ASX RELEASE 25th January 2022

2021 Annual General Meeting

Paradigm Biopharmaceuticals Ltd (ASX: PAR) (Paradigm or the Company), a clinical stage biopharmaceutical company focussed on repurposing existing molecules for new indications with unmet clinical needs, is pleased to provide a copy of the Chairman's address delivered by Mr Paul Rennie at today's Annual General Meeting (AGM) to shareholders. Following the Chairman's address, Dr Donna Skerrett, Interim CEO and Chief Medical Officer will provide the CEO and business update.

Investors wishing to attend today's AGM can find details to access the meeting in the Notice of Meeting lodged with the ASX on the 24th December 2021.

-Ends-

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2021 AGM Chairman's Address

Dear Shareholders,

Good morning and I welcome you to this **Annual General Meeting of Paradigm Biopharmaceuticals Ltd.** I am Paul Rennie Non-Executive Chairman. Today's meeting is being held online via the Computershare Meeting Platform. This allows Shareholders, Proxies and Guests to attend the meeting virtually. Wherever you're joining us from today, I thank you for your participation.

Paradigm Biopharmaceuticals is a global Australian-based pharmaceutical company focused on repurposing existing molecules to meet high unmet medical needs. Paradigm's purpose is to develop and commercialise pentosan polysulfate sodium (PPS) for the treatment of arthralgia driven by injury, inflammation, aging, degenerative disease, infection, or genetics.

The immediate commercial focus is the repurposing of the historic drug pentosan polysulfate sodium (PPS or brand name Zilosul®) for the treatment of pain associated with osteoarthritis (OA). This is a global unmet need and Paradigm has advanced towards phase 3 trials for this indication. There is strong scientific evidence that the drug PPS addresses all aspects of the disease: inflammation, pain, and cartilage preservation, suggesting PPS has OA disease modifying potential.

Other indications include the treatment of pain and arthropathy and other disease complications in patients with the rare genetic disorder mucopolysaccharidoses (MPS); treating alphavirus induced arthralgia (in patients with Ross River virus and Chikungunya); chronic heart failure (CHF) and potentially acute respiratory distress syndrome (ARDS).

I am pleased to report that the company has continued to progress the development of Zilosul® for the treatment of pain associated with osteoarthritis by submitting an IND (Investigational New Drug) application with the US FDA in March 2021. The IND submission was the result of many years of substantial work by the entire Paradigm team as well as several meetings with key regulatory agencies the FDA, EMA and TGA to develop a clinical protocol acceptable for registration by these regulators.

Paradigm achieved the significant milestone of an open IND application following notification from the US FDA, which was announced to the market on 3rd November 2021.

In addition to pursuing the phase 3 trial, we continue to progress development of Zilosul® with the commencement of the PARA_OA_008 study in Australia. This study seeks to evaluate molecular biomarkers in the synovial fluid of the knee joint to demonstrate the mechanism of action and OA disease modifying potential of Zilosul® on the diseased joint. The biomarker analysis aims to provide key scientific evidence about the local activity of Zilosul® in the knee joint of OA subjects. The biomarkers analysis will include an analysis of inflammatory cytokines, pain mediator nerve growth factor (NGF), cartilage degrading enzymes, and products of cartilage degradation. Additionally, clinical, and radiographic assessments will be obtained.

The significance of this study is also the commercial potential of Zilosul In the amount that the market is prepared to pay for Zilosul.

In addition to the progress being made in the clinical development program for osteoarthritis, development of PPS for MPS (where Paradigm has received orphan status from the FDA and EMA for MPS I and MPS VI) continues with two major milestones achieved in FY21.

In November 2020 we announced that the first patient was dosed in a Phase II study in Adelaide, South Australia evaluating the safety and efficacy of PPS on pain and functional symptoms in MPS type I patients who have received ERT and/or haemopoietic stem cell transplantation (HSCT).

In June 2021, the company announced that it had received approval from the ANVISA, the Brazilian regulator, to commence a Phase II study in Brazil to evaluate the safety, tolerability, and effect of PPS on pain, function, and glycosaminoglycan (GAG) levels in patients with MPS type VI. Brazil has the highest concentration of MPS type VI sufferers globally. The first participant in this study was reported in September and the clinical program under Principal Investigator Dr. Roberto Giugliani continues to progress.

Much of the investment in FY21 was focused on identifying and then meeting the requirements of the regulatory pathways for clinical development for the lead programs. Infrastructure and organisational support were strengthened for current and upcoming clinical trial activities. We engaged key opinion leaders and industry experts to work alongside our in-house teams to enhance success in advancing the programs. Investment will continue as we progress with both the global clinical pivotal program and projects to optimise commercial and partnering attractiveness for Zilosul®.

