ASX RELEASE 19 November 2024

Chairman's Address to 2024 Annual General Meeting

Dear Shareholders,

Welcome everyone to the 2024 Annual General Meeting of Paradigm Biopharmaceuticals. It's a pleasure to extend a warm welcome to all our shareholders here today and to those joining us through the Automic online meeting platform.

In 2024, Paradigm achieved several milestones and delivered positive clinical data across both our osteoarthritis (OA) and mucopolysaccharidosis (MPS) programs. However, we recognise and share the disappointment with the current share price performance, which, in my view, does not accurately reflect the ongoing progress, positive data, and strong engagements with global regulators and commercial partners. We are on the cusp of initiating a pivotal phase 3 trial in the multi-billion-dollar OA market, an area that remains underserved by available treatments. The level of demand we receive annually for our injectable pentosan polysulfate sodium product via the Special Access Scheme (SAS) reinforces the immense need for a new therapeutic option, and we are committed to providing a solution for all those affected by the debilitating impact of OA.

This year at Board level, we welcomed Mr. Matthew Fry as Non-Executive Director. Matthew brings more than 25 years of experience in healthcare, diagnostics, and regulatory engagement, and he has been a critical asset as we navigate global regulatory pathways and advance the commercialisation of iPPS.

Today also marks the last day of Dr. Donna Skerrett serving as an executive Director of Paradigm. Donna's fierce dedication to iPPS and her commitment as a director, while managing multiple global clinical trials across various time zones, has been truly inspiring. Moving forward, Donna's focus will be fully dedicated to executing the phase 3 clinical program and progressing iPPS toward market approval.

Our work over recent years has focused on de-risking this program and applying valuable learnings from each clinical trial to shape our phase 3 PARA_OA_012 clinical protocol. This deliberate approach ensures we provide the highest probability of success for iPPS, both clinically and commercially, as a treatment for the millions of people suffering from OA.

On behalf of the Paradigm Board, I extend my heartfelt thanks to all shareholders, employees, commercial partners, and other stakeholders for their continued support. The

Board is working on ways to reward loyal shareholders, particularly those who have held their PAR stock over the past 12 months. Together, we are advancing Paradigm's vision of providing new hope to those affected by OA and other musculoskeletal diseases.

Yours Sincerely,

Paul Rennie

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 is currently developing pentosan polysulfate sodium for the treatment of pain associated with musculoskeletal disorders driven by injury, inflammation, ageing, degenerative disease, or genetic predisposition, such as osteoarthritis (phase 3) and mucopolysaccharidosis (phase 2).

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.

To learn more please visit: www.paradigmbiopharma.com

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PARADIGM BIOPHARMA

ANNUAL GENERAL MEETING | 19 NOV 2024

Welcome

Board of Directors

Experienced team to drive clinical success and commercialisation

PAUL RENNIE
Founder & Managing Director

DR. DONNA SKERRETT
Executive Director & Chief Medical Officer

Matthew Fry
Non-Executive Director

AMOS MELTZER
Non-Executive Director

Company Update

Paul Rennie, Managing Director

Agenda

- Company Update
- Notice of meeting & formal business
- Questions relating to Company Update

Disclaimer

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2024

What we set out to achieve

- Phase 3 OA program protocol acceptance from US FDA for progression with lowest effective dose (2 mg/kg twice weekly).
- Regional licensing agreement(s) in OA and MPS.
- Pivotal study commencement of recruitment.
- TGA provisional approval determination application submission.
- Peer-reviewed manuscript submissions for publication of PARA_OA_008 phase 2 clinical trial in key scientific journals.

2024 | Key Company Milestones

Q1

- **OARSI Conference:** Paradigm presented phase 2 data at the Osteoarthritis Research Society International (OARSI) Congress
- **R&D Tax Incentive**: Received a $7.3 million refund, aiding cash flow
- **Board Addition**: Welcomed Matthew Fry as Non-Executive Director
- **Type D Meeting with FDA**: Discussion with the FDA on requirements for the phase 3 clinical program in osteoarthritis

Q2

- **Bio International Conference**: Paradigm executives attended the event to engage with global industry leaders and potential partners
- **TGA Application:** Submitted provisional approval application to the Australian TGA
- **FDA Submission**: Submitted phase 3 clinical program response package, including key nonclinical and clinical data

