PARADIGM BIOPHARMACEUTICALS LIMITED

ASX RELEASE 30 April 2019

MARCH 2019 QUARTERLY REPORT

KEY HIGHLIGHTS (INCLUDING SIGNIFICANT EVENTS POST END OF QUARTER)

- **Paradigm reported on the positive secondary end-points of its successful phase 2b randomised double-blind placebo-controlled multi-centre clinical trial (n=112)** treating participants with knee osteoarthritis (OA) and concurrent bone marrow lesions (BML) with injectable Pentosan Polysulfate Sodium (iPPS).
- The positive secondary end-points reported on were:
    - **Improved knee function** (Activities of Daily Living or ADL) showing improved physical function to Day 165;
    - **Pain reduction to 6 months** (reduction in KOOS pain score from baseline to Day 165). This means the pain reducing effects of iPPS are durable over a 6 month period.
    - At 6 months (Day 165) **the proportion of subjects receiving iPPS with a greater than 50% reduction in KOOS pain score is clinically meaningful and statistically significant** over placebo; and
    - **Objective data of reduction in BML Grade, Size and Volume** in the iPPS groups as measured on MRI. This demonstrated that the number of subjects receiving iPPS treatment had a clinically meaningful reduction in the Grade of their BML compared to placebo with strong trends in reduction of size and volume of the BML.
- **Reduction of BML Grade, Size and Volume on MRI highlights the potential of iPPS to slow the progression of the disease.**
- **These objective data corroborate previously reported Top-Line-Data <u>that iPPS is safe and clinically effective</u>** (as measured by >KOOS 10, percentage of subjects with >50% reduction in pain) and statistically significant improvement of Patient Global Impression of Change (PGIC) (p=0.0062).
- **Orphan indication.** Paradigm conducted a satellite meeting on 3-4th February at the "WORLD Symposium 2019, 15th Annual Research Meeting on Lysosomal Storage Disease Research" in Orlando, USA to discuss plans for its upcoming randomised double-blind placebo-controlled multicentred multinational Phase 2/3 clinical trial for the Orphan Indication of Mucopolysaccharidosis (MPS).
- **Key Executive Appointments**. During the quarter, Paradigm appointed two very experienced full time staff members ie Global Head of Clinical Development and Global Head of Regulatory Affairs.
- **Peer Review Publication.** During the quarter Paradigm submitted, for peer review and publication, a manuscript detailing the Mechanism of Action (MOA) of iPPS in reducing pain in people with osteoarthritis.

- **Successful Capital Raising** comprised of ~$52m institutional placement and ~$26m underwritten entitlement offer should see Paradigm with a **cash position of >A$81m** upon completion of the entitlement offer component, leaving the company fully capitalised to execute on its clinical development and commercialisation strategy for OA and MPS.
- **Planning for Phase 3 OA clinical trial progresses and partnering discussions have already commenced** on the back of the robust Phase 2b data package.

Paradigm Biopharmaceuticals Limited (ASX:PAR) ("Paradigm" or " the Company") is pleased to provide its quarterly report for the three months ending 31st March 2019 including significant events to the date of this report to accompany its Appendix 4C cash flow report for the period.

SUMMARY OF PHASE 2B OA/BML SECONDARY ENDPOINTS RESULTS

On the 15th April Paradigm announced the positive secondary end-points of improved knee function (Activities of Daily Living or ADL) and pain reduction to 6 months (reduction in KOOS pain score from baseline to Day 165). Additionally, Paradigm reported the secondary end-point objective data of reduction in BML Grade, Size and Volume in the iPPS groups as measured on MRI.

These objective data corroborate previously reported Top-Line-Data that iPPS is safe and clinically effective (as measured by >KOOS 10, percentage of subjects with >50% reduction in pain) and statistically significant improvement of Patient Global Impression of Change (PGIC).

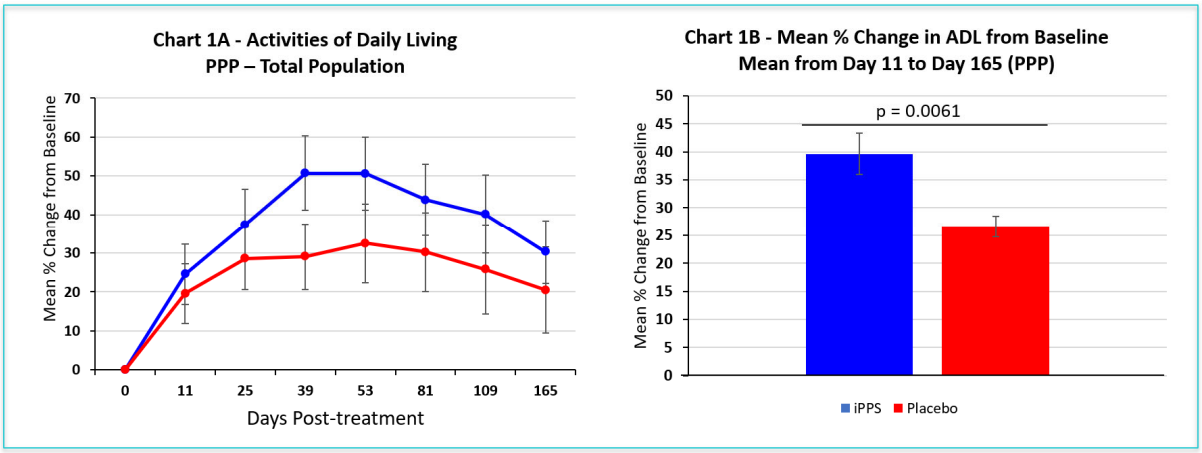
A summary of the positive secondary end-points reported is as follows:

