PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE 20 December 2018

PARADIGM PROVIDES SUPPLEMENTARY PHASE 2B CLINCIAL TRIAL DATA OF iPPS IN KNEE OSTEOARTHRITIS PAIN

Further to our ASX Announcement about Paradigm's successful Phase 2b clinical trial released on Tuesday 18 December 2018, Paradigm would like to provide further information to its shareholders and the wider investment community to explain the significance of our Phase 2 data and our path to commercialisation. Paradigm confirms to have the entire study peer-reviewed and published in CY2019.

KEY HIGHLIGHTS

- Clinical trial met the primary endpoint - change in the KOOS pain from baseline at Day 53 for the total trial population ($p < 0.0001$);
- Mean Change in KOOS Pain from Baseline – Total Population. Clinically meaningful and statistically significant results – see chart 1 below;
- Mean Change in KOOS Pain from Baseline – NRS:4-6 Strata. Clinically meaningful and statistically significant results – see chart 2 below;
- Mean Percentage Change in NRS Pain from Baseline – NRS:4-6 Strata. Clinically meaningful and statistically significant results ($p<0.028$) – see chart 3 below;
- Number of subjects with a >50% Reduction from Baseline in KOOS Pain Score at Day 53 – NRS:4-6 Strata. Clinically meaningful and statistically significant results ($p<0.026$) - see chart 4 below;
- Number of subjects with a >50% Reduction from Baseline in KOOS Pain Score at Days 11-81 – NRS:4-6 Strata. Clinically meaningful and statistically significant results ($p<0.021$) - see chart 5 below;
- Number of subjects with a >50% Reduction from Baseline in NRS Pain Score at Days 11-81 – NRS:4-6 Strata. Clinically meaningful and statistically significant results ($p<0.02$) - see chart 6 below;
- A key measure in pain outcomes is the Patient Global Impression of Change[1] (PGIC) the total population and placebo was statistically (PGIC, $p=0.0062$);
- All secondary endpoints will be reported on Q1/Q2 CY2019;
- All data will be the subject of a peer-review publication in CY2019;
- Safety of drug confirmed; and
- Paradigm believes there is a high probability that the drug will be successful in a Phase 3 clinical trial and therefore will have big pharma licensing/partnering interest.

Paradigm Biopharmaceuticals Ltd (ASX: PAR) is pleased to announce it has met its primary endpoint of its phase 2b randomised double-blind placebo-controlled multi-centre clinical trial. The primary outcome of the trial is to evaluate the effects of injectable pentosan polysulfate sodium (iPPS) on knee pain in subjects with knee osteoarthritis and subchondral bone marrow edema lesions (BMELs) as assessed by the Knee injury and Osteoarthritis Outcome Score (KOOS) Pain subscale.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2891384/

Paradigm's CEO, Mr Paul Rennie said that *"I would like to confirm the Paradigm Phase 2b clinical trial met its primary endpoint. In addition to that, Paradigm wanted to present top-line results and that Paradigm achieved a clinically meaningful and a statistically significant result between iPPS and Placebo in the total population and highly clinically meaningful and highly statistically significant results in the NRS 4-6 strata. If you have both a clinically meaningful and statistically significant result you have a high probability that the drug will be successful in a Phase 3 clinical trial and once registered a drug that can penetrate the market.*

The rationale to focus on the clinically meaningful effect is because for products to be commercially successful it must firstly produce clinically meaningful effects.

