ASX RELEASE 19 November 2025

2025 Annual General Meeting
Chairman's Address

Dear Shareholders,

As Chair and Managing Director, I am pleased to report on the strong progress Paradigm Biopharmaceuticals has delivered over the past 12 months. 2025 has been a year defined by operational execution, disciplined financial management, and meaningful strategic advancement as we continue to progress our pivotal Phase 3 clinical program in knee osteoarthritis (OA).

2025 marked Paradigm's transition from planning to full execution of the global PARA_OA_012 Phase 3 program, the final step before potential registration of injectable pentosan polysulfate sodium (iPPS) for knee OA. Following extensive regulatory dialogue and careful protocol refinement, the U.S. FDA completed its 30-day protocol review without further questions. This outcome enabled Paradigm to efficiently advance into the ethics and regulatory approvals needed to activate trial sites across Australia and the United States.

Site activation commenced in May 2025, led by our global CRO, Advanced Clinical, and by June we had successfully consented our first participant in Australia. Since then, screening and recruitment have continued to accelerate across both geographies, supported by refined inclusion criteria and strong site engagement. To further strengthen global oversight and enhance trial robustness, Paradigm recently engaged NBCD as a complementary CRO. NBCD brings additional on-the-ground regulatory and operational expertise across Europe and Asia, improving geographic diversity, governance efficiency, and data quality throughout the Phase 3 program.

We remain firmly on track to achieve our key clinical milestones. Both the 25% and 50% recruitment markers are now in sight, with hundreds of participants currently progressing through screening. Our independent interim analysis remains scheduled for mid-2026, once half the study cohort reaches Day 112. This analysis will represent a major value inflection point for Paradigm, providing early efficacy signals and informing ongoing regulatory, commercial, and partnering discussions.

While advancing iPPS remains our highest priority, 2025 was also notable for a strategic broadening of Paradigm's osteoarthritis portfolio. In June 2025, we completed the acquisition of Proteobioactives Pty Ltd, securing global intellectual property rights for Pentacoxib™, a novel oral combination of PPS and a COX-2 inhibitor designed for earlier-stage OA and veterinary applications.

This acquisition positions Paradigm across the full OA treatment continuum, addressing both early symptomatic disease with Pentacoxib and moderate-to-severe OA with Zilosul®. The veterinary development pathway for Pentacoxib also creates a capital-efficient route to generate early data and potentially revenue, supporting a measured and scalable expansion of our musculoskeletal pipeline.

In response to clear feedback from shareholders during the 2024 AGM and subsequent meetings, the Board prioritised a balanced, flexible and minimally dilutive funding strategy in 2025. In December 2024, Paradigm successfully raised $16 million through an equity

placement at $0.40 per share, enabling accelerated site activation and manufacturing readiness. In July 2025, we supplemented this with a US$27 million (approximately A$41 million) convertible note facility with Obsidian Global Partners, secured following a competitive international process.

The Obsidian facility provides staged access to capital while preserving balance sheet strength and maintaining strategic optionality. Importantly, it provides funding runway through 100% recruitment and the interim analysis in mid-2026.

Our Loyalty and Piggyback Option Program further supports a long-term, shareholder-aligned capital structure. While we acknowledge the options are not yet in the money, the potential for up to $112 million in future non-dilutive capital underscores Paradigm's commitment to creating value for long-standing shareholders. We are focused every day on delivering the progress needed to ensure these options can be exercised and reward those who have supported the Company through this phase.

2025 has been characterised by disciplined execution across all operational pillars. Trial site selection, activation and recruitment scaling have been supported by global systems and experienced clinical, regulatory and operational teams. These efforts are designed to optimise data integrity, trial consistency, and overall probability of success. Early screening data demonstrates improved performance and lower screen-failure rates relative to previous studies, reflecting the refinements implemented after FDA feedback.

Parallel progress continues across supply chain and CMC readiness, ensuring that commercial-scale manufacturing capability remains aligned with our clinical and regulatory timeline.

As we enter the next phase of execution, Paradigm does so with strengthened operational momentum, increased regulatory clarity, and the financial runway required to deliver one of the most important milestones in the Company's history, the interim analysis of the Phase 3 PARA_OA_012 trial in mid-2026.

