ASX RELEASE 9 September 2025

Paradigm to Present at the Evans & Partners Small Cap Healthcare Conference

Paradigm Biopharmaceuticals Ltd (ASX:PAR) ("Paradigm" or "the Company"), a late-stage drug development company focused on delivering new therapies to address unmet medical needs, today announced it will be presenting at the 4th Annual Evans & Partners Small Cap Healthcare Conference on 9 September 2025.

The presentation, delivered by Paradigm's Founder and Managing Director Paul Rennie, will outline the significant burden of osteoarthritis disease and how Paradigm is seeking to address this unmet need through its ongoing global Phase 3 clinical trial of injectable pentosan polysulfate sodium (iPPS) for the treatment of knee OA.

A copy of the presentation is available attached, or available via the company's website via:

https://investors.paradigmbiopharma.com/link/PBJlmP

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About Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals Ltd. (ASX: PAR) is a late-stage drug development company driven by a purpose to improve patients' health and quality of life by discovering, developing, and delivering pharmaceutical therapies. Paradigm's current focus is developing iPPS for the treatment of diseases where inflammation plays a major pathogenic role, indicating a need for the anti-inflammatory and tissue regenerative properties of PPS, such as in osteoarthritis (phase 3).

Forward Looking Statements

This Company announcement contains or may contain 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.

To learn more please visit: https://paradigmbiopharma.com

Approved for release by the Paradigm Board of Directors.

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PARADIGM BIOPHARMA

Evans & Partners

4th Annual Small Cap

Healthcare Conference

MD | Paul Rennie

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What is Osteoarthritis

Overview

- A degenerative joint disease causing pain, swelling, and stiffness.
- Affects entire joints (cartilage, bone, ligaments, muscles).
- Most common in knees, hips, spine, and hands.
- Chronic, progressive, and a leading cause of disability.

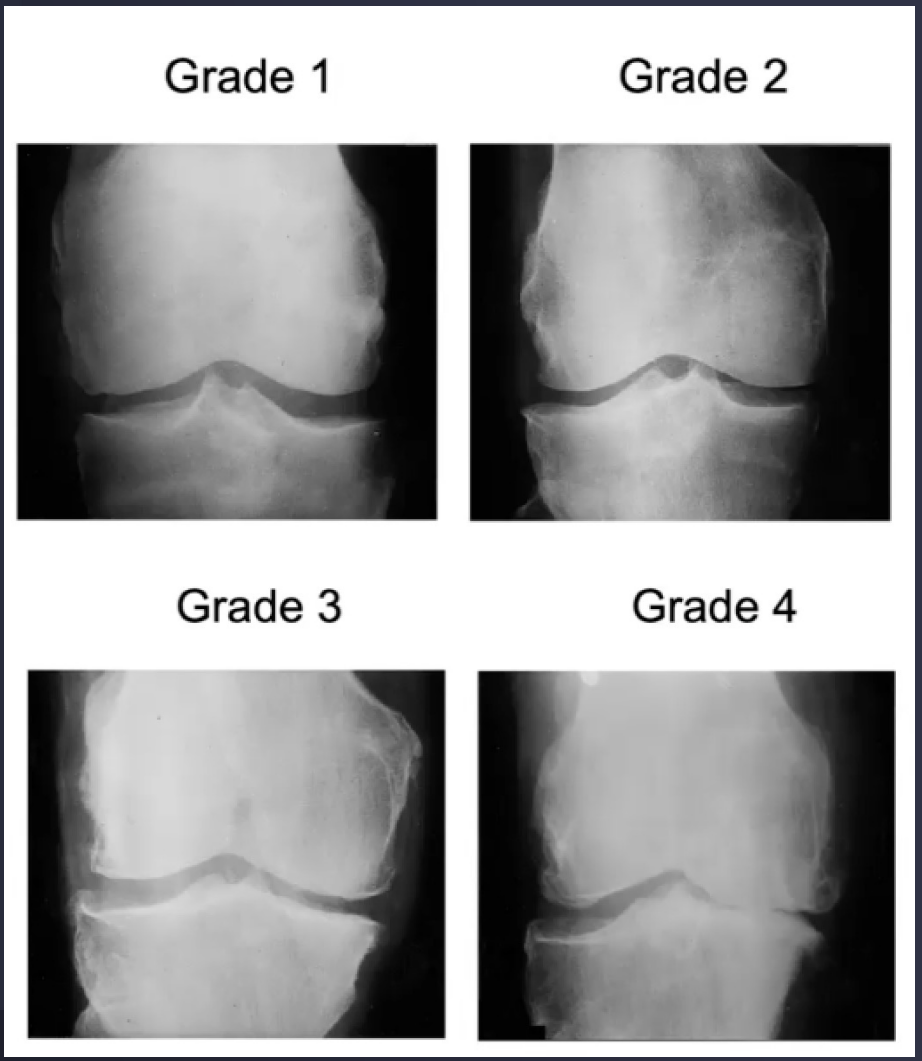
Impact

- Restricts movement, daily activities, and quality of life.
- Can lead to mental health issues, sleep disturbance, and social withdrawal.