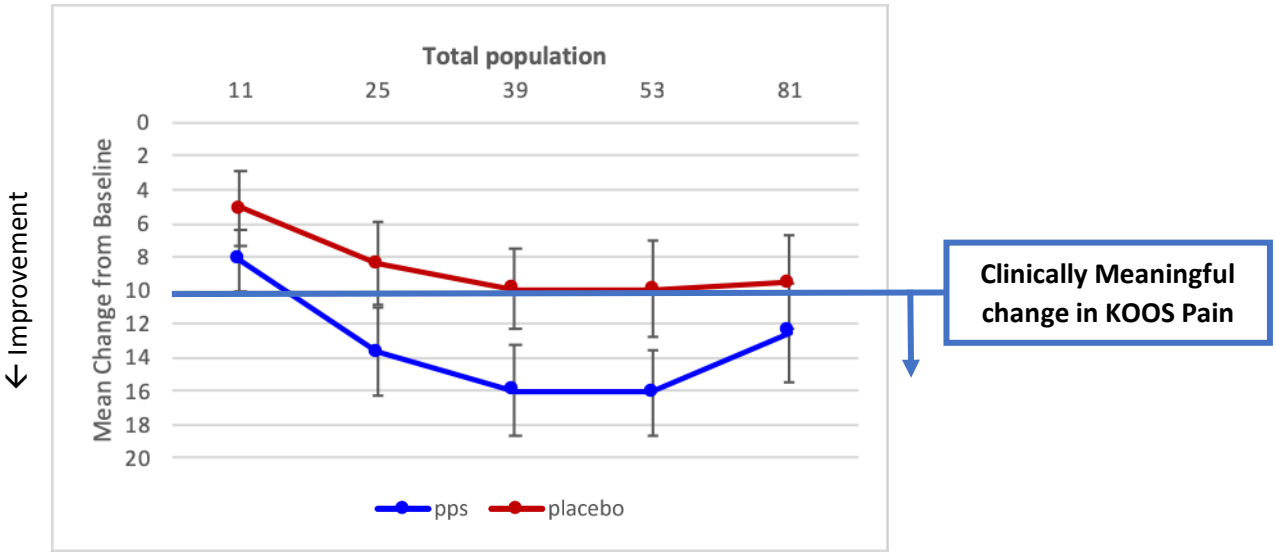
There are many scientific publications on how to interpret pain outcomes in clinical trials. One such peer reviewed example is the US NIH publication that specifically deals with clinical meaningfulness and statistical significance in reference to pain as an end-point.

(*source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2891384/*)

" To determine clinical significance, the clinician or researcher must first choose a metric (e.g., percent reduction of pain), and then choose a cut-off that indicates a clinically meaningful change (e.g., 30% reduction of pain). When deciding on a cut-off value for clinical significance, we must determine the minimal amount of change in pain that would be valuable and important to patients. Many different approaches to determining this minimal important clinical difference have been proposed. A well-researched cut-off method suggests that a 30% reduction of pain can be considered clinically significant. This level corresponds with a "much improved" or "very much improved" response from patients on a global impression of change, or 2 points on a 0 to 11 pain intensity numerical rating scale."

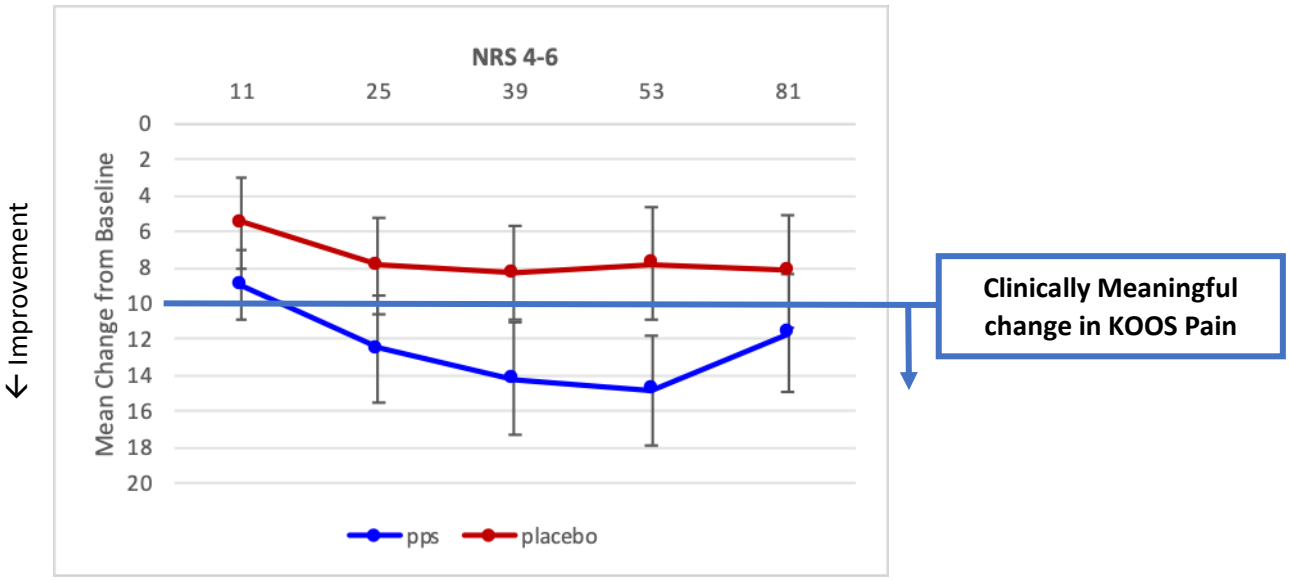
Note: Paradigm used a 50% reduction of pain for its results!

