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SUCCESSFUL COMPLETION OF $16M PLACEMENT TO COMMENCE GLOBAL PHASE 3 CLINICAL TRIAL

KEY HIGHLIGHTS

- **Successful $16 Million Capital Raising:** Paradigm receives firm commitments to raise $16 million through a placement to institutional and sophisticated investors, through the issue of 40 million shares at $0.40 each. This will fund the global Phase 3 clinical trial setup and other strategic initiatives.
- **Phase 3 Clinical Trial Focus:** The funds to primarily support global Phase 3 trials for osteoarthritis treatment with iPPS, beginning in Australia (Q1 CY2025) and expanding to key U.S. sites (Q2 CY2025). The study aims to demonstrate improvements in pain and function.
- **Loyalty Option Incentive Program:** Shareholders anticipated to receive one Loyalty Option for every four shares held at the Record Date (defined below), exercisable at $0.65 within 12 months from the Record Date. This could raise up to an additional ~$63 million by early 2026, enhancing shareholder value.
- **Use of Funds:** The $16 million expected to be allocated as follows: $5.5M for trial setup, $6.1M for site recruitment, $1.5M for manufacturing, $1.2M for NDA studies, and $1.7M for working capital and covering costs of the capital raise. Pro forma cash balance post-raise is expected to be $26.9 million
- **Cash Position**: Approximately $26.9m December pro forma cash balance post capital raising providing runway into 2H CY2025.

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, is pleased to announce that it has received firm commitments for a capital raising totalling $16 million through a placement of fully paid ordinary shares In the capital of the Company (Shares) to sophisticated and institutional investors (Placement). This funding will support the Company's phase 3 global start-up, site initiation commencing firstly in Australia and other strategic initiatives.

The Placement received strong interest from new and existing institutional and sophisticated investors both domestically and internationally.

Paradigm Managing Director Paul Rennie stated: "*The capital raise, priced at $0.40, represents a 3% premium to the 30 VWAP. The size of the raise of $16M provides Paradigm with sufficient cash reserves to commence the start-up of the Phase 3 clinical trial and working capital into 2H CY2025. We received support from our current and new investors which highlights the strength of our clinical programs and positions Paradigm to immediately advance our global phase 3 clinical trial setup and deliver on critical milestones. We chose to reward all shareholders with a loyalty option with the record date likely to be mid – late January 2025. 2024 has been an important year of dealing with regulatory agencies and now we are looking forward to the execution of our phase 3 clinical trials to move ever closer to bringing iPPS to those suffering seriously debilitating*

pain and dysfunction. We are grateful for the continued support and enthusiasm of our shareholders".

Capital Raise Summary

The Placement will involve the issue of 40 million Shares at an issue price of $0.40 per Share, comprising:

- 40 million shares to be issued under the Company's available placement capacity under Listing Rule 7.1.

The Placement price of $0.40 per Share represents:

- 10.6% discount to 15-day volume weighted average price ("VWAP"); and
- 2.9% premium to 30-day VWAP.

Bell Potter Securities Limited acted as sole lead manager and bookrunner to the Placement. Blue Ocean Equites Limited acted as co-manager to the Placement.

Loyalty Option

As a way to reward shareholders, the Company currently intends to issue one (1) listed option for every four (4) Shares held at the Record Date ("Loyalty Options"). The Loyalty Options will be exercisable at $0.65 and have a 12-month expiry from the Record Date. The record date for the Loyalty Options will be 4 business days following lodgement of a prospectus for the Loyalty Options, expected in late January 2025 ("Record Date").

Upon exercise of every two (2) Loyalty Options, the holder will receive one (1) piggyback option, exercisable at $1.00, expiring 24 months from the date of expiry of the Loyalty Options.

Summary Use of Funds

The proceeds of the capital raising will be allocated to support the following:

- Phase 3 Clinical Trial Setup: Global initiation and site recruitment in Australia (Q1 CY2025) and United States (Q2 CY2025);
- Manufacturing and Inventory: Preparation for Phase 3 and NDA submission;
- Regulatory Enabling Studies: To support eventual regulatory submissions;
- Working Capital: Including hiring and offer-related expenses; and
- Costs of the capital raise.