Risk Factors & Management

- Age, sex, obesity, joint injury, overuse, metabolic disease, genetics.
- Exercise, weight management, physical therapy, braces.
- NSAIDs, Opioids for pain control.
- Joint replacement surgery in severe cases.

Kellgren and Lawrence Grade



Osteoarthritis By Numbers

Zilosul® is a non-opioid subcutaneous injectable aimed to treat pain and function in moderate-to-severe osteoarthritis.

People affected by OA Globally[1]

528m+

Knee OA most prevalent[2]

365m+

Knee OA is the most common form of OA, accounting for around 69% of all cases, followed by hip and hand OA[2].

Moderate – to – Severe OA[3]

65% of all OA

OA patients dissatisfied with current treatments[4]:

81%

Target uptake: 10% dissatisfied market

Zilosul indicative price: US$2500 per year[5]

- **Significant TAM**
- **Prevalence continues to rise due to ageing, obesity and injury.**

1. GBD 2019: Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. https://vizhub.healthdata.org/gbd-results/
2. Long H, Liu Q, Yin H, Diao N, Zhang Y, Lin J et al. Prevalence trends of site-specific osteoarthritis from 1990 to 2019: Findings from the global burden of disease study 2019. Arthritis Rheumatol 2022; 74(7): 1172-1183.
3. Cieza A, Causey K, Kamenow K, Wulf Hansen S, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020 Dec 19; 396(10267): 2006–2017.
4. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.
5. Global Pricing Research conducted by Paradigm.US, UK Germany, France

Unmet Need

- **Limited treatment options**: Current treatments (NSAIDs, steroids, HA) focus on short-term pain relief.
- **High economic burden**: OA costs the US healthcare system over **$136B annually**[1].
- **Strong demand for alternatives**: A safe, effective treatment with long-term benefits is urgently needed.

Analgesics, NSAIDS	• Daily use • GI, CV risk with prolonged use.
Opioids	• Severe side-effects • Addictive
*Hyaluronic Acid Injectable*Platelet-rich Plasma, *Stem Cells	• Limited pain relief • Royal Australian College of General Practitioners hold a 'strong against' recommendation.
Steroid injectable	• Limited pain relief • Evidence of further cartilage degradation
Surgery - Total Knee Arthroplasty	• High cost • Patients opting for alternative treatments

CV = Cardiovascular; GI = Gastrointestinal

1. Source: https://www.tandfonline.com/doi/full/10.1080/03007995.2023.2234727?scroll=top&needAccess=true&role=tab

Advancing iPPS Toward a Differentiated OA Therapy

Robust data and regulatory momentum underpin a well-defined path through Phase 3

01

SAFTEY & EFFICACY PROFILE

- Strong efficacy and safety shown across a broad dataset
- Durable benefits sustained to 12 months in Phase 2 studies
- Imaging and biomarker data suggest effects beyond symptom relief

02

PHASE 2 AND REAL-WORLD EVIDENCE

- Multiple Phase 2 studies underpin Phase 3, showing consistent efficacy across patient types and timepoints
- Real-world insights from Australia's SAS program show long-term benefits with repeat courses.