In the near term, our focus remains on accelerating recruitment, maintaining data quality, driving operational efficiency, and we continue to assess regional licensing and strategic partnership opportunities to support global positioning for both iPPS and Pentacoxib™.

With these two complementary assets, Paradigm is now uniquely positioned across the full osteoarthritis treatment spectrum, from early symptom management to potential disease-modifying treatment for moderate to severe OA. This portfolio breadth, combined with our strong clinical, regulatory, and manufacturing foundations, provides a compelling long-term value proposition.

I would like to extend my sincere thanks to our shareholders for their confidence and support, to our clinical investigators and patients for their invaluable participation, to our employees and partners for their ongoing dedication, and to my fellow Directors for their continued guidance and commitment.

2026 will be a defining year for Paradigm, one in which we expect to complete recruitment, deliver the interim analysis, and advance the next stage of our growth strategy. Our purpose remains steadfast: to provide new hope to millions of people worldwide living with chronic pain.

Thank you.

Paul Rennie

Chair and Managing Director
Paradigm Biopharmaceuticals Ltd

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 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.

Authorised for release by the Paradigm Board of Directors.

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Paradigm Biopharma

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PARADIGM BIOPHARMA

ANNUAL GENERAL MEETING | 19 NOV 2025

BOARD OF DIRECTORS

Experienced team to drive clinical success and commercialisation

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Non-Executive Director

PAUL RENNIE

Chair & Managing Director

AMOS MELTZER

Non-Executive Director

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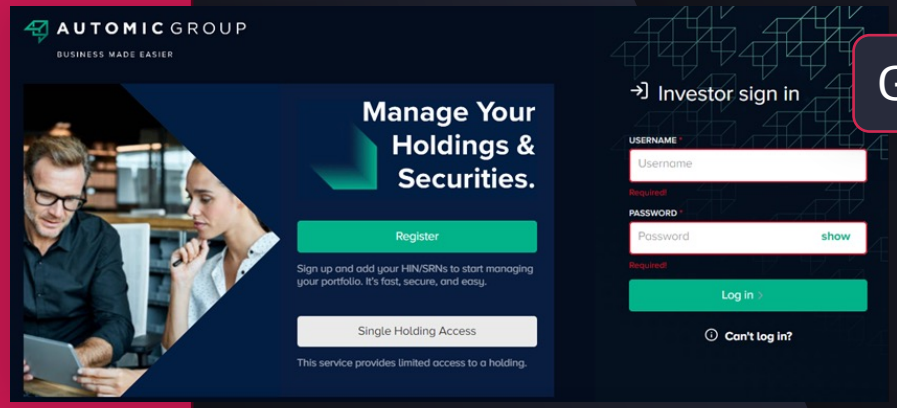

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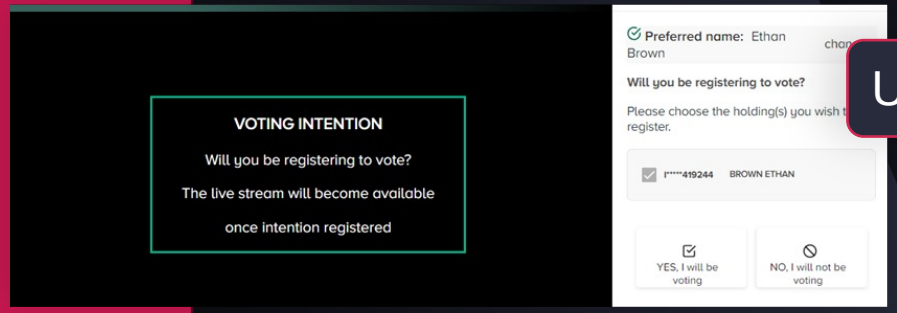

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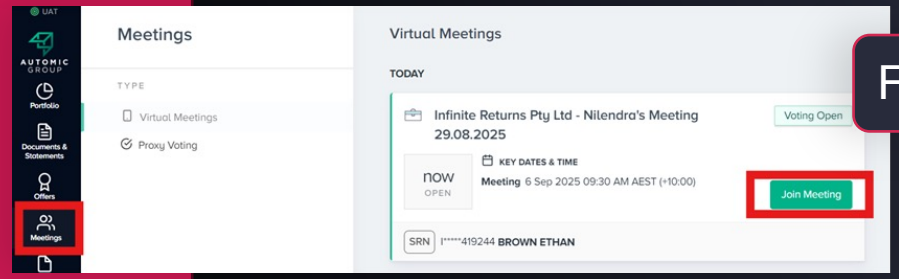