Q3

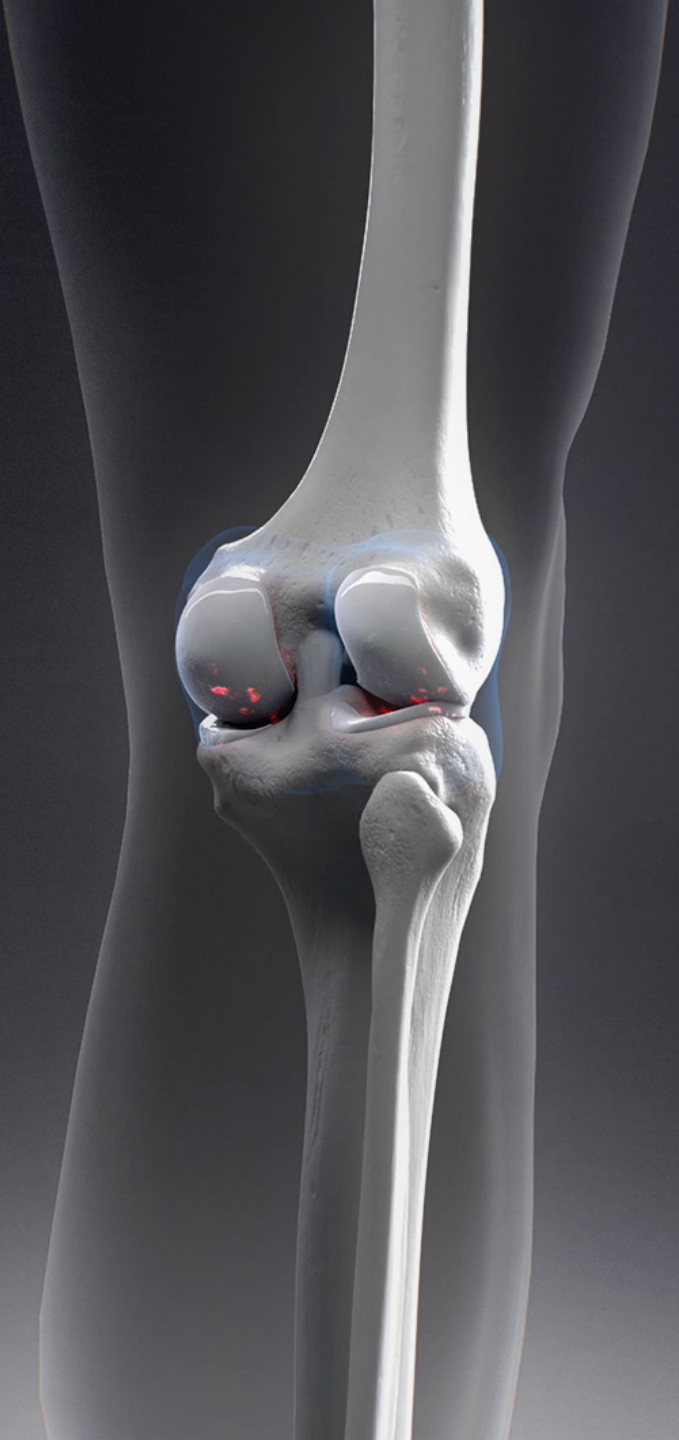
- **Manuscript Completion and Peer Review Submission**: Manuscripts on the PARA_OA_008 phase 2 trial results and comparative analysis of iPPS vs. other OA treatments completed and submitted for peer review.
- **Phase 3 Protocol Submission**: Submitted final phase 3 protocol to the FDA, with review completion expected by November 2024
- **FDA Feedback**: Received guidance on phase 3 program, finalising protocol adjustments

Q4 (Projected)

- **FDA Approval**: Anticipated FDA review and agreement of phase 3 protocol for PARA_OA_012
- **CRO Selection**: Finalising the selection of Contract Research Organisation for phase 3 trial
- **TGA Response**: Determination response on provisional approval application in Australia.
- **R&D Rebate Completion**: Expected rebate of $5-6mt o support ongoing activities

Osteoarthritis

OA



Lead Program Osteoarthritis

Global Phase 3 Progress

Achievements

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.