03

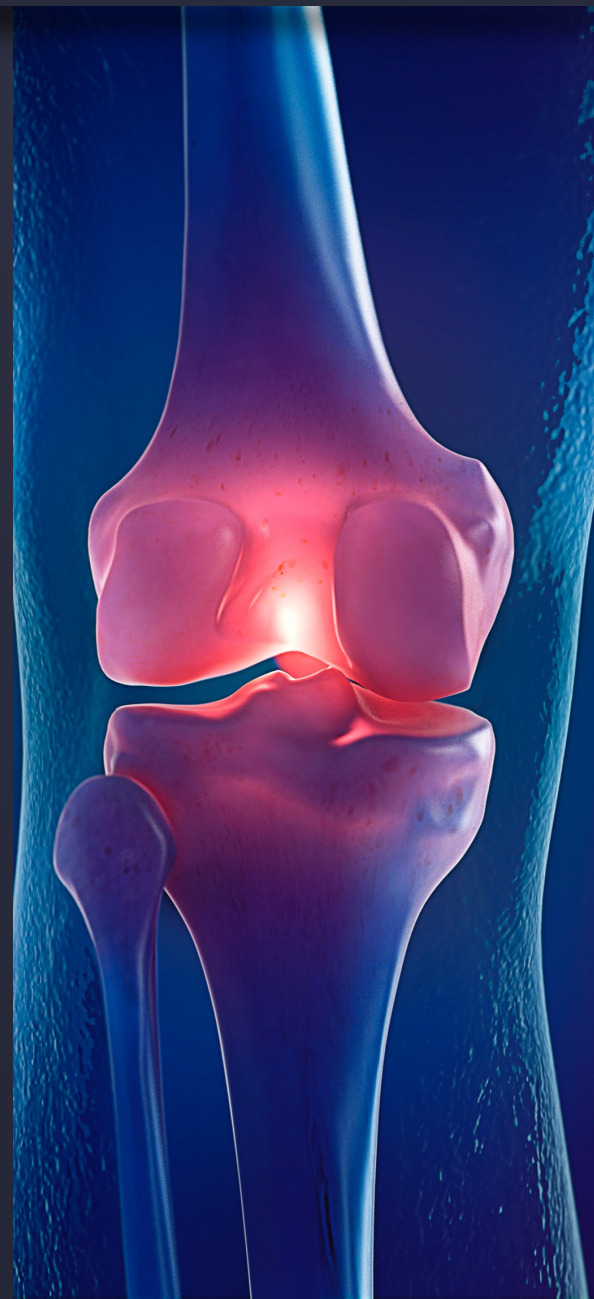
MECHANISM OF ACTION

- Demonstrated across preclinical models and human studies
- Anti-inflammatory, cartilage-protective, and matrix-restoring properties
- Biomarker data from Phase 2 suggests activity beyond symptom relief

04

OPTIMISED PHASE 3 PROGRAM

- Fast Track designation granted by FDA
- Protocol refined following extensive FDA engagement (Type C and D meetings)
- Endpoints, statistical powering, and assessment windows aligned with regulatory expectations



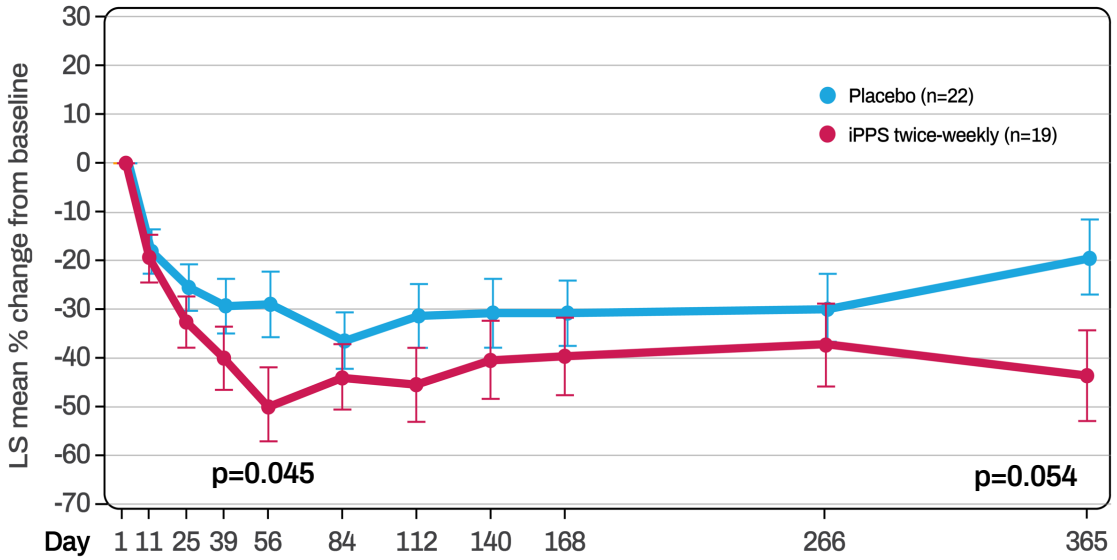
Confidence in IPPS | Clinical & Real-World Evidence