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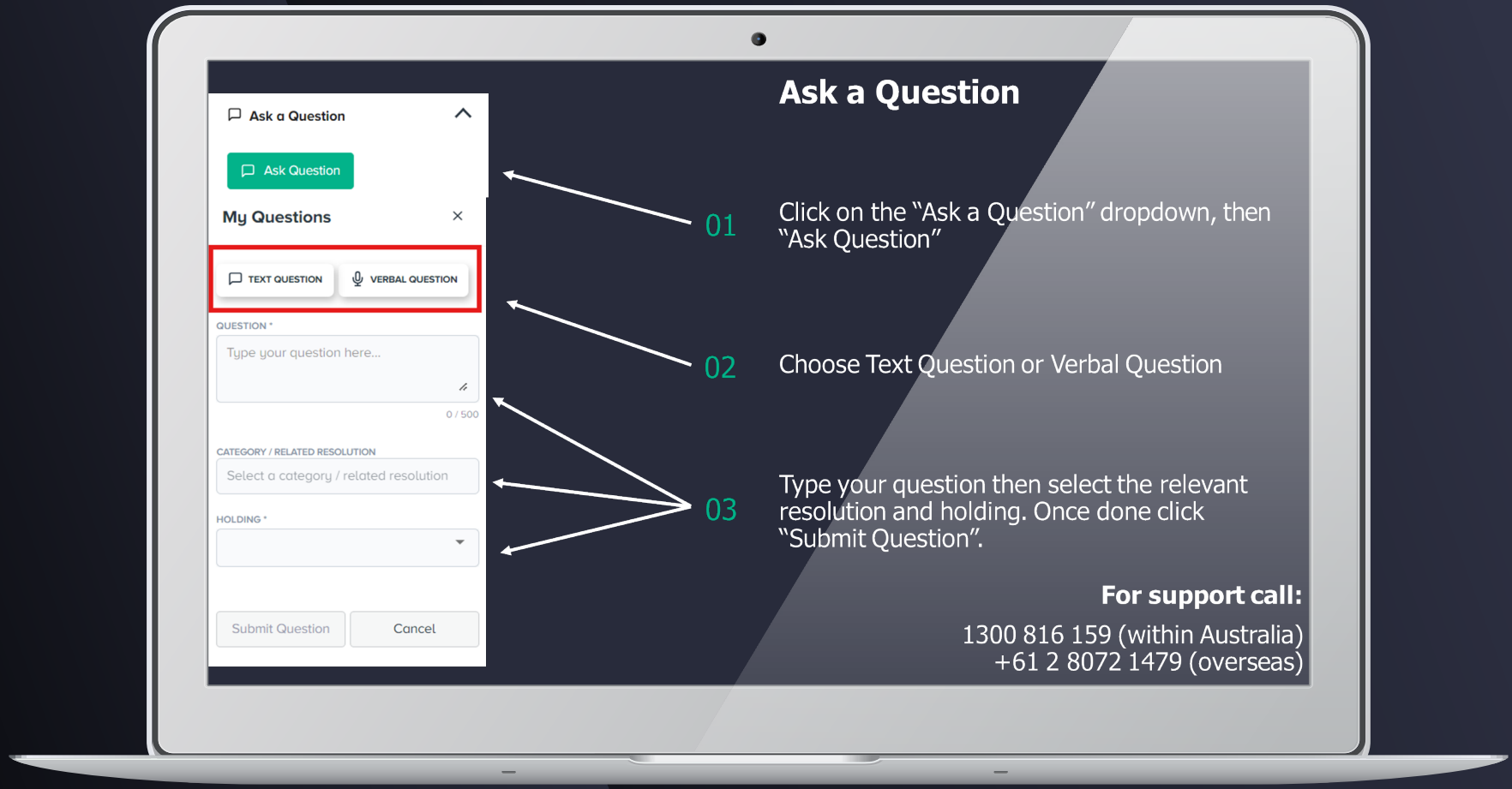