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

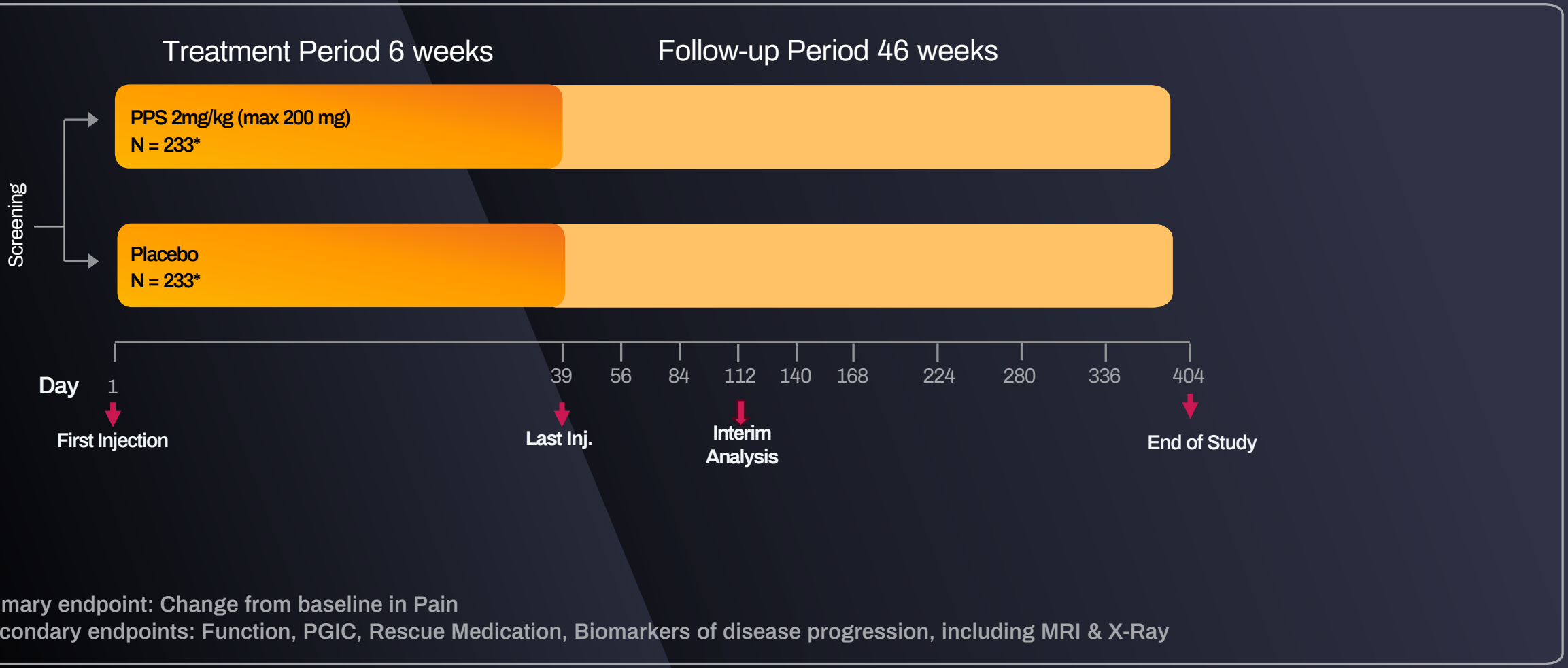
- FDA feedback on clinical endpoints and statistical procedures.
- Structural changes will be evaluated via X-ray and MRI as secondary endpoints consistent with regulatory guidance.