Chart 1: Mean Change in KOOS Pain from Baseline – Total Population



In the **Total Population** Paradigm demonstrated a statistically significant mean change in KOOS Pain from Baseline versus Placebo at day 39 and day 53.

Chart 2: Mean Change in KOOS Pain from Baseline – NRS:4-6 Strata



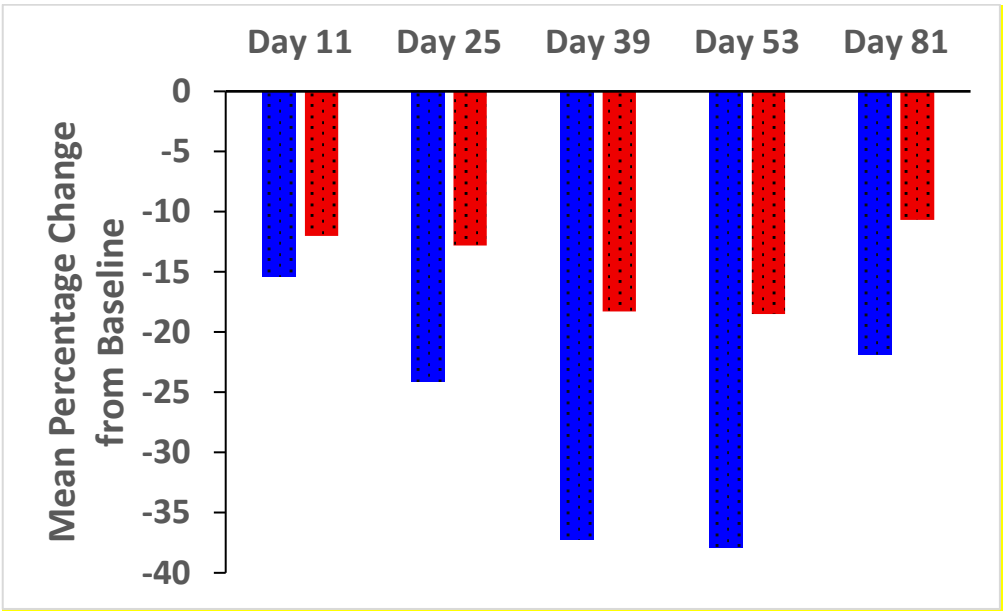
In the **NRS: 4-6 Strata** Paradigm demonstrated a statistically significant mean change in KOOS Pain from Baseline versus Placebo at day 39 and day 53.

Clinically Meaningful

A change of 10 from Baseline is considered a clinically meaningful change in KOOS Pain Subscale

- iPPS returned clinically meaningful results from day 25 onwards in both the Total Population and the NRS:4-6 strata

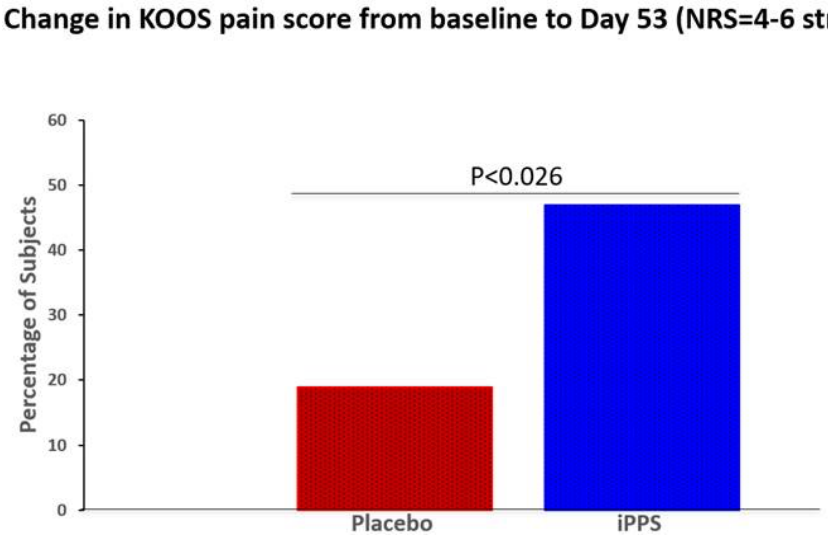
Chart 3: Mean Percentage Change in NRS Pain from Baseline – NRS:4-6 Strata