iPPS Study	Study Type	Dosing Regimen	Key Findings
Ghosh et al. (2005)	Randomised, double-blind, placebo-controlled (n=114)	3 mg/kg IM once weekly for 4 weeks	Significant pain reduction at rest (out to 24 weeks); Improved joint stiffness and global assessment
Kumagai et al. (2010)	Open-label clinical trial (n=20)	2 mg/kg SC once weekly for 6 weeks	Improved range of motion and pain reduction (out to 52 weeks); Reduced serum C2C (cartilage degradation marker)
PARA_OA_005	Phase 2b (n=128)	2 mg/kg SC twice weekly for 6 weeks	Clinically significant pain & function improvement; 5x lower rescue medication use; Sustained relief to 6 months
PARA_OA_008	Phase 2 (n=61)	2 mg/kg SC twice weekly for 6 weeks	Significant pain and function improvement out to 12 months; Reduced cartilage degradation biomarkers; MRI evidence of bone marrow lesion reduction
PARA_OA_002	Phase 2b/3 (n=601)	Dosing study, 6-week treatment, 18-week follow-up	Confirmation of minimum effective dose for Phase 3 trial; Safety profile consistent across all doses
TGA SAS	Real-World (n>700)	2 mg/kg SC twice weekly	Meaningful clinical improvements in pain and mobility

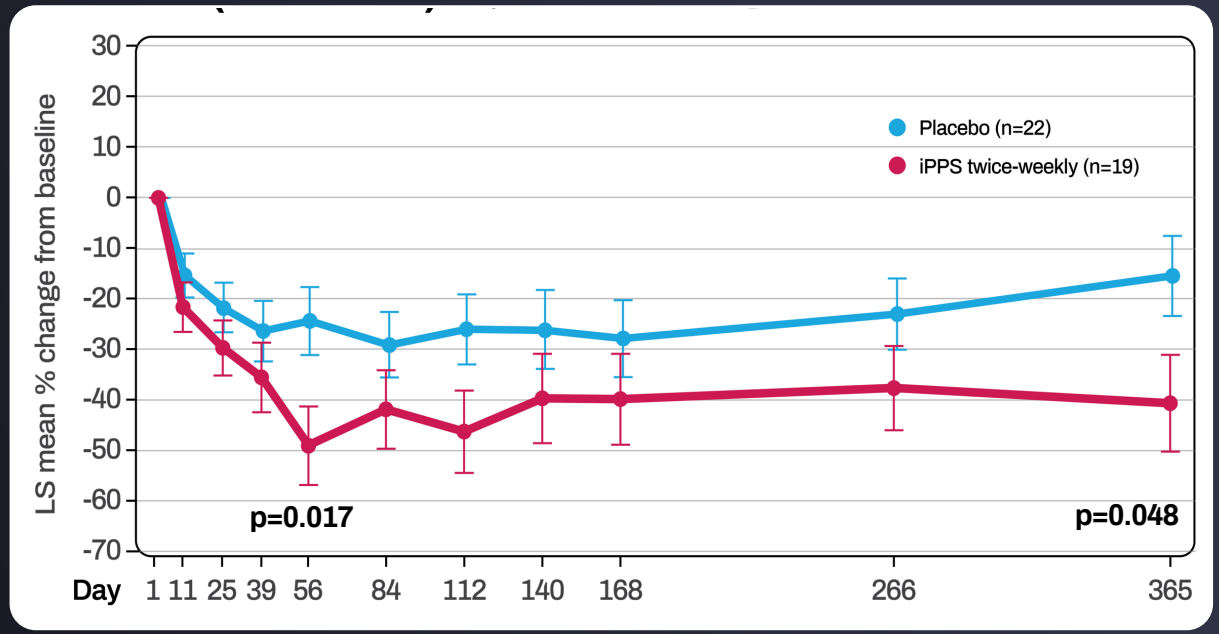
Phase 2: PARA_OA_008 | 2 mg/kg IBW SC twice weekly v placebo for 6 weeks, followed up for 12 months (n=61)

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.