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

Lead Program Osteoarthritis

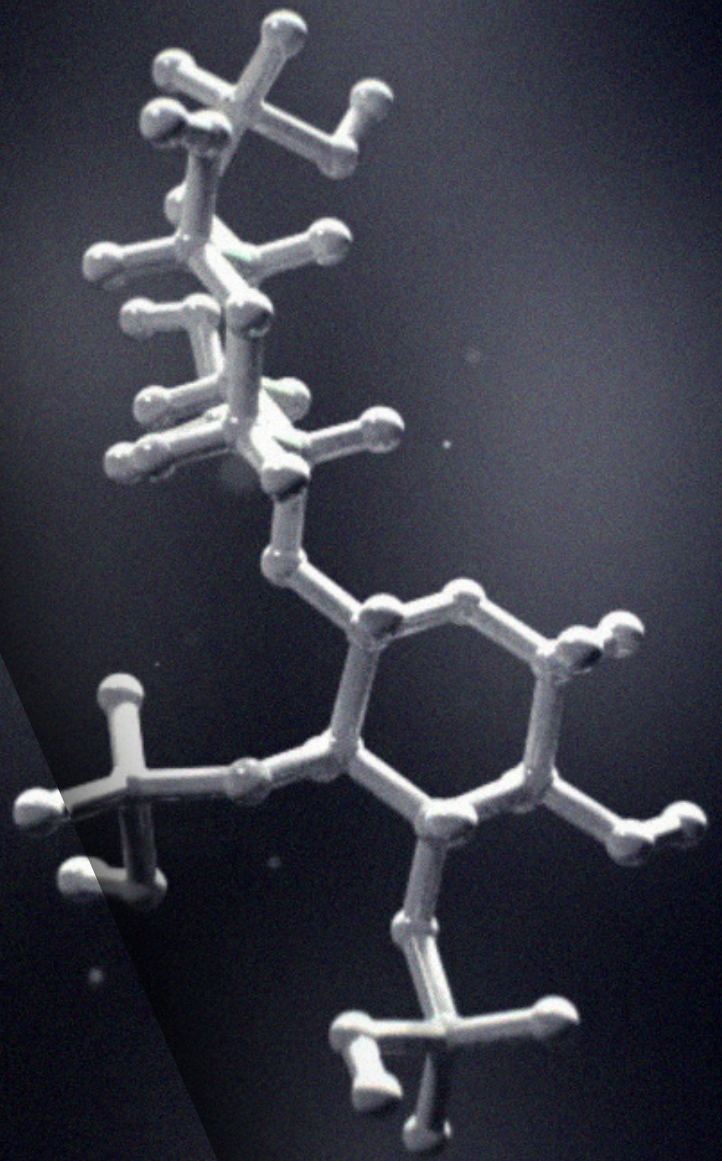
Global Phase 3

Key Expected Milestones Next 12 Months

Key plans for the next 12 months for Paradigm's global Phase 3 OA program include:

- **FDA Protocol Review and Approval**: Complete the FDA review of the Phase 3 protocol, expected by November 2024, to proceed with the Pivotal clinical trial.
- **CRO Selection**: Finalise the selection of a Clinical Research Organisation (CRO) to manage the global Phase 3 trial, and complete site selection by the end of Q4 2024.
- **Commence Patient Enrolment**: Begin patient pre-screening and enrolment activities in Q1 2025 at approximately 10 Australian trial sites.
- **Global Roll Out**: Activation of sites in US, CAN, UK for Pivotal phase 3 program and commence patient enrolment.
- **TGA Provisional Approval Pathway**: TGA determination on provisional approval; if positive, prepare a full dossier submission to expedite Australian market entry.

Company UPDATE



Partnering Update

Commercial strategy for iPPS

Ongoing Commercial Partnering Efforts

- Active engagement with key potential partners to support and co-fund late-stage development and future commercialisation.
- Feedback: FDA phase 3 trial acceptance is a critical milestone to further those discussions.
- Assuming FDA clearance, Paradigm can progress discussions with potential partners to indicative terms.

Milestone: Green Light for Global Phase 3

- Paradigm anticipates a critical regulatory milestone with the green light from the US FDA for the Global Phase 3 trial of iPPS for OA, expected by end of 2024.

Finance

Significant Reduction in Cash Burn Achieved

Targeted Reduction:
- Cash outflows for recent quarters under forecast, with September quarter reduced to $4.72M, below the $7M guidance.

Strategic Financial Management:
- December quarter forecast to remain at or below $7M, focusing on critical research and operational efficiency.
- Tight quarterly budget controls to align funding with key clinical and regulatory milestones.

Aggressive Cost Containment:
- Operational overheads reduced by over $1M per quarter from early 2024.
- Streamlined team post-MPS phase 2 completion to prioritise OA Phase 3 trials.

Optimisation of R&D Spending:
- Prioritising high-impact research, reducing R&D costs while progressing Phase 3 OA programme.
- Enhancing efficiencies in site management and participant recruitment to minimise enrolment costs.

Supplier and Contract Efficiency:
- Renegotiating service contracts to secure favourable terms and control trial expenses.
- Exploring options for fixed price budget structure from CRO for phase 3 clinical trial.

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.

Contingency Planning:

- The company guided that the option exercise of approximately 60 million shares at $0.65 could provide further funding to extend cash runway until at least mid-2025.
- Option exercise success appears low, and we are exploring a range of alternative funding strategies to replace this cash runway.
- While non-dilutive funding is preferred, convertible notes or equity raises remain viable solutions if additional capital is required to maintain momentum into pivotal clinical programme.

Maintaining Cash Conservation Measures:

- Continued focus on cost management and prioritisation of expenditures to extend cash runway.

Clear 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

* Subject to Regulatory approvals and funding.

Thank you for your attendance

For more information please visit:
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