Allocation of Funds (A$ millions)	$16.0
Phase 3 Trial Setup	$5.5
Site Recruitment	$6.1
Inventory & Manufacturing	$1.5
NDA Enabling Studies	$1.2
Working Capital and costs of the capital raise	$1.7

The Company expects approximately a $26.9m December pro forma cash balance post Placement. The Company also intends to seek non-dilutive funding from a partnering or regional licensing deal to materially extend its runway. In addition, the exercise of all

Loyalty Options could raise up to an additional ~A$63.3 million from shareholders by early CY2026.

Indicative Timeline

Event	Date
Trading Halt	Thursday, 5 December 2024
Placement Closes	Friday, 6 December 2024
Announcement of Completion	Monday, 9 December 2024
Settlement	Thursday, 12 December 2024
Allotment	Friday, 13 December 2024

This timetable is indicative only and subject to change. The Company reserves the right to vary the above dates and times, subject to ASX Listing Rules and the Corporations Act 2001 and other applicable laws.

Upcoming Catalysts

Event	Target Date
FDA 30-day review completion, proceed to Pivotal Phase 3 PARA_OA_012 trial	Complete
Australian Ethics Submission – Phase 3 PARA_OA_012	Q4 CY2024
Regional licensing agreement(s) in OA and MPS.	CY2025
PARA_OA_012 – First Australian participant enrolled.	Q1 CY2025
PARA_OA_012 – First US participant enrolled.	Q2 CY2025
PARA_OA_008 Peer Review Publications – 2 manuscripts submitted to separate journals for review and anticipated publishing in CY25.	1H CY2025
PARA_OA_012 – 50% Recruitment of participants	2H CY2025*
PARA_OA_012 Interim Analysis – 50% participants reach Day 112	1H 2026*

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

Company Update

Paradigm wishes to also provide the following update on recent developments and ongoing initiatives. Below are key updates regarding recent option expiry, regulatory progress, and the Paradigm employee long term incentive plan. The Company remains focused on advancing its clinical programs, delivering value to shareholders, and addressing the significant unmet medical need in osteoarthritis.

Expiration of Listed PARO Options

Paradigm advises that the listed PARO options expired on 30 November 2024. The Company received less than $500 in funds from the exercise of options by eligible holders. As discussed during the recent Annual General Meeting (AGM), the Paradigm Board is committed to rewarding shareholders and plans are underway to introduce a new option program in the future as part of this initiative. Shareholders will be provided with further details on this program at an appropriate time. The Company thanks its shareholders for their continued support as it progresses its pivotal clinical activities.

Therapeutic Goods Administration (TGA) Determination

Based on recent feedback from the TGA, Paradigm has been informed that the TGA acknowledges the preliminary clinical results for PPS demonstrated benefits that could be clinically meaningful to patients suffering from moderate to severe osteoarthritis (OA) of the knee. However, the TGA noted that for patients with minor or mild osteoarthritis, this is not considered seriously debilitating.

After reviewing the currently available clinical data, the TGA concluded that the data supports PPS entering the therapeutic landscape through the traditional registration pathway (CTX), rather than via a provisional determination application. The TGA further recognised that Paradigm provided sufficient evidence to support its plan to submit comprehensive clinical data on PPS's safety and efficacy. Additionally, the TGA agreed that the proposed phase 3 OA program, if successfully executed, will provide the necessary evidence to support full registration of PPS in Australia.

Paradigm remains committed to pursuing this route and emphasises the U.S. FDA's recognition of iPPS through its Fast Track designation for the OA program, highlighting the potential importance of this treatment.

Phase 3 PARA_OA_012 Trial Details

Eligible patients will have a clinical and radiographic diagnosis of knee OA with (Kellgren-Lawrence [K-L] grade 2, 3, or 4), knee OA pain unresponsive to conservative non-pharmacologic and pharmacologic therapy. Randomisation to treatment will be stratified by K-L grade and baseline average daily pain (ADP) NRS score in the index knee.

The objective of this study is to demonstrate the improvement in pain and function with subcutaneous injections of pentosan polysulfate sodium (iPPS) compared with subcutaneous injections of placebo in participants with knee OA pain. Study details include:

- The study duration will be up to 64 weeks.
- The treatment duration will be 6 weeks.
- The visit frequency will be twice weekly during treatment.
- The visit/contact frequency will be every 4–6 weeks during the 52-week follow-up.

Objectives and Key Endpoints for iPPS Treatment in Knee OA Pain

Primary Objective: Evaluate the effectiveness of PPS in reducing knee pain.

- **Primary Endpoint**: Change from Baseline (CFB) at Day 112 in knee pain as assessed by the weekly ADP (average daily pain) score on the numerical rating scale (NRS) 11-point (0–10) scale.

