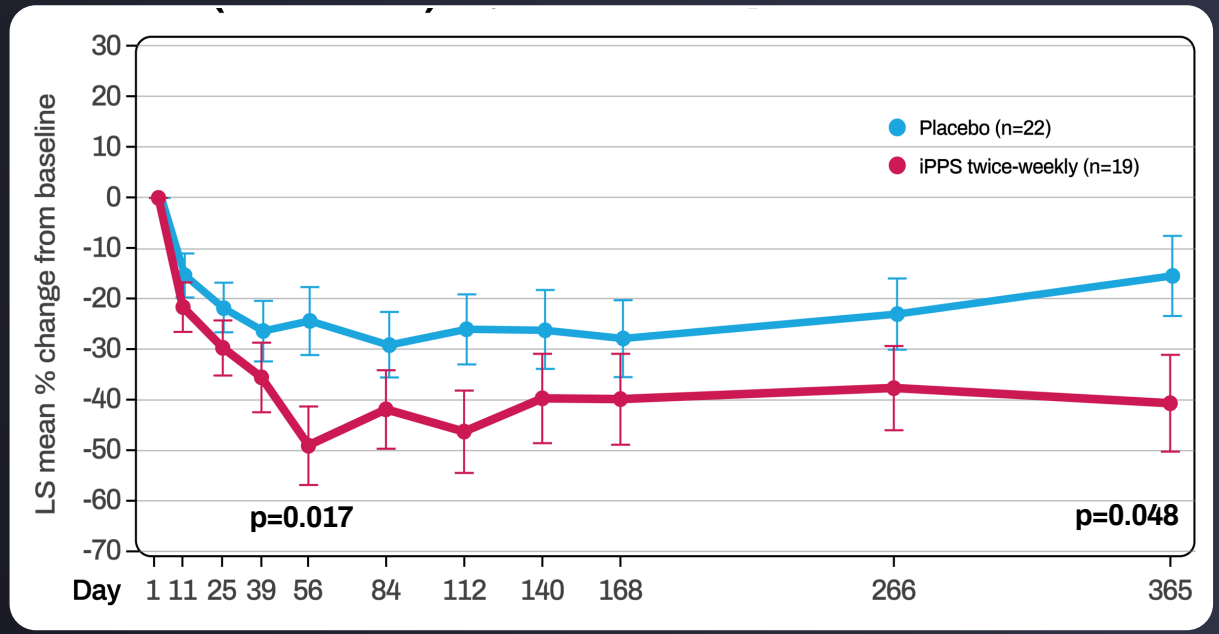
Phase 2: PARA_OA_008 | 2 mg/kg IBW SC twice weekly v placebo for 6 weeks, followed up for 12 months (n=61)

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.

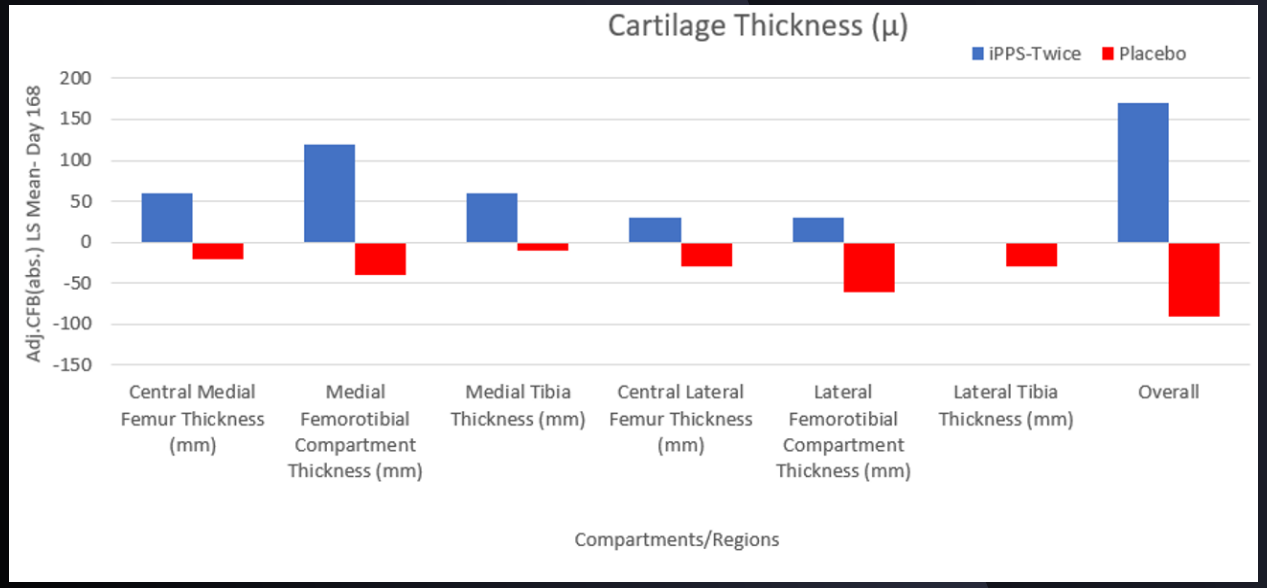


Rescue medication use

- 5x lower cumulative use of rescue medication in iPPS group.