COMPANY UPDATE

PAUL RENNIE,
Managing Director

Agenda

01 Company Update

02 Notice of meeting & formal business

03 Questions relating to Company Update

DISCLAIMER

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COMPANY OVERVIEW

Paradigm is advancing pentosan polysulfate sodium (PPS) as a novel, non-opioid therapy to transform the treatment of osteoarthritis. By targeting the underlying inflammation and structural degeneration that drive disease progression, Paradigm aims to deliver safer, more effective options that move beyond symptom relief.

Mission

Develop and commercialise safe, effective and non-opioid therapies for musculoskeletal diseases, targeting inflammation, pain relief, and disease modification.

Unmet need

- Osteoarthritis (OA) affects more than 500 million people worldwide and is the leading cause of pain-related disability in adults.
- Current treatment options are largely symptomatic, relying on opioids or NSAIDs that offer limited long-term relief and carry significant safety risks.
- The U.S. FDA has reinforced the urgent need for new **non-opioid** therapies for chronic pain, creating a supportive regulatory environment for novel OA treatments such as iPPS.

OA Portfolio – Addressing full OA Spectrum

- **Early OA** → Pentacoxib™ (oral PPS + COX-2)
- **Moderate to Severe** → Zilosul® (injectable PPS)
- **Full OA Treatment Spectrum:** Veterinary → Early Human OA → Moderate–Severe Knee OA

COMPANY ACHIEVEMENTS

2025 YTD

Phase 3 trial transitioned from setup to active dosing across AUS & US.

Acquisition of Proteobioactives → broadened OA pipeline.

Advanced Clinical appointed as global CRO with NBCD engaged in a complementary role, broadening geographic footprint.

Secured US$27m Obsidian funding facility, fully funded through interim analysis.

Submission of Peer Review Publications.

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].

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

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]

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.

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

UNMET NEED


Effective
Non-validated
Ineffective
Invasive
Analgesics,NSAIDS
• Daily use
• GI, CV risk with prolonged use.
Opioids
• Severe side-effects
• Addictive
*Royal Australian College of General Practitioners hold a 'strong against' recommendation
*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
Grafe 1
Minor OA
Grade 2
Mild OA
Grade 3
Moderate OA
Grade 4
Severe OA

ADDRESSING FULL OA SPECTRUM

01.

Dual PPS-based therapies transforming osteoarthritis management across the full disease spectrum.

02.

Together, they aim to shift treatment earlier, reduce opioid reliance, and improve long-term outcomes.

03.

Aligned with FDA focus on non-opioid chronic pain solutions.

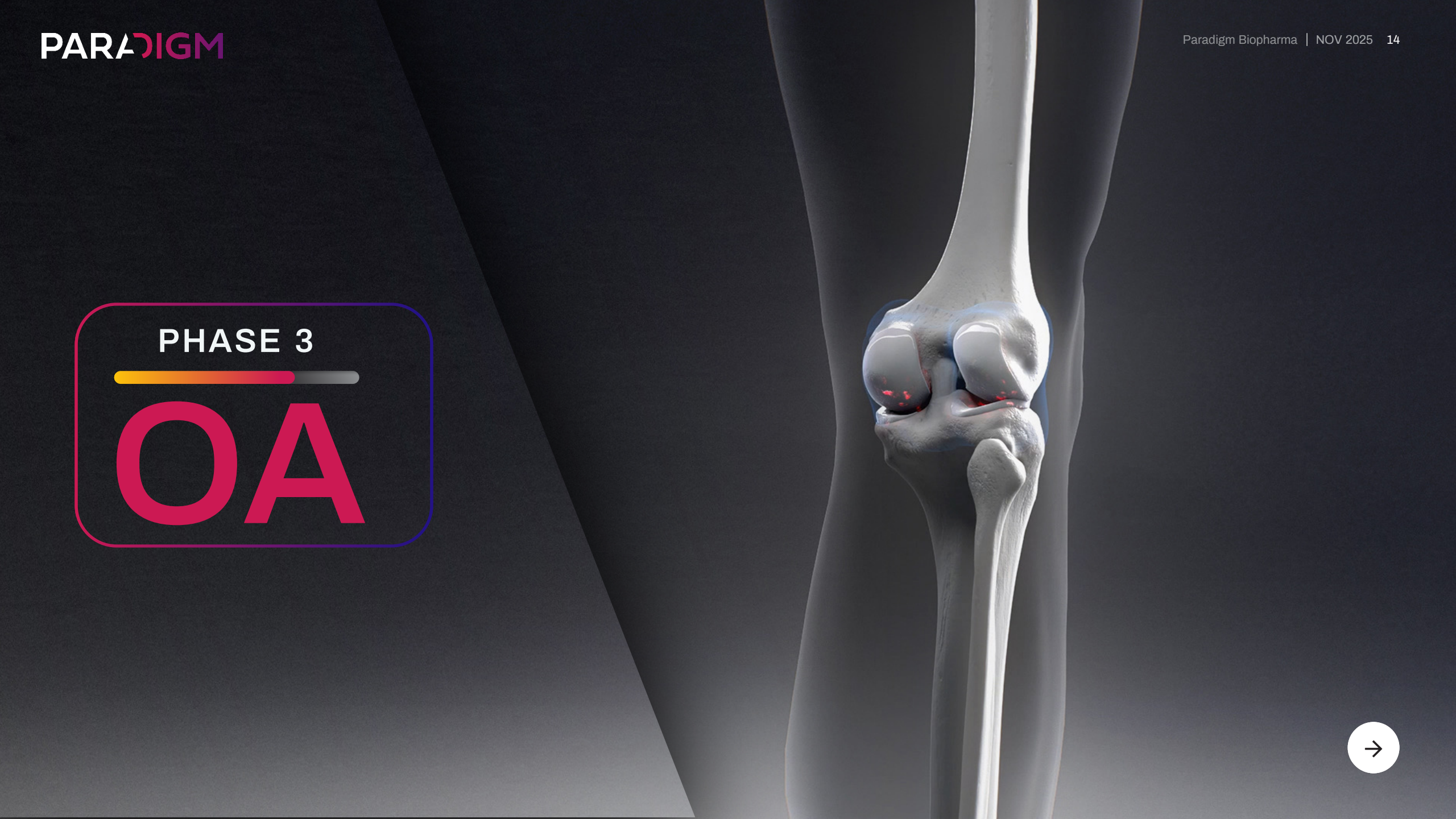
ADDRESSING FULL OA SPECTRUM

- Pentacoxib™ (oral PPS + COX-2) – safe, non-opioid option for mild-to-moderate OA.
- Applications across vetinary and human OA

- Zilosul® (injectable PPS) Phase 3 program for moderate-to-severe OA with disease-modifying potential.
- Current P3 program

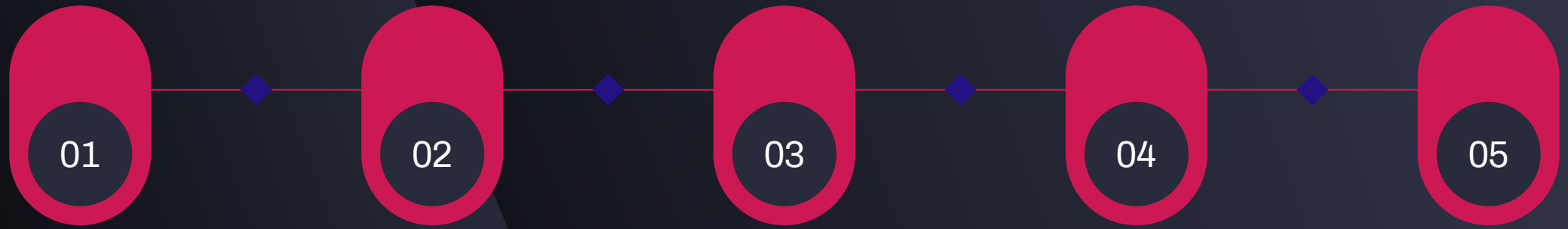
PHASE 3

OA



PARA_OA_012 PHASE 3 PROGRAM OVERVIEW

Global Pivotal Phase 3 Trial Progressing Toward Mid-2026 Interim Analysis



Study design

466-patient, randomised, placebo-controlled trial evaluating injectable pentosan polysulfate sodium (iPPS, Zilosul®) for moderate-to-severe knee OA.

Dosing regimen

2 mg/kg twice weekly for six weeks (12 injections).

Primary endpoint

Change in average daily pain at Day 112; key secondary endpoints include WOMAC pain and function, PGIC, and imaging biomarkers.

Trial oversight

Conducted under FDA Fast Track designation with Advanced Clinical as global CRO and NBCD engaged in a complementary role to expand operational reach and data robustness.

Interim analysis

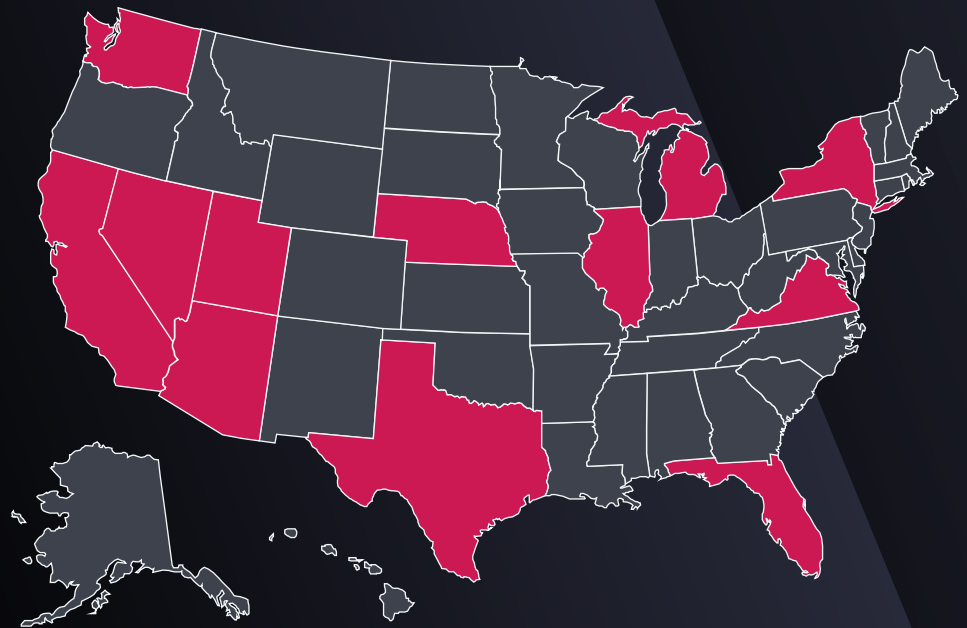
Planned for mid-2026, when 50 % of participants reach Day 112; independent DSMB oversight in place.