Key Secondary Objectives

- Assess the impact of PPS on knee function.
    - **Key Measure**: CFB in function based on WOMAC NRS 3.1 Index (functional subscale) at Day 112.
- Evaluate overall patient-reported improvement.
    - **Key Measure**: Patient Global Impression of Change (PGIC) scores at Day 112.

- Analyse the proportion of participants with meaningful and substantial improvement:
  - **Pain**: ≥30% and ≥50% reduction in pain scores by Day 112 and other intervals.
  - **Function**: ≥30% and ≥50% improvement in function scores.

Additional Secondary Endpoints

- Effects on pain and function from baseline through day 365
- Changes in knee stiffness, quality of life (QoL), and use of rescue medication.
- Long-term assessment of knee structure via MRI (cartilage volume, synovitis, bone shape) and X-ray (joint space width).
- Evaluation of work productivity and activity (WPAI scores).

Safety and Exploratory Outcomes

- Monitor adverse events, adverse events of special interest and overall treatment tolerability.
- Explore PPS effects on biomarkers and pharmacokinetics (PK).

Interim Analysis Criteria

The interim analysis (IA) will be conducted by the independent DMC. Statistical rules for the analysis will be documented in the statistical analysis plan for the interim analysis. An early conclusion of efficacy may be established if a rigorous effect size is demonstrated. A conclusion of futility may be established for minimum treatment effect with low probability of success. Should early efficacy or futility not be established at the IA, the trial will proceed to the final analysis with the full sample size (N=466).

Strategic Enhancements to Trial Design

Paradigm's Type D discussions with the FDA provided meaningful feedback regarding the trial design of this pivotal phase 3 study. Establishing a primary endpoint at least 8 weeks post-final injection (Day 112) was emphasised as important for a chronic OA treatment indication. This timeframe aligns with regulatory and market expectations for sustained efficacy in chronic conditions. Paradigm has increased the study's sample size by approximately 60 participants based on the target effect size of 0.3 for the sample size determinations. This provides statistical power for demonstrating clinically meaningful and statistically significant outcomes for regulatory and commercial expectations.

Advantages of Average Daily Pain as a Primary Endpoint

The selection of average daily pain (ADP) as the primary endpoint for this trial reflects advantages over traditional measures such as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale. Average daily pain provides a more data points for the assessment of patients' pain experiences, thus providing a more consistent assessment of the response to pain. This approach increases sensitivity to detecting changes in pain levels between treatment groups over time. The adoption of average daily pain as the primary endpoint enhances the reliability of pain outcome measurements and aligns with the FDA's guidance on best practices for chronic pain assessments. The last product registered, by the US FDA, for the treatment of OA pain

(2017), was the slow-release intraarticular steroid, which used the daily average pain score to 24 weeks as its primary endpoint[3].

Long-Term Incentive (LTI) Plan

Paradigm is pleased to announce the implementation of its Long-Term Incentive (LTI) program for staff. This initiative is designed to drive employee retention, align their efforts with shareholder interests, and foster long-term value creation for the Company.

Under the LTI program, performance shares will be granted to employees, with vesting based on achieving three critical milestones over a three-year term:

1. **Shareholder Target**: Achieving a compound annual growth rate (CAGR) of 40% in total shareholder return.

2. **Employee Target**: Staff remaining employed until the vesting date and meeting performance standards under the Company's performance management system.

3. **Company Target**: Successful completion of the Phase 3 trial for iPPS for OA and filing a New Drug Application (NDA) with the U.S. FDA.

This program highlights Paradigm's commitment to building a high performing, aligned team capable of delivering significant shareholder value. The Company will continue to support its employees in achieving these milestones and looks forward to their contributions to Paradigm's success.

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About Paradigm Biopharmaceuticals Ltd.

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 focus is developing injectable (subcutaneous) pentosan polysulfate sodium (iPPS) for the treatment of diseases with inflammatory pathogenesis, where the anti-inflammatory and chondroprotective properties of iPPS may be transformative to current care.

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.

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References

1. Cash balance of A$13.15 million as of 30 September 2024, expected December 2024 quarter spend of $7.00m maximum and R&D Refund provision estimate of $5.5m.

2. All dollar amounts are in Australian dollars unless otherwise stated.

3. https//zilrettapro.com/efficacy,

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

Approved for release by the Paradigm Board of Directors.

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