Adjusted Mean Relative Change from Baseline and 95% Confidence limits (CI)

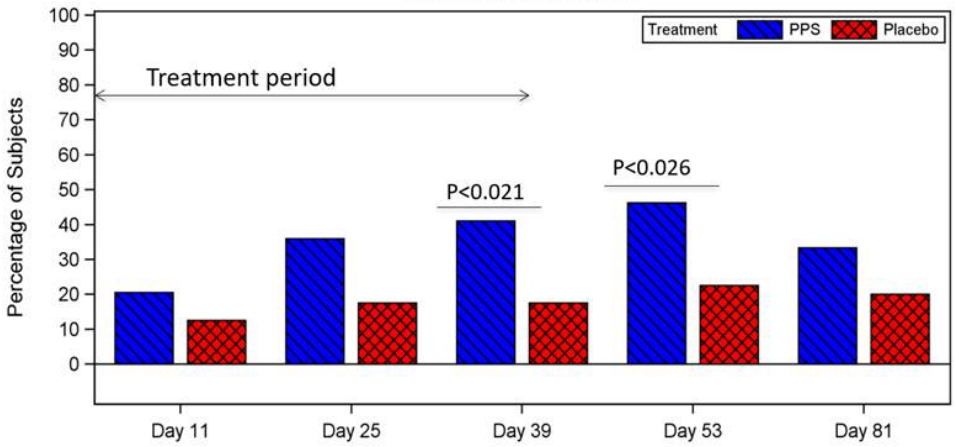
- ***Day 39** iPPS (Blue) vs Placebo (Red) p=0.028*
- ***Day 53** iPPS (Blue) vs Placebo (Red) p=0.039*

Chart 4: Number of Subjects with >50% Reduction KOOS pain score at Day 53 (NRS:4-6 stratum)



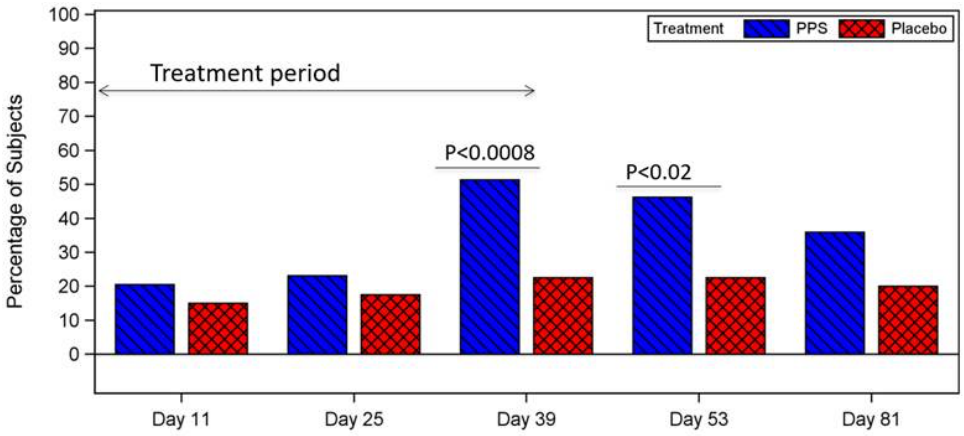
- **>50% Reduction from Baseline in KOOS Pain Score at Day 53**
- iPPS treatment is statistically significant compared to placebo (Chi-square analysis)
- iPPS treatment showed a clinically meaningful response to pain

Chart 5: Number of Subjects with >50% Reduction from Baseline in KOOS Pain Score at Days 11-81 – NRS:4-6 Strata



- 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)

Chart 6: Number of subjects with a >50% Reduction from Baseline in NRS Pain Score at Days 11-81 – NRS:4-6 Strata



- 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)

Secondary Endpoints

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.

The complete Secondary Endpoint Data is still being evaluated, however in regard to secondary endpoints that have been analysed to date, in comparisons with placebo, statistical differences are achieved in NRS pain score (day 39 and 53), Patient Global Impression of Change (PGIC, p=0.0062), and proportions of patients with 25% and 50% reductions in timepoints other than day 53.

As with all biotechnology/drug development companies, primary end-point (top-line) data is always presented before and separately to secondary end-point data, generally because it is analysed first as a priority. If a company has no new or novel data to submit for peer-review publication it is unlikely to be accepted and therefore the company misses the opportunity to gain scientific community/pharma recognition for its trial data.

To further assist the market's understanding of the significance of this successful Phase 2b trial the company, with the input from independent doctors from several of the clinical trial sites, has produced a video describing the OA market, the importance of the data and of having a product that is *both clinically meaningful and statistically significant*. The video presenters are Prof. Andrew Östör (Principal Investigator), Dr David Martin (orthopaedic surgeon), Dr Phil Bloom (sports physician) and retired AFL footballer Andrew Walker. This video can be found on the following link on Paradigm's website at www.paradigmbiopharma.com

Real Commercial Potential for iPPS as a Treatment for OA

Furthermore, Paradigm, would like the reiterate the real and significant commercial potential of iPPS as a safe, effective, durable, repeat (year on year) treatment for OA. Especially in the context of the

nearest comparator treatments currently going through clinical development, the anti-NGF class of small molecules. Both iPPS and the anti-NGFs are administered via several sub-cutaneous injections – for example Tanezumab is intended to be administered at 8-week intervals (seven doses total) for up to ~1 year[2]; & iPPS is administered twice weekly for 6 weeks with SAS data indicating potential durability up ~12 months (we do note 6 month duration of effect data via the Phase 2b trial is yet to be collected and therefore cannot be reported on as yet, but the company is very encouraged by the duration of effect witnessed in the TGA SAS patients).

However, in the true context of partnering/licensing attractiveness, the safety profile of iPPS versus the anti-NGFs cannot be underestimated. The anti-NGF's have all been put on clinical hold by the FDA at various stages due to serious adverse events (AEs) such as rapid joint disintegration or rapidly progressive OA.

Despite these serious safety issues numerous big pharma transactions have occurred over recent years with one of the largest being Elly Lilly partnering with Pfizer on Tanezumab for US$200m upfront and up to US$1.6bn in milestones[3] (i.e. US$1.8bn total potential transaction size). Paradigm, therefore feels very confident in the partnering/licensing potential of iPPS and as previously announced remains committed to progressing this pathway as part of the commercialisation of its OA program.

ABOUT PARADIGM BIOPHARMACEUTICALS LTD

Paradigm Biopharmaceuticals Limited (ASX: PAR) 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 over 60 years.

On 18 December 2018 the Company will announce the results of a phase 2b randomised, double blind, placebo controlled multicentre trial, investigating subjects with osteoarthritis and concurrent bone marrow edema lesions. The recruitment of the 126 subjects into the clinical trial commenced in November 2017 and concluded in August 2018. There is a global trend for safe and effective non-opioid and non-steroid pain relief for chronic disease such as osteoarthritis which presents a huge market opportunity for Paradigm's PPS treatment.

Post these successful phase 2b results, the Company is aiming to achieve Fast-Track designation and begin a phase 3 trial in the US in CY2019. Successful phase 2b trials and Fast-Track designation would be expected to generate significant big pharma interest.

In July 2017 the Company commenced a phase 2a clinical trial to treat people recently infected with the Ross River virus. The results of this trial are also expected to be released in Q1CY2019.

Paradigm recently executed an Exclusive In-License Agreement for the use of iPPS in the treatment of mucopolysaccharidoses (MPS), a group of inherited lysosomal storage disorders. A key unmet medical need in this class of inherited disease is the lack of treatment of joint pain and dysfunction akin to osteoarthritis, hence the applicability of iPPS in treating these rare joint diseases.

The Company continues to execute on its drug repurposing strategy. The key benefits of this strategy are lower costs, accelerated development timelines and higher success rates than the standard clinical development timeline.

To learn more please visit: www.paradigmbiopharma.com

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5764290/

[3] https://www.fiercebiotech.com/partnering/eli-lilly-spells-out-1-8b-deal-to-partner-pfizer-on-tanezumab

For more information, please contact

CORPORATE ENQUIRES

Paul Rennie
Director & CEO
Paradigm Biopharmaceuticals Ltd
E: info@paradigmbiopharma.com

INVESTOR ENQUIRIES

Dirk van Dissel
Adelaide Equity Partners
E:dvandissel@adelaideequity.com.au
M: +61 408 326 367

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