PARA_OA_012

Phase 3 Site Locations by State

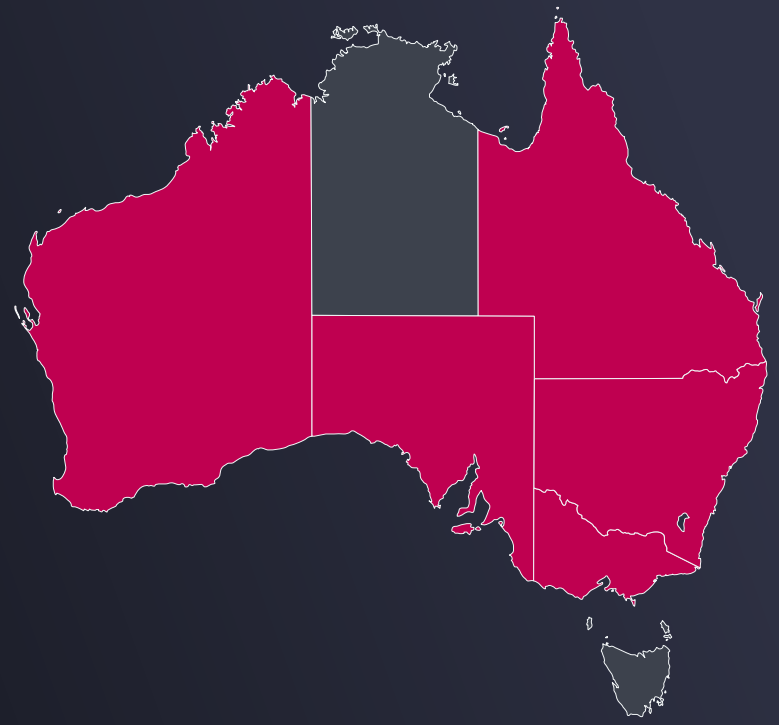
United States

45 sites



Australia

11 sites



LEAD PROGRAM OSTEOARTHRITIS

Phase 3 Achievements

Site Activations

- 60 sites across Australia, US, Hong Kong and Moldova on track for full activation by December 2025.
- New sites in Hong Kong and Moldova broaden diversity and support regional regulatory pathways including the *“1+”* framework.

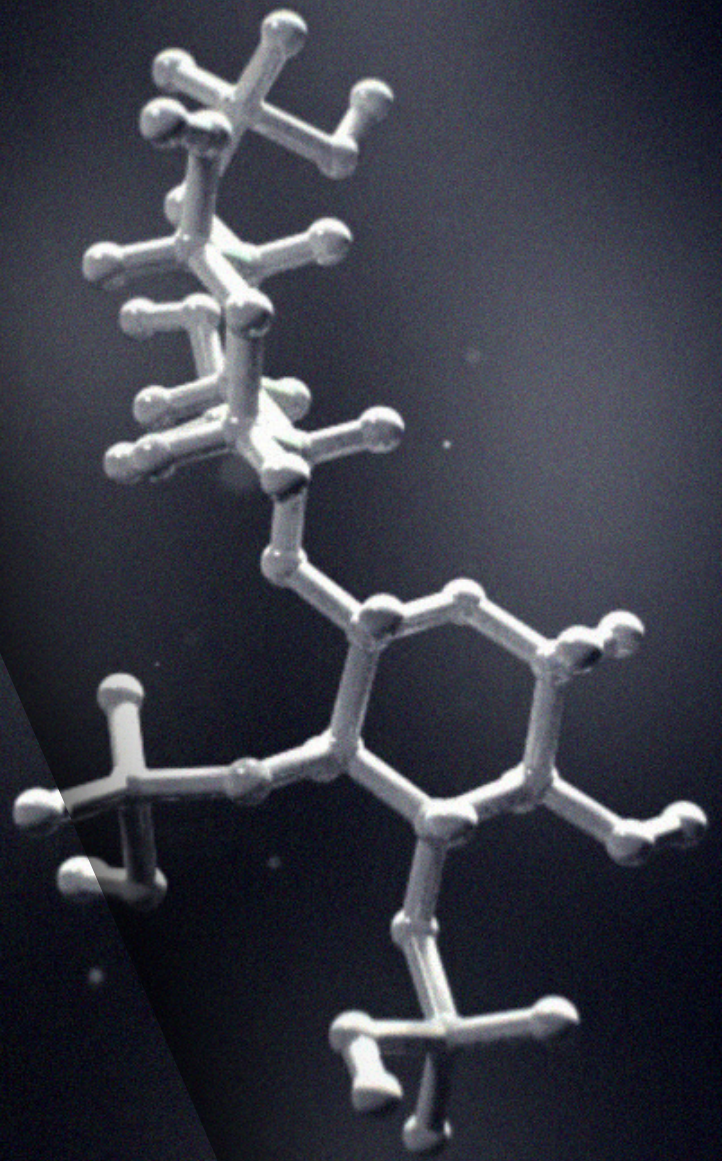
Enrollment

- Hundreds in screening with strong conversion to randomisation.
- Improved screen-failure rates vs PARA_OA_002 from refined criteria and site training.
- Recruitment and retention on plan; interim analysis mid-2026 (50 % of patients, DSMB-overseen).

Addition of NBCD as Complimentary CRO

- NBCD engaged alongside Advanced Clinical to enhance operational reach across Europe & Asia.
- Strengthens site activation, data quality and overall trial governance efficiency.

Company UPDATE



FINANCE

Strong Capital Position to Deliver Key Milestones

Obsidian Facility

01

Key focus has been to secure flexible sources of capital while minimising shareholder dilution wherever possible.