During FY21 Paradigm welcomed Non-Executive Directors Ms. Helen Fisher and Mr. Amos Meltzer and Executive Director Dr Donna Skerrett to the Board. Ms. Fisher, previously a Tax Partner at Deloitte, Mr. Meltzer who has a background in science and commercialisation and is an intellectual property lawyer, and Dr Skerrett, who has three decades of experience in clinical research and development, bring a wealth of experience to Paradigm. These appointments improve the composition of the board in terms of independence and governance, experience, gender diversity and will contribute to the success of Paradigm into the future.

Today, Paradigm's fundamentals remain very strong:

- We are repurposing the only FDA approved version of the drug PPS (Pentosan Polysulfate Sodium) for which we have a 25-year period of exclusivity from market authorisation.

- There is a very significant unmet medical need, i.e., the need to treat chronic pain with non-opioid based medicines.

- Our Company has a clear regulatory pathway to commercialisation with our Phase 3 clinical program, which is harmonized with the regulators in our key markets: EU - EMA, the US - FDA and Australia - TGA.

To learn more please visit: www.paradigmbiopharma.com

Approved for release by the Paradigm Board of Directors

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PARADIGM

BIOPHARMA

Annual General Meeting

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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.

Paul Rennie, Chairman

Welcome

Dr. Donna Skerrett, CMO & Interim CEO

CEO & Business Update

Paradigm's Vision

Paradigm Biopharmaceuticals Limited (PAR) is a global biopharmaceutical company driven to improve patients' lives through repurposing existing drugs and pioneering new solutions for unmet medical needs.

Objectives FY 2021 - Repurpose Pentosan Polysulfate Sodium

1. Conduct research and pivotal studies to gather data for successful harmonized global registration/reimbursement and commercialisation-open IND and initiate global phase 3 program
2. Strengthen continuity of supply and product exclusivity
3. Quantify commercial opportunity for each disease state for global sales and by region to guide resource use
4. Achieve commercial sale of PPS for OA in AUS as early as possible
5. Assess commercialisation options
6. Explore customer focused solution for differentiation and patient convenience
7. Increase investor interest and confidence in Paradigm
8. Create a company culture of inclusion and accountability for successful delivery of programs while being mindful of maximising shareholder value

1. Lead Program Osteoarthritis

De-risked phase 3 asset in blockbuster indication with large unmet medical need

Clear Harmonised Pathway

- Obtained regulatory feedback (FDA, TGA, EMA) for a harmonised clinical protocol to achieve simultaneous registration in key jurisdictions.
- 002 and 003 protocol designed to achieve pain and function label.
- 26 GLP nonclinical studies and western PK studies completed and submitted to FDA IND, IND and regional ethics cleared to start
- Incorporated additional outcomes into clinical trial program; expected to facilitate reimbursement outside of US.

Actively screening and enrolling participants

- Enrolment initiated in AUS & US, UK and EU site ongoing
- First subjects randomised and commenced dosing.

DMOAD (disease modifying OA drug)

- Study in progress (PARA_OA_008) to evaluate DMOAD and support TGA provisional application. Study extended for single in addition to biweekly injection for translation with phase 3 dosing.

2. Exclusive Supply & Manufacture

Supply chain ready to partner

- Extension of exclusive supply agreement with bene pharmaChem, 25 years from the date of marketing approval.
- Expansion of indications covered under the agreement.
- Collaboration agreement to co-fund new projects. Bene and Paradigm will jointly fund the new R&D activities and work collaboratively on new Intellectual Property creation which Paradigm will commercialise.
- IP generation ongoing.

Scalable Model to accommodate Future Indications

3. Pricing and Reimbursement

Market research conducted with specialists, funding authorities and patients in US, UK, DE and FR.

- Representative cross section of global pricing and reimbursement scenarios.
- Blinded - product and company not identified.
- Product profile based on preliminary clinical data.

Outcomes

- Place in therapy: pain and function-second line after oral NSAIDS, DMOAD may be used earlier in therapy.
- Current clinical program sufficient for funding evaluations in the US.
- Confirmed early PAR price estimation of US$2500 per year for pain and function (P&F) is likely acceptable for the US market, potential increase to US$6000 per year for DMOAD.
- Optimize funding determinations in non-US reimbursed markets by incorporating additional outcomes (e.g. duration of effect, retreatment) into clinical trial program.
- Ongoing advice to provide further guidance.

4. PPS via SAS and EAP

Special Access Scheme (SAS)

- First revenue via the provision of Zilosul® (injectable Pentosan Polysulfate Sodium (**iPPS**)) under the pay-for-use SAS.
- Under the TGA SAS, Zilosul® has been made available to physicians with SAS approval to treat previous SAS participants seeking re-treatment and other subjects that would not qualify for recruitment into the Para_OA_008 or Para_OA_002 clinical trials.

