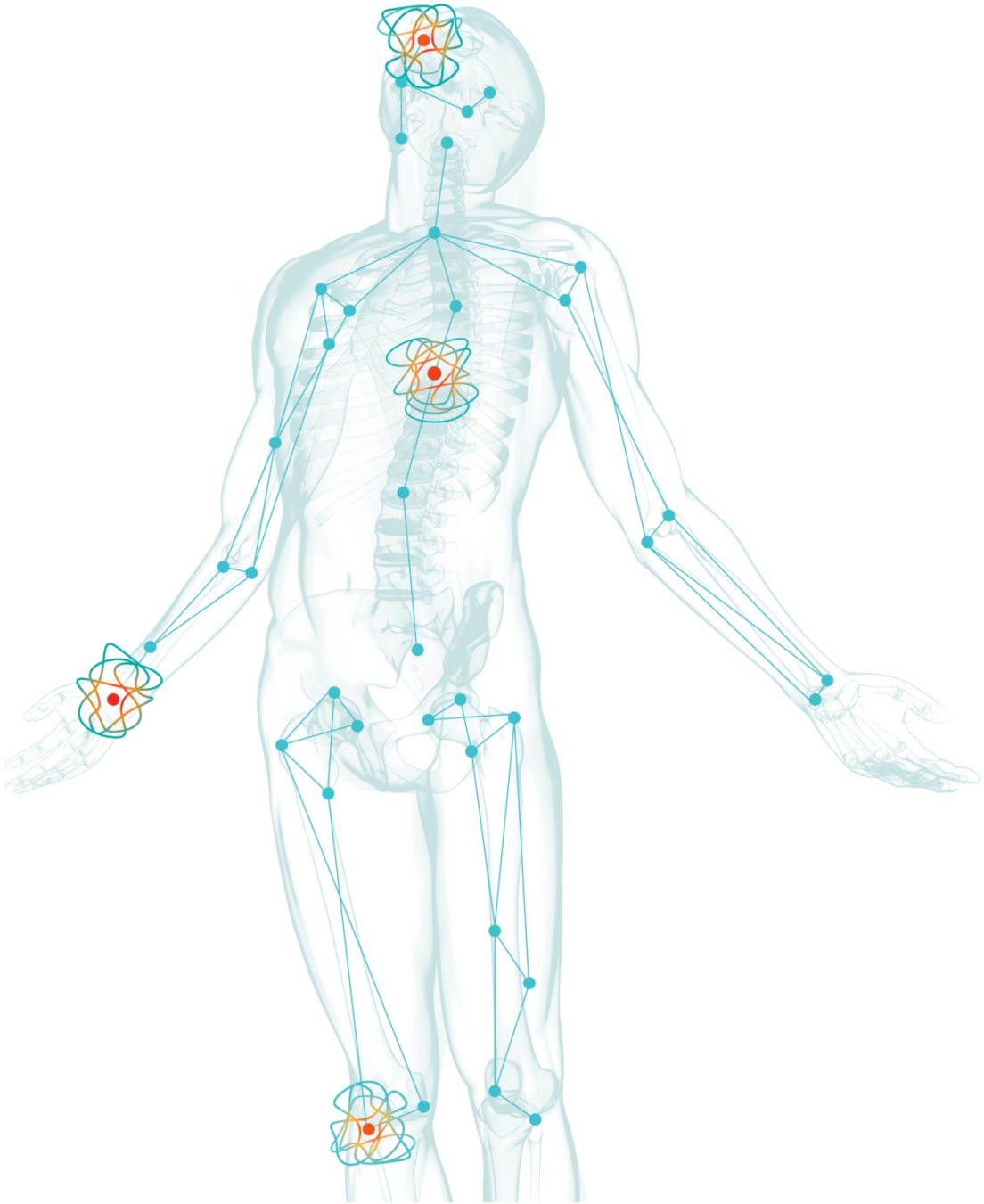
paradigm
BIOPHARMA

Phase 2b OA/BMEL Clinical Trial Results Presentation



18 December 2018

Disclaimer

This document, together with any information communicated by Paradigm Biopharmaceuticals Ltd (known as “Paradigm”, “Paradigm Biopharma” or “the Company”), in any presentation or discussion relating to this document (collectively, “Information”) is confidential, and has been prepared by the Company on the condition that it is for the exclusive information and use of the recipient. The Information is proprietary to Paradigm and may not be disclosed to any third party or used for any other purpose without the prior written consent of the Company.