02

Each conversion to date under the US$27 million Obsidian facility has occurred at a higher price than a traditional equity raising would have achieved at the time.

03

The most recent US$5 million drawdown increased cash reserves to approximately A$26 million, with US$15 million still available at the company's discretion.

FINANCE

Runway and Funding Outlook

Fully funded through to the mid-2026 interim analysis of the Phase 3 program.

R&D investment averaging A$5–6 million per quarter as global site activation and recruitment continue to scale.

Forecast cash outflows for Q4 CY25 of A$13–15 million, reflecting peak clinical execution period.

Loyalty and Piggyback Options provide potential A$111.9 million in additional non-dilutive capital if exercised.

Ongoing focus on targeted capital allocation and disciplined financial management to preserve balance-sheet strength.

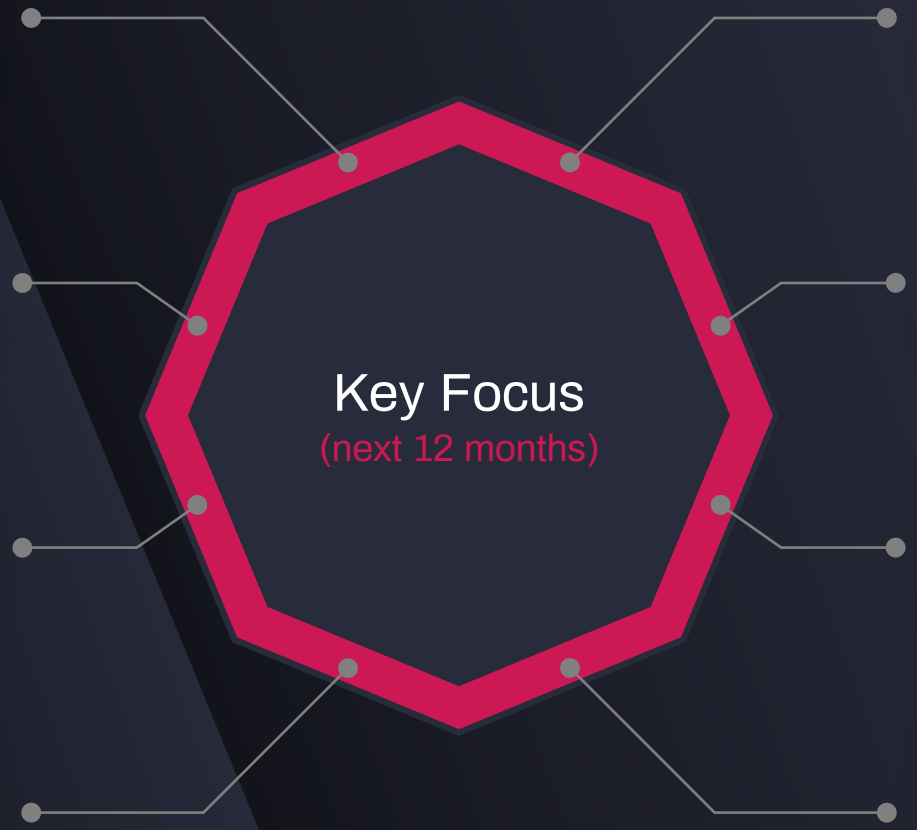
OUTLOOK

Recruitment Completion (1H 2026)
Global enrolment completion with strong retention and adherence.

Regulatory Engagement
Continued collaboration with key regulatory agencies on expedited approval pathways.

Pentacoxib™ Development
Formulation optimisation and progression of development for veterinary and early OA markets.

Scientific Publications
Preparation and publication of peer-reviewed papers from Paradigm's clinical programs.



Interim Analysis (Mid-2026)
Key efficacy and safety readout to guide next regulatory and commercial steps.

Confirmatory Trial
Protocol and site planning underway; clearance anticipated **post-IA**.

Commercial Strategy
Advancing market-readiness and access planning in key regions.

Loyalty Options
Exercise of loyalty options providing non-dilutive funding.

NEWS FLOW & CATALYSTS

Upcoming Catalysts

Event	Target Date
PARA_OA_012 – 25% & 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*

THANK YOU FOR YOUR ATTENDANCE

For more information please visit:

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