Expanded Access Program (EAP)

- 65% mean reduction in WOMAC pain from baseline at week 12 (day 81-83) across total patient population (n=10) using WOMAC Pain Subscale.
- Under the protocol agreed with the US FDA for the EAP, clinical monitoring of participants concluded following the 12-week follow-up.
- Paradigm has regular contact with the 10 participants all whom are over 18-months post treatment phase and are exploring a re-treatment EAP.

5. Commercialisation Options

Preference is to partner

- Maintain optionality to bring Zilosul to market ourselves

De-risked phase 3 asset with globally accepted trial design in key markets

Increased inbound interest in partnering OA since open IND

- Global / regional partnerships preferred
- Option to partner pipeline indications to a single partner, or partner by indication
- Interested party discussions taking place in OA and MPS

Re-purposing Opportunities

- R&D pipeline advanced in HF and Respiratory
- Evaluated five repurposing opportunities.
- Each opportunity is subject to a multidisciplinary assessment

5. Pipeline

- Developing new indications in parallel to lead program in OA

Indication / Action of PPS	Stage of Development
Mucopolysaccharidosis (MPS) • Reduction of tissue GAGs • Pain target: NGF • Anti-inflammatory target: NF-kB • Cartilage degeneration target: ADAMTS-5; MMPs	• MPS I (AUS) :Open label trial currently enrolling up to 10 subjects. Dosed weekly for 12-weeks then every other week for a total of 52 • MPS VI (Brazil): A double-blind placebo-controlled trial with 12 subjects. Dosed weekly for 24-weeks.
Alphavirus induced arthralgia • Anti-inflammatory target: NF-kB • Pain target: NGF • Cartilage degeneration target: ADAMTS-5; MMPs	• Phase 2 Clinical study in participants with RRV (completed) • Preclinical Proof-of concept for CHIK-V: • (Institute for Glycomics; Queensland)
Heart Failure • Adverse tissue remodeling target: ADAMTS-4 • Anti-inflammatory target: NF-kB • Vascular endothelial inflammation target: CAM (Cell Adhesion Molecules)	• Preclinical Dose translational study: • (Center for Heart Failure Research & Institute for Experimental Research, Oslo University, Oslo)
Respiratory (ARDS, AR, SARS-Cov-2) • Cytokine storm anti-inflammatory target: NF-kB • Inhibition of complement activation • Anti-viral effects	• Preclinical Proof-of-concept study mouse model of ARDS mediated by influenza infection • In Vitro study in collaboration with bene pharmaChem and Ronzoni Institute on PPS inhibition on attachment and infection by SARS-CoV-2.

6. Improving value of the Asset

Clinical program will support broad label, maximise reimbursed price and market penetration from launch.

Clinical and commercial activities to improve Zilosul label

- 006 & 007 determine long term durability of effect
  - Differentiate from current therapies and improve cost effectiveness for payers.
- 009 retreatment study
  - Establish safety and efficacy of repeated dosing for regulatory bodies and payers.
- 010 OA in Hip (approx. 19% of the OA market, potential $3B value based on market size and indicative price of Zilosul)
  - Expand label with selected dose from 002

All studies to support label claims, registration and funding in reimbursed markets

- Seeking to align clinical studies to maximise product launch value to mitigate against further studies for pain and function after launch.
- Delivery device for patient & prescribing physician convenience.
- Market Access Strategy (by Region / Country) under development to streamline market access post registration

Activities are occurring in parallel to clinical program

7. Investor Engagement

- **Company Rebranding**: In January 2021 Paradigm successfully rebranded at the JP Morgan Healthcare conference. Central to this rebrand is the focus on repurposing molecules.
- **Global and Aus Conference Presentations**: JP Morgan Healthcare Conference, Evercore ISI HealthCONx, Truist Life Sciences Conference, Goldman Sachs SMID Cap Conference, BIO Partnering Conferences, Bell Potter, MST Access and other broker Healthcare days.
- **Investors**: Consistent news-flow updates, R&D Day presentation, road shows.
- **Publications**: RRV, CHIKV, MPS

8. Global Focus

During the year we took several steps to continue to build our organisation to support commercialising Zilosul®, these include:

- **Incorporating a US entity:** Several strategic roles in our Clinical and Safety functions now reside in the US with plans to add further resources as we progress our clinical efforts to commercialisation of PPS.
- **Commenced Commercial reimbursement and outcomes research**.
- **Additions to Paradigm Team:** Paradigm has added further resources in Clinical Operations, Global Head of OA, R&D and Safety.

Newsflow Remainder of FY 2022

- ✓ First Ph3 AU patients dosed
- UK ethics approval
- First patient dosed US – 002 recruitment update
- EAP retreatment approval
- 008 last patient randomised (100% recruitment)
- Pipeline indications – Next Steps
- EU ethics approval
- First sites open UK
- First patients dosed UK - 002 recruitment update
- New CEO appointment

For more information please visit:
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