The Information is based upon management forecasts and reflects prevailing conditions, which are accordingly subject to change. In preparing the Information, the Company has relied upon and assumed, without independent verification, the accuracy and completeness of all information available from public sources, or which was otherwise reviewed by it. In addition, the analyses are not and do not purport to be appraisals of the assets, stock or business of the Company. Even when the Information contains a kind of appraisal, it should be considered preliminary, suitable only for the purpose described herein and should not be disclosed or otherwise used without the prior written consent of Paradigm. The Information is provided on the understanding that unanticipated events and circumstances may occur which may have significant valuation and other effects.

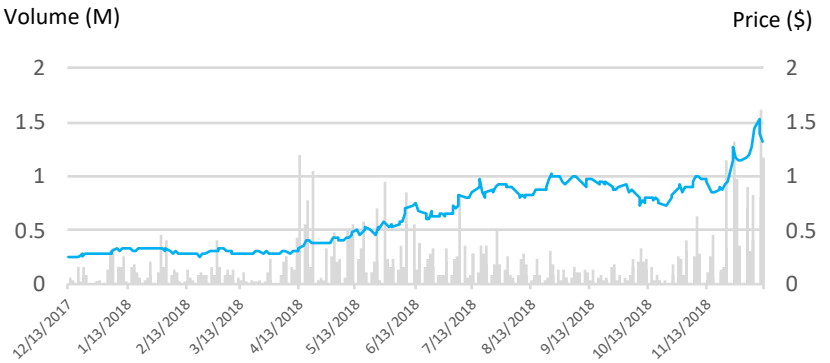
Corporate Overview

- **Paradigm Biopharmaceuticals Ltd** is an ASX-listed biotechnology company focused on repurposing pentosan polysulfate sodium (PPS), an **FDA-approved drug** that has a **long track record** of safely treating inflammation
- Drug repurposing uses the 505(b)(2) pathway - **lower cost, minimises risk** and has accelerated development timelines
- **Several clinical indications** such as Osteoarthritis/Bone Marrow Edema Lesions, MPS, Ross River virus and Chikungunya, gives Paradigm **"multiple shots on goal"**
- Strategy is to **establish commercial partnerships** with multiple leading pharmaceutical companies

Financial Information

Share price (13-December-2018)	A$1.32
Number of shares	139.8m
Market capitalisation	**A$184m**
Cash (Dec 2018) – no debt	~A$10.5m

Top shareholders[1,2]	Shares (m)	%
Paul Rennie (Managing Director)	21.6	15.4%
MJGD Nominees *(technology vendor)*	6.9	4.9%
Other Board and management	7.1	5.1%
Irwin Biotech *(technology vendor)*	6.3	4.5%
J.P. Morgan Nominees Aust Pty Ltd	4.2	3.0%
Citicorp Nominees Pty Ltd	3.2	2.3%



Note: 1. Blue shading represents Board and management holdings 2. MJGD Nominees and Irwin Biotech are select vendors of Xosoma, which was acquired by Paradigm prior to listing

Osteoarthritis Pain

Osteoarthritis – Facts and Figures

- **Most common form of joint disease** and **the leading cause of disability** for people greater than 65 years of age[1]
- **OA is a progressive disease strongly correlated with bone marrow edema lesions (BMEL),** affecting the entire joint, including synovial inflammation, cartilage loss and bone remodelling
- **Blockbuster market** – 31m Americans have been diagnosed with OA - ~10% of the total population[2]
- **Significant cost –** OA currently costs the US economy ~US128+ billion per annum[3]
- **Growing crisis –** Due to an aging population and high obesity rates the number of OA sufferers in the US is expected to exceed 67m (116% growth) by 2030[4]
- **Significant limitations, in efficacy, tolerability and safety of available treatments for patients with moderate – severe OA**
- **Opioid Epidemic –** The US and Australia are experiencing unprecedented opioid addiction and overdoses. The FDA is highly supportive of new, safe and effective, non-opioid treatments for pain
- **Timing of Phase 3 critical** - There is a time-limited market opportunity for safe and effective non-opioid non-steroidal therapies to treat moderate – severe OA.