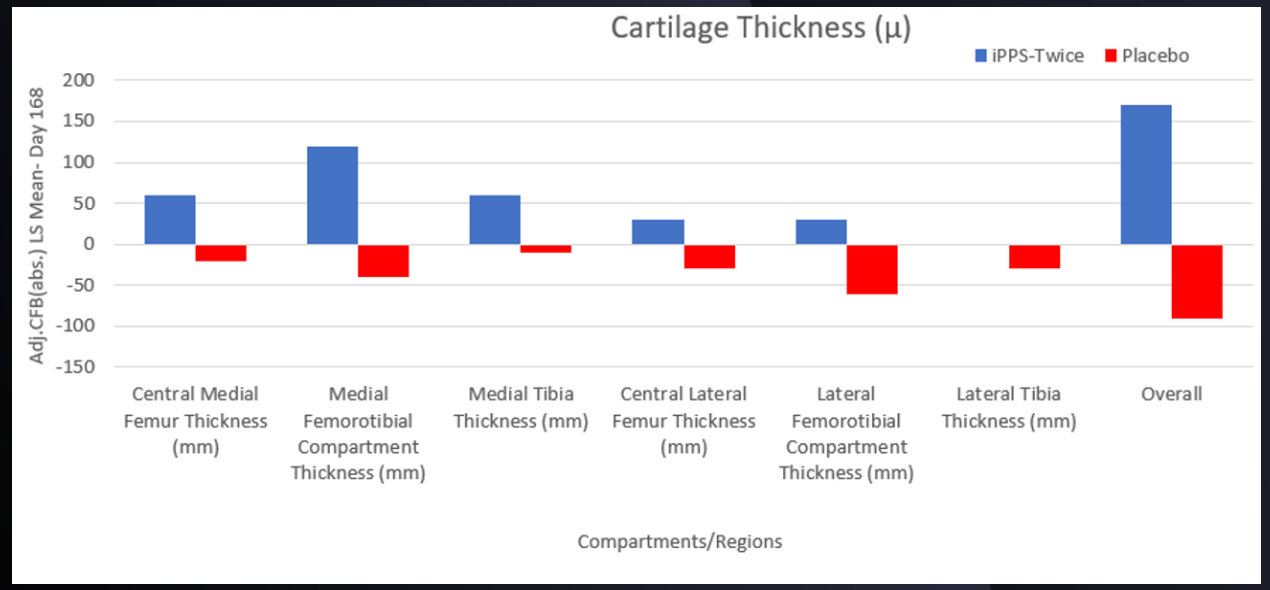


Rescue medication use

- 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

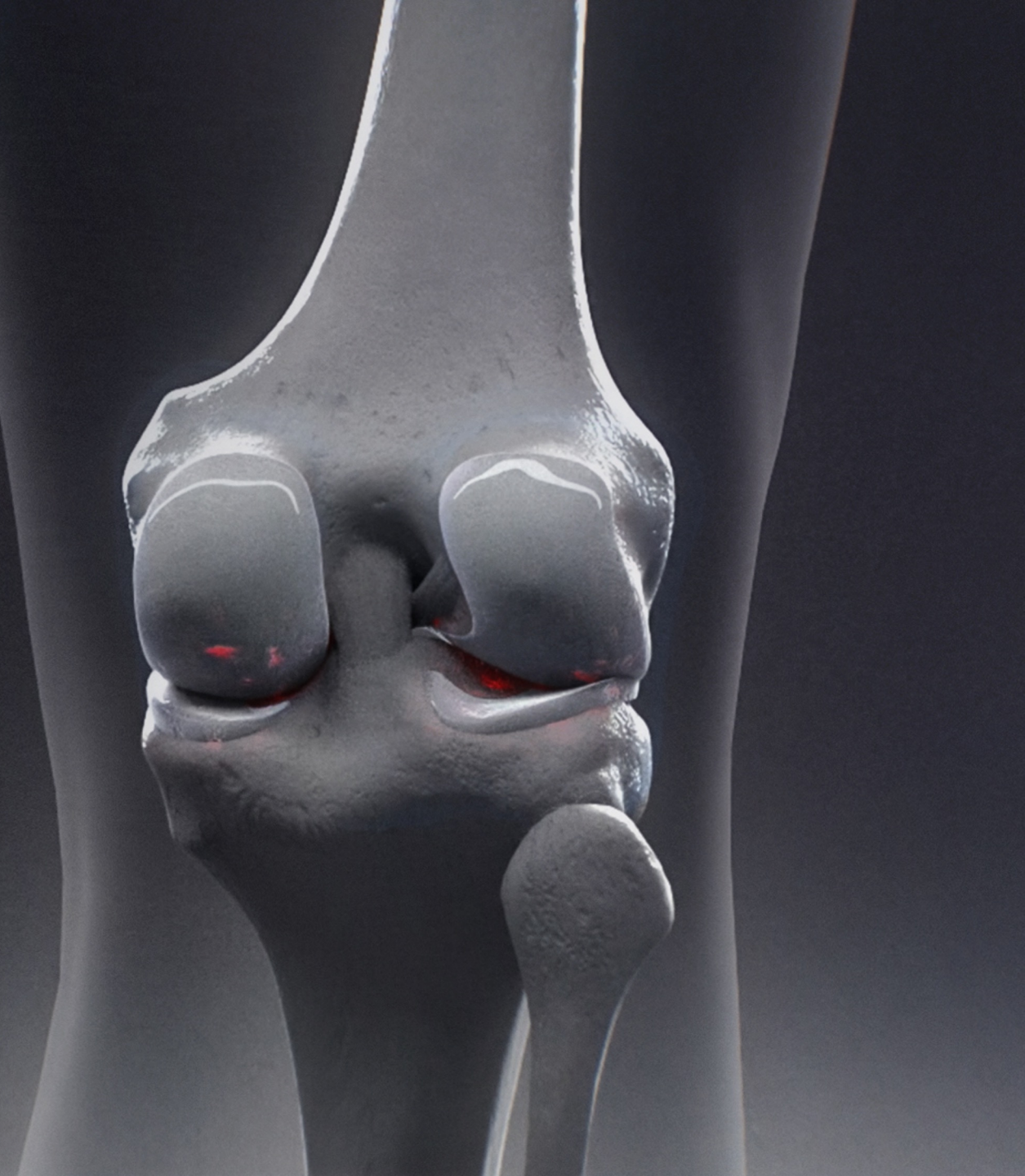
Changes in Cartilage Thickness from baseline

- 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).

PARADIGM

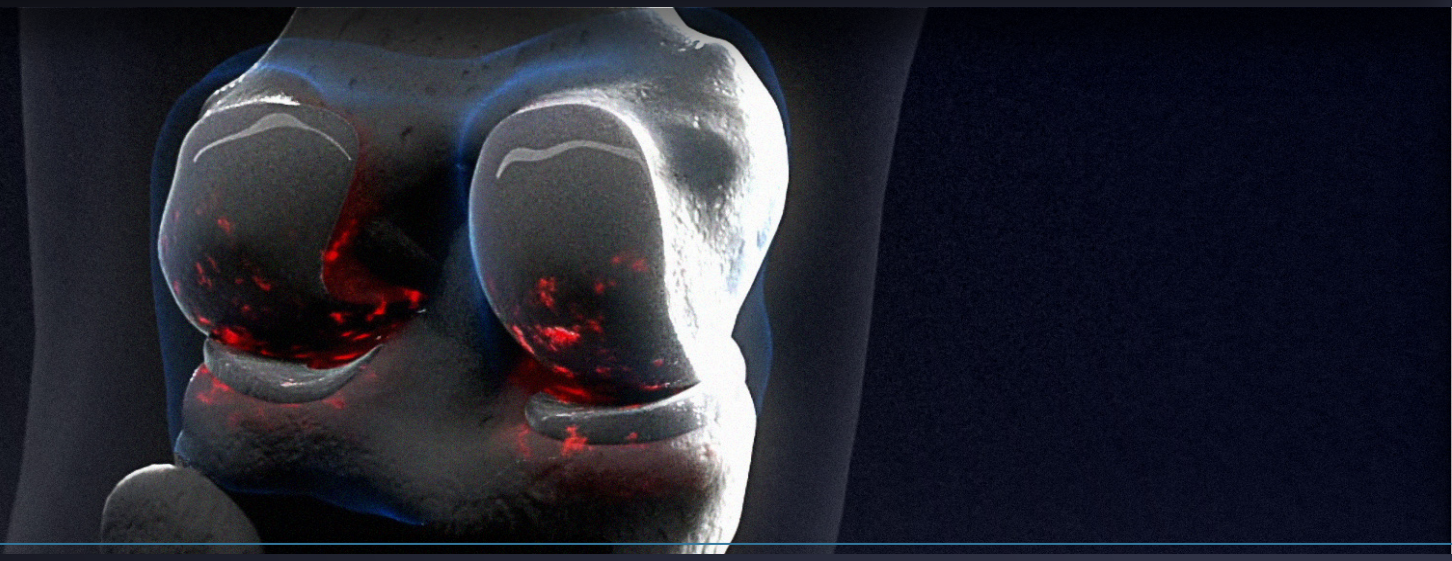
Osteoarthritis

Pivotal PH3 Trial



Phase 3 Objectives

Key objectives for the Phase 3 PARA_OA_012 study



Primary Objectives

- To evaluate the treatment effect of PPS on knee pain in participants with knee OA pain. (Weekly Average ADP Day 112)

Key Secondary Objectives

- To evaluate the treatment effect of PPS on knee pain function in participants with knee OA pain. (WOMAC Day 112)
- To evaluate the effect of PPS treatment on PGIC in participants with knee OA pain. (PGIC Day 112)
- To evaluate the efficacy of PPS treatment on knee pain, function, stiffness, and overall, in participants with knee OA pain.

Secondary Objectives

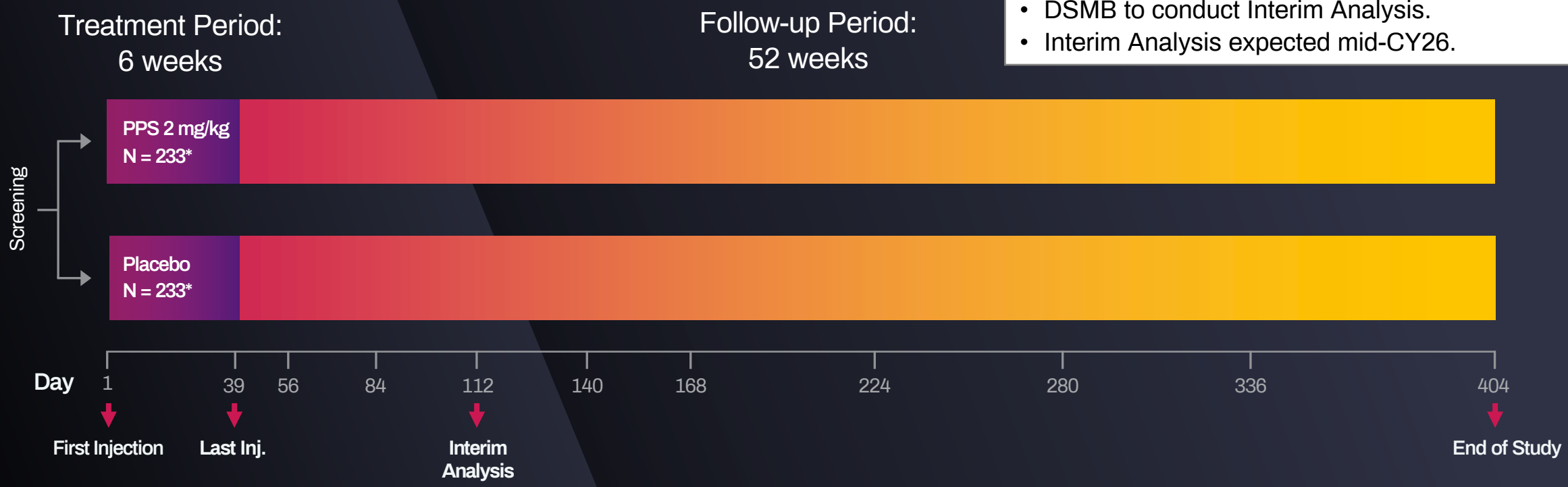
- WOMAC Pain and function assessments at multiple timepoints to Day 404.
- IPPS effects on Rescue Medication use.
- Structural changes via X-Ray and MRI from baseline day 168, 404

PARA_OA_012

Phase 3 trial design

Interim Analysis (IA)

- Conducted once 50% of subjects (~233) reach Day 112.
- Plan assess efficacy and possible early conclusion of trial based on target effect size.
- DSMB to conduct Interim Analysis.
- Interim Analysis expected mid-CY26.



Primary endpoint: Change from baseline in weekly ADP NRS pain score at Day 112.

Secondary endpoints: Function, PGIC, rescue medication, biomarkers of disease progression, including MRI & X-Ray.

*May be subject to change

PARA_OA_012 – Powered for Success

Statistical Power Based on Phase 2 Data Validates

The table summarises modelled power at effect sizes established in Phase 2 studies.

Effect Size (ES)	Estimated Power (n=233/arm)
0.3 *(Phase 2 pooled)*	>86%
0.4	>98%

- High statistical power supports confidence in replicating prior Phase 2 clinical benefit.
- Model assumes observed Phase 2 variance and full sample size.
- Success estimates based on historical trial performance and standard assumptions*.

* Does not account for executional risk.

ASX PH3 Comparison Table

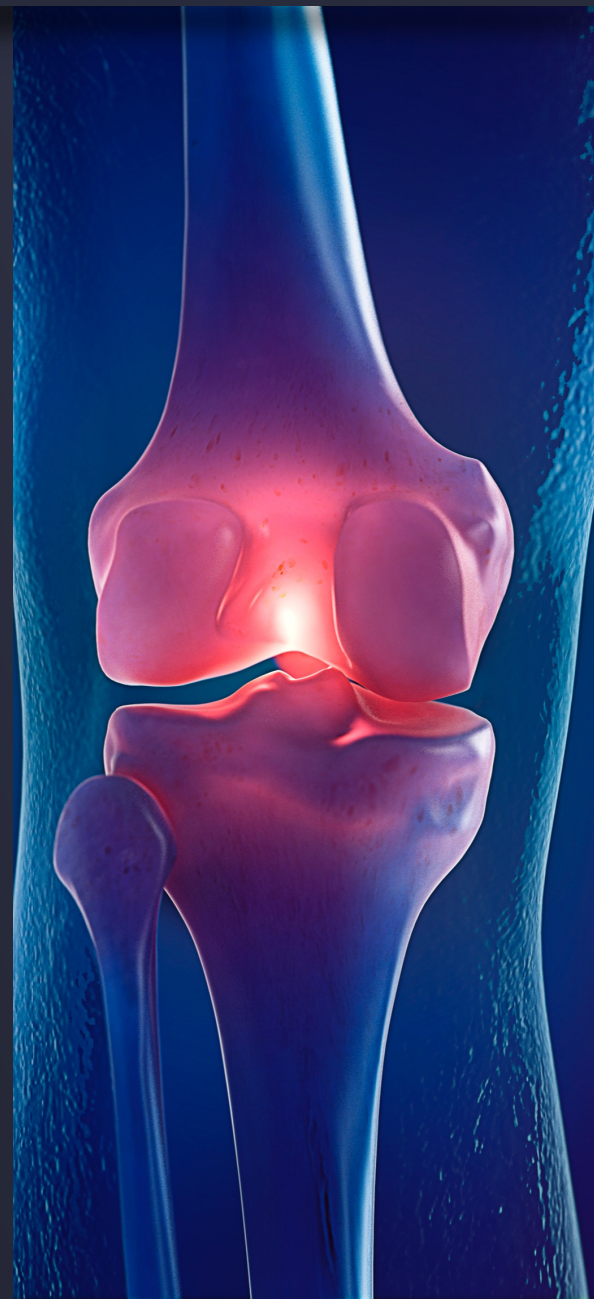
Upside from current valuation

Company	P3 Trial Indication	FDA Designations	Valuation (Market Capitalisation $Am)	
			At IND Clearance	Current
Mesoblast Ltd (MSB)	GVHD (paediatric refractory to standard of care)		~A$1,500	~A$2,931
Immutep Ltd (IMM)	Metastatic non-small cell lung cancer		~A$535	~A$382
Dimerix Ltd (DXB)	Focal segmental glomerulosclerosis (FSGS)	Orphan	~A$90 (May-22)	~A$291
Neuren Pharmaceuticals Ltd (NEU)	Phelan-McDermid syndrome (PMS)	Orphan	~A$500 (Mar-22)	~A$2,250
Botanix Pharmaceuticals Ltd (BOT)	Primary axillary hyperhidrosis		~A$190 (Oct-23)	~A$314
Paradigm Biopharmaceuticals Ltd (PAR)	**Osteoarthritis of the knee**	**Fast track**	**~A$112**	

Source: Market capitalisations are approximate only. IRESS as of 12 August 2025. NEU, MSB and BOT have since completed PH3 studies and are in production likely to positively effect current market capitalisation above.

Investment Highlights

- ✓ **Multiple Positive Phase 2 Trials:** Consistent efficacy and safety demonstrated across studies, with signals of disease-modifying activity on MRI and biomarkers.
- ✓ **Real-World Evidence:** Long-term benefits observed in Australia's SAS program, including sustained improvements with repeat courses.
- ✓ **Optimised Phase 3 Design:** Refined following extensive FDA engagement, aligned with regulatory expectations, and powered to detect clinically meaningful effects.
- ✓ **Fast Track Designation:** Accelerated regulatory pathway secured with the FDA.
- ✓ **Large, Unmet Global Market:** 500M+ people affected by OA, 81% of patients dissatisfied with current treatments
- ✓ **Near-Term Inflection Point:** Interim analysis expected mid-2026 at 50% patient completion, representing a major value catalyst.



News flow & catalysts

Upcoming Catalysts

Event	Target Date
PARA_OA_012 – First participant dosed.	Q3 2025
PARA_OA_012 – 50% Recruitment of participants	2H 2025*
Regional licensing agreement(s) in OA	Ongoing
PARA_OA_008 – Phase 2 clinical trial data manuscripts peer reviewed and published.	End of CY2025
PARA_OA_012 – 100% Recruitment	1H 2026*
PARA_OA_012 Interim Analysis – 50% participants reach Day 112	Mid-2026*

**The above is a statement of current intentions as at the date of this presentation. Investors should note that the above upcoming events are subject to funding or new circumstances.*

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