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

PARA_OA_008 | Top-Line Day 168 Quantitative MRI Results



Cartilage Thickness (µm) Adj. CFB (abs.) LSM results by key regions of the medial and lateral compartments in knee

Changes in Cartilage Thickness from baseline

- Twice weekly iPPS arm, demonstrated a consistent pattern of improvement in cartilage thickness across all key regions of medial and lateral compartments at 6 months
- Placebo showed a loss in cartilage thickness in all key regions 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 group demonstrated cartilage loss rate consistent with the natural progression of knee OA (-40µm or 0.04mm per year).

Real World Evidence

iPPS use in Aus through Special Access

	Andrew Walker AFL	*"I was a 10/10 pain in my knee and had trouble with simple daily tasks which lead to my retirement from AFL. Following iPPS I am back to a 1 or 2 pain and am back playing local league football"*
	Rebecca Cole Basketball	*"Not being in pain everyday has been life changing"*
	Liffort Hobley NFL	*"I stopped running due to my doctor telling me I was bone on bone in my knee. Following the treatment, I could probably run 2-3 miles today".*
	Marc Murphy AFL	*"I have gone from taking medication and having my knee drained weekly to functioning normally again."*

TGA Special Access Scheme

- iPPS has been available via the TGA Special Access Scheme since 2016.
- Prescribing Doctors able to treat patients who have failed available medications.
- To date 600+ Australians have received Paradigm's Zilosul® (iPPS) via TGA approved Special Access.
- Significant previous publicity with elite athletes utilising iPPS.

Lead Program Osteoarthritis

Global Phase 3 Progress

FDA Progress to Phase 3

January

- Type D meeting with US FDA to discuss stage 1 PARA_OA_002 results and optimal dose to progress development program.

April

- Submission of key documents to the US FDA in April 2024, for review and agreement on the progression of the Phase 3 clinical program for osteoarthritis utilising the optimal dose.
- Response includes the results of five nonclinical studies, data from the successful Phase 2 clinical trial, PARA_OA_008, and clinical data from 600 participants dosed in stage 1 of PARA_OA_002.
- Submitted a draft of the Phase 3 pivotal clinical trial protocol for agency review and comment

September

- Response received from US FDA for progression of phase 3 knee OA program.

Summary of FDA Feedback

Phase 3 PARA_OA_012

FDA Type D Meeting Response

- Positive feedback and recommendations from the Agency with key feedback items:
  - Acceptability of 2mg/kg dose regimen.
  - Reduction to safety monitoring and mitigation compared to prior stage.
  - Recommendations on statistical analysis for P3 study and the timing of planned assessments.
- Agreement to proceed with final submission of the protocol to the IND when suggested changes have been implemented.
- Protocol amendment completed and filed with the Agency on 29th October 2024.

Designed for Trial and Label Success

Pivotal Phase 3 PARA_OA_012

Phase 3 PARA_OA_012 Clinical Program: Key Details

Program Focus

- De-risked, efficient program with high probability of success.

Primary Endpoint

- Change from baseline in pain.

Key Secondary Endpoints

- Pain and function assessments (change from baseline) up to Day 404.
- Patient Global Impression of Change (PGIC) .

Regulatory Alignment

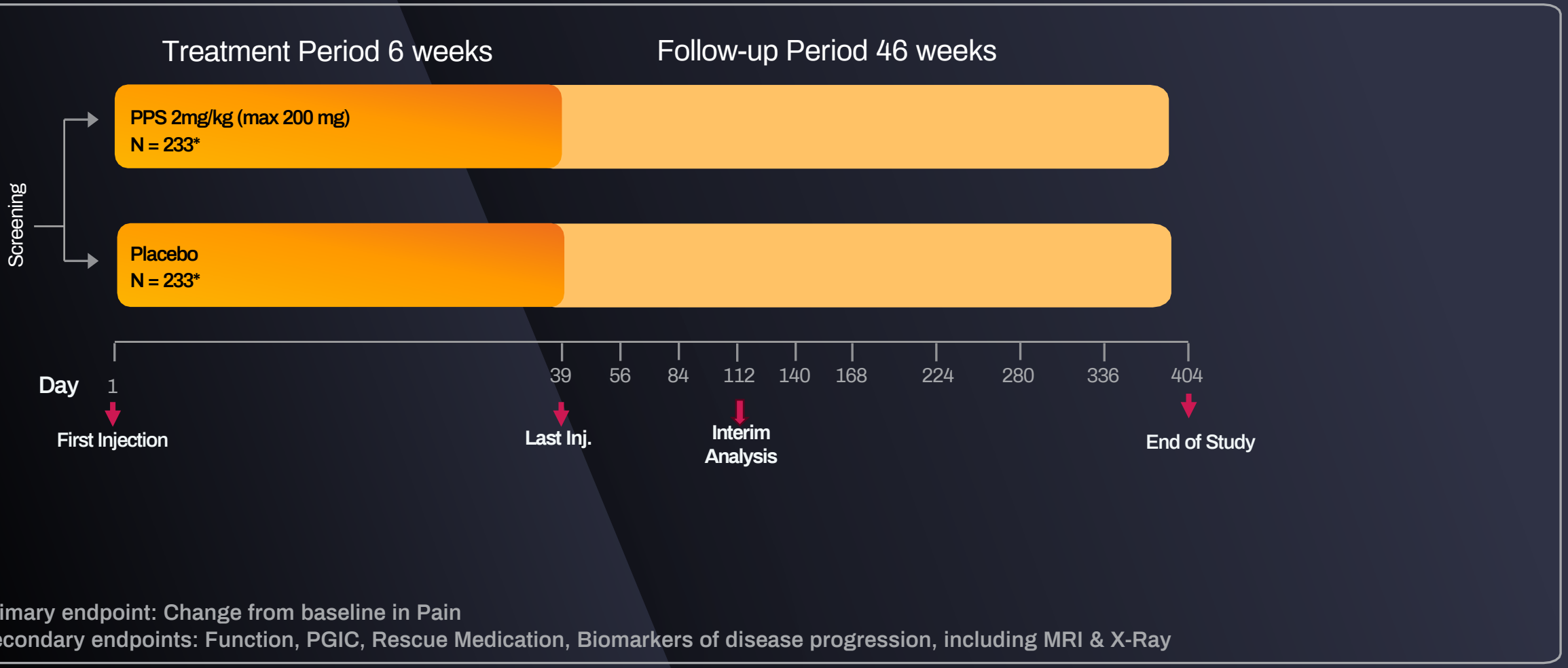
- FDA feedback on clinical endpoints and statistical procedures.
- Structural changes will be evaluated via X-ray and MRI as secondary endpoints consistent with regulatory guidance.

Trial Scale

- Approximate enrolment: 466 participants. 1:1 randomization.

PARA_OA_012

Phase 3 trial design



Primary endpoint: Change from baseline in Pain
Secondary endpoints: Function, PGIC, Rescue Medication, Biomarkers of disease progression, including MRI & X-Ray

Finance

Exploring Multiple Funding Pathways

Focus on Non-Dilutive Funding

- Priority on securing non-dilutive or less dilutive sources, including government grants, R&D rebates, and milestone payments or direct investment from potential commercial partnerships.

Strategic Partnerships and Collaborations:

- Ongoing discussions with potential commercial partners aimed at securing key regional partnerships.
- Key milestone is FDA Phase 3 clearance.

Contingency Planning:

- While non-dilutive funding is preferred, convertible notes or equity raises, remain viable solutions if additional capital is required to maintain momentum in pivotal clinical programme.

Pathway to Commercialisation:

- Funding plans are aligned with key upcoming milestones, including TGA and FDA regulatory responses, and the start of patient enrolment for the Phase 3 trial in early 2025.

Near-term News flow

Upcoming Catalysts

Event	Target Date
FDA Phase 3 Protocol Review - FDA Agreement to proceed to with PARA_OA_012 study	Q4 CY2024
TGA Provisional Approval OA - TGA Determination Decision	Q4 CY2024
Australian Ethics Submission – Phase 3 PARA_OA_002	Q4 CY2024
Phase 3 OA program – First participant enrolled, subject to regulatory agreement.	Q1 CY2025
TGA Provisional Approval OA - Dossier Submission, pending determination application approval.	1H CY2025
PARA_OA_008 Peer Review Publications – 2 manuscripts submitted to separate journals for review and expected publishing in CY25.	1H CY2025
PARA_OA_012 – 50% Recruitment of participants	2H CY2025
Regional licensing agreement(s) in OA and MPS.	Ongoing

Summary

Opportunity

- Pivotal phase 3 PARA_OA_012 to commence enrolment early 2025
- Extensive clinical data and Real-world evidence of iPPS effect in OA.
- FDA Fast tracked phase 3 OA program. Stage 1 completed randomising over 600 patients across 120 sites globally.
- 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.
- Phase 3 clearance critical milestone for commercial discussions.

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