Osteoarthritis is the last frontier of blockbuster diseases with no treatment

1.Neogi T. (2013). The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis and cartilage*, *21*(9), 1145-53.2. http://ard.bmj.com/content/annrheumdis/early/2017/07/12/annrheumdis-2017-211396.full.pdf
3. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September. 4. Neogi T. (2013). The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis and cartilage*, *21*(9), 1145-53.

Phase 2b Knee OA Clinical Trial Design Strategy

- **Paradigm Clinical team –** extensive clinical trial experience with pain as a primary endpoint.
- **Ultimate objective of clinical development:** To succeed in Phase 3 for successful marketing registration in Australia and abroad.
- **Previous clinical trial design experience allows Paradigm to identify pitfalls** in conducting pain studies and the potential for clinically and statistically significant placebo effect in the clinical trial setting.

Strategic Underpinning of Clinical Trial Design

- To evaluate the effectiveness of injectable Pentosan Polysulfate Sodium (iPPS) on pain compared with baseline (clinical and statistical significance) in the controlled clinical trial setting *ie confirm Therapeutic Goods Association Special Access Scheme (TGA SAS) data.*

- To evaluate the optimal design for phase 3 clinical trial, including:
  - Target population: Numeric Rating Score (NRS) strata groups, 4-6 (moderate pain) and 7-8 (high pain)
  - Clinical measurements best able to demonstrate statistically significant and clinically meaningful benefits over placebo

Phase 2b Knee OA – Clinical Trial Design

The Phase 2b, placebo controlled clinical trial was conducted to evaluate the effects of injectable Pentosan Polysulfate sodium (iPPS) on the treatment of pain in subjects with osteoarthritis of the knee and concurrent subchondral bone marrow edema lesions

Trial Design	Phase 2b, randomised double blind placebo controlled multicentre study
Primary Endpoint	**Change in Knee injury and Osteoarthritis Outcome Score (KOOS) (Pain Subscale) from baseline to Day 53**
Secondary Endpoints	Safety, KOOS Pain, KOOS Symptom, KOOS Function, KOOS Quality of Life, BMEL Volume, Patient Global Impression of Change (PGIC)
No. Participants	112 completed study protocol
Active : Placebo	First stratified by baseline pain score: NRS 4-6 (moderate pain) NRS 7-8 (high pain) Then randomised 1:1 iPPS: Placebo
Dosing	2mg/kg Pentosan Polysulfate Sodium (100mg/ml injectable solution), administered by subcutaneous injection, twice weekly for 6 weeks.
Placebo	Saline (0.9% saline solution)
Recruitment Sites	6 sites throughout Australia (VIC, SA, WA and QLD)

Phase 2b Knee OA – Subject Population

Key Inclusion Criteria

- Subjects with a clinical diagnosis of osteoarthritis in one or both knees and a radiographic diagnosis of knee osteoarthritis showing a Kellgren-Lawrence score 2, 3 or 4 (i.e. moderate to severe Knee OA), and baseline pain score of NRS 4-8 inclusive (stratified 4-6, 7-8)
- Symptomatic pain for at least 6 months
- Males and females aged 40 to 75 years
- Body Mass Index (BMI) of 18 to 35.0 kg/m2
- Presence of subchondral bone marrow lesions as determined by MRI

Baseline Statistics of Placebo and Treatment Arms

Per Protocol Population	**iPPS**	**Placebo**
Age, yrs (mean, (min,max))	**57.1** (40, 74)	**57.6** (40, 75)
Sex (M:F)	M **36** : F **19**	M **38** : F **19**
Total (n)	55	57
NRS Pain Strata 4-6 (n)	39	40
NRS Pain Strata 7-8 (n)	16	17

Key outcomes from Osteoarthritis Clinical Trials

The main goals of clinicians, patients and regulatory authorities of a phase 2 clinical trial for OA

- Safety
- Clinically meaningful reduction in pain >50% and statistical significance over placebo
- Looking for other signs of meaningful clinical improvements such as patient wellbeing, quality of life and knee function
- Inform Phase 3 trial design

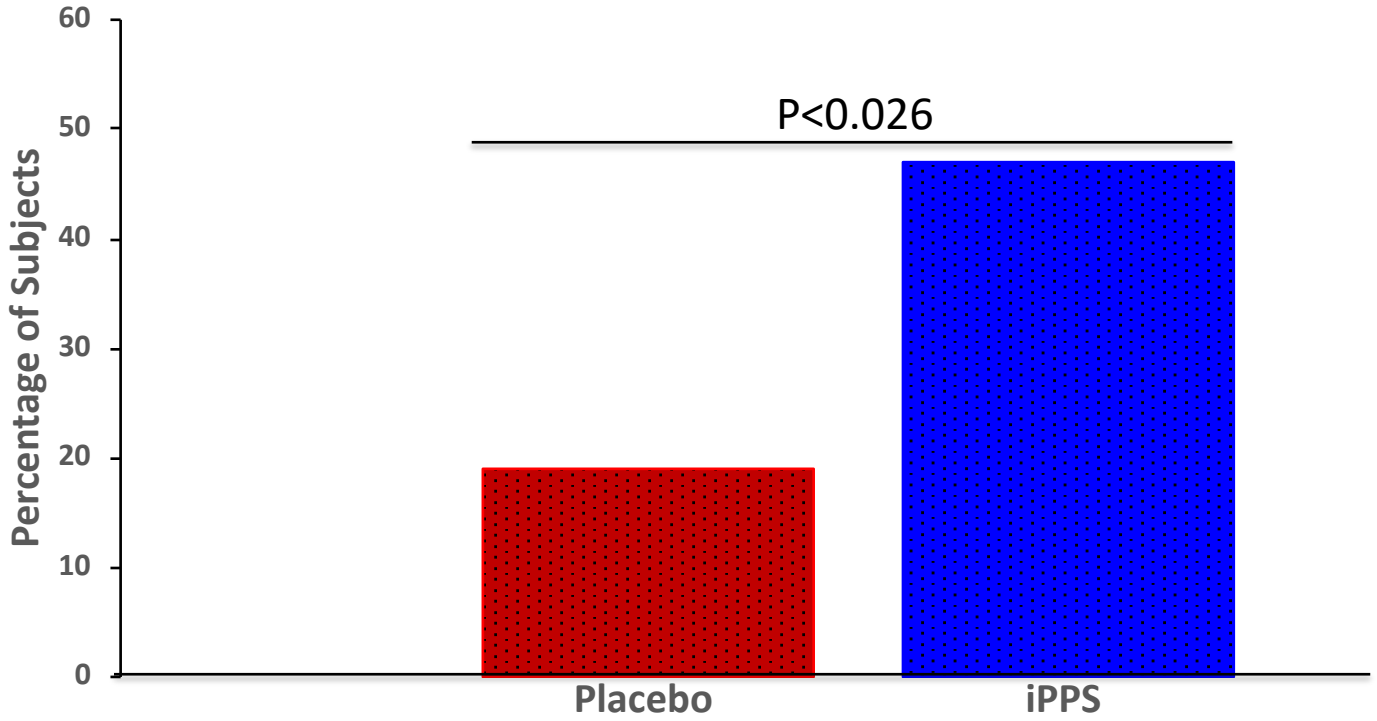
Top Line Report: Primary End point at Day 53

- **Primary Endpoint of "Change in KOOS pain from baseline" met, with statistical and clinical significance compared with Baseline**

- Distribution of subjects in the NRS stratum of 4-6 was 70% and subjects in the NRS stratum of 7-8 was 30% of the total study population
- NRS stratification 4-6: Change in KOOS Pain score from baseline to Day 53 reached statistical significance compared with placebo at day 39 and 53 (refer to graph on page 10)
- The secondary End point of the Patient Global Impression of Change (PGIC) from baseline to Day 53 between iPPS treatment and Placebo was statistically significant at p=0.0062

iPPS Treatment Meets its Primary End Point

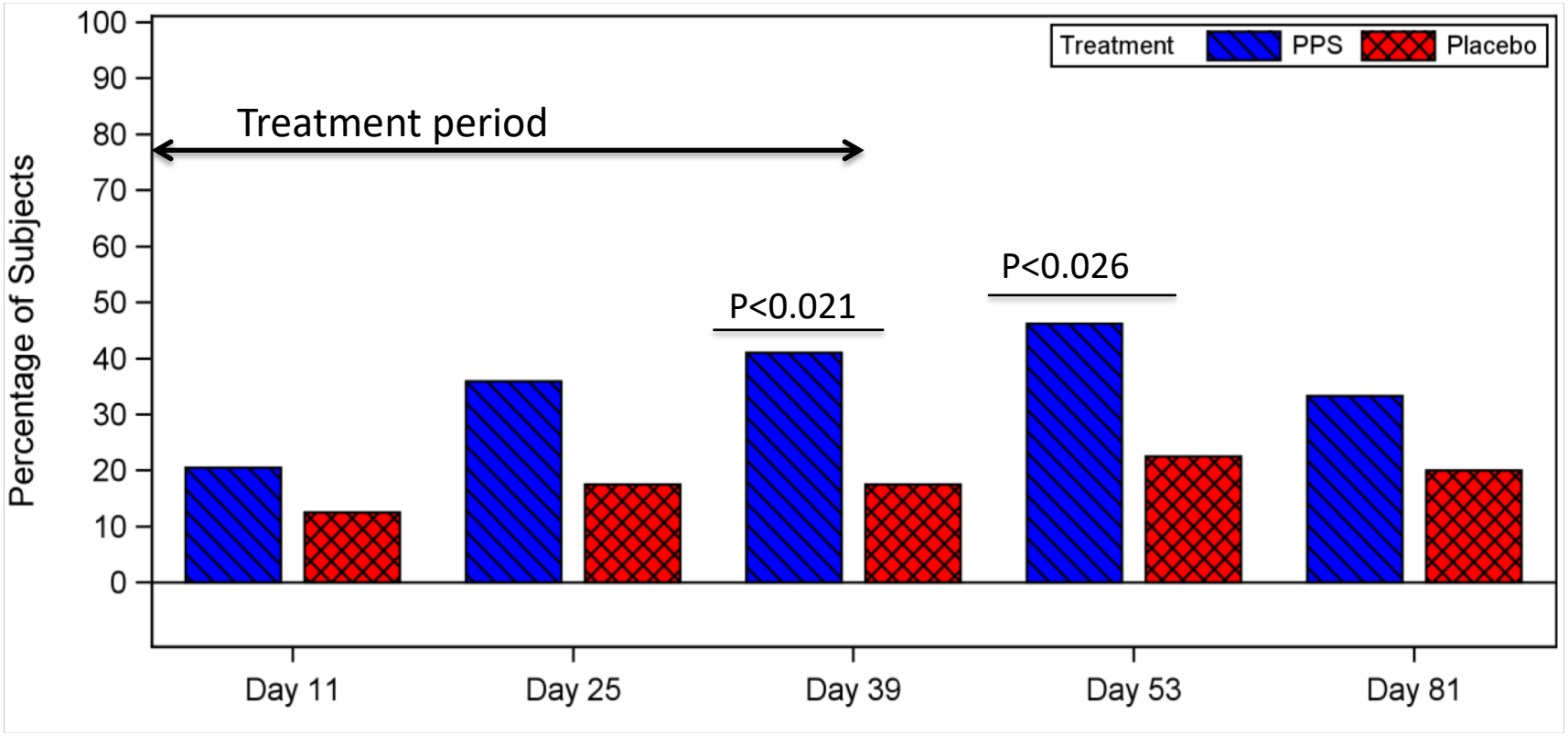
>50% Reduction from Baseline in pain as measured in KOOS Pain Score at Day 53 (NRS: 4-6 stratum)



- **iPPS treatment is statistically significant compared to placebo (Chi-square analysis)**
- **iPPS treatment showed a clinically meaningful response to pain**

KOOS Pain Subscale – Clinically Meaningful Pain Reduction of >50% from Baseline

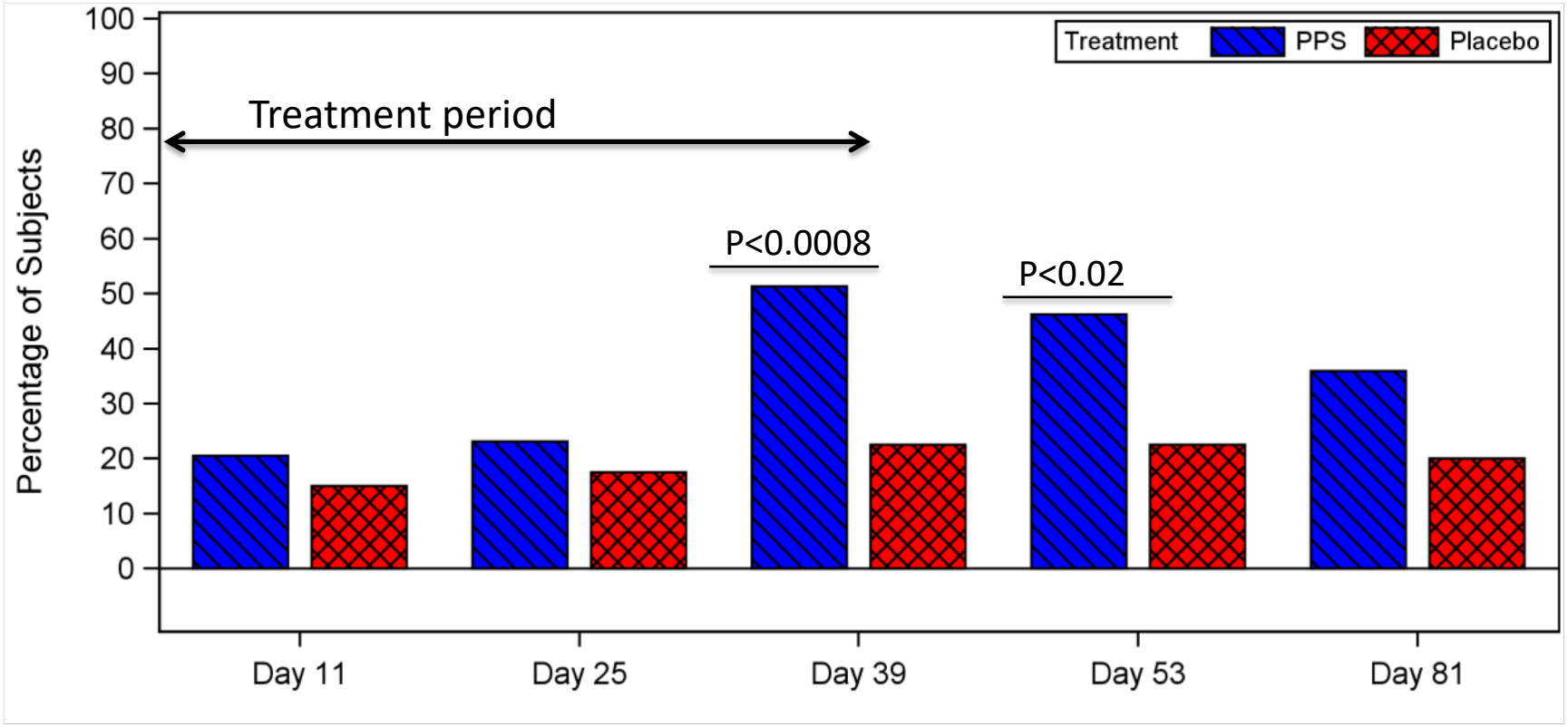
KOOS Pain Subscale – NRS Stratification: 4-6



- **Statistically greater proportions of subjects with >50% reduction in pain from Baseline after iPPS as measured by KOOS Pain subscale (Chi-square analysis)**
- **> 50% pain reduction corresponds to high reduction in pain (OARSI definition)**

NRS Pain Score – Clinically Meaningful Pain Reduction of >50% from Baseline

NRS Pain Score – NRS Stratification: 4-6



- **Statistically greater proportions of subjects with >50% reduction in pain from Baseline after iPPS as measured by NRS pain score (Chi-square analysis)**
- **> 50% pain reduction corresponds to high reduction in pain (OARSI definition)**

Phase 2b OA Results – Conclusions

- **Clinical trial met the primary endpoint -** Change in KOOS pain score from baseline at Day 53
- **Clinically meaningful and statistically significant results** between iPPS and Placebo in the total population (p=0.031) and highly clinically meaningful and highly statistically significant in the NRS pain = 4-6 strata
- **46.2% of subjects receiving iPPS showed a greater than 50% reduction in pain** from baseline compared to 22.5% of subjects receiving Placebo. This is statistically significant at p=0.026 and clinically meaningful i.e. pain reduction of 50% or more
- **Data are consistent with TGA-SAS** with an average of 51.4% reduction of pain from baseline with NRS scores reduced from 6.3 to 3.1
- **Safety profile confirmed –** Expected AE's mild/moderate severity with no life threatening AE's.
- **Confirmed target population for the Phase 3 clinical trial**

Phase 2b Knee OA Results

Key Outcome

In the total study population, iPPS achieved a safe, well tolerated, clinically meaningful, statistically significant result over placebo as demonstrated by higher number of subjects with >50% reduction in KOOS pain score from baseline.

NRS strata 4-6, produced highly clinical and statistically significant results over placebo and is the target population in our Phase 3 clinical trial.

- As a result of Paradigm's Phase 2b results, Paradigm intends to file a NDA (with USA FDA) for a pivotal Phase 3 in CY2019
- Today Paradigm reported primary end point data and secondary end points will be reported on in Q1CY2019
- Outstanding Phase 2b results are likely to reach higher effect and statistical significance in larger Phase 3 clinical trial
- NRS = 4-6 strata data very consistent with TGA SAS data

2019 Objectives and Catalysts

Paradigm is well positioned to execute many valuable milestones throughout CY19

- ✓ File IND for Phase 3 trial in OA/BMEL with the possibility of being granted "fast track status" for the Phase 3 trial
- ✓ Ross River Phase 2a trial results release – Q1CY2019
- ✓ CY2019 file IND for recently in-licensed MPS indication
- ✓ Dose first Compassionate Use OA patient in the US
- ✓ Recruit US based medical and clin/reg staff
- ✓ Possibility of early revenue in 2019 via receiving 'Provisional Approval' from TGA to sell Zilosul (iPPS)
- ✓ Ongoing release of additional TGA special access scheme results – Potential for new joints and/or new orthopaedic indications
- ✓ Upcoming release of peer review scientific paper/s in conjunction with Phase 2b secondary end-point data
- ✓ Discussions with big pharma

Contacts

Office

Level 2, 517 Flinders Lane,
Melbourne, VIC, 3000
info@paradigmbiopharma.com

CORPORATE ENQUIRIES:

Managing Director & CEO

Paul Rennie - prennie@paradigmbiopharma.com

INVESTOR RELATIONS:

Dirk van Dissel - Adelaide Equity Partners Ltd

E: dvandissel@adelaideequity.com.au D: +61 408 326 367

Alastair Murray - Adelaide Equity Partners Ltd
E: amurray@adelaideequity.com.au D: +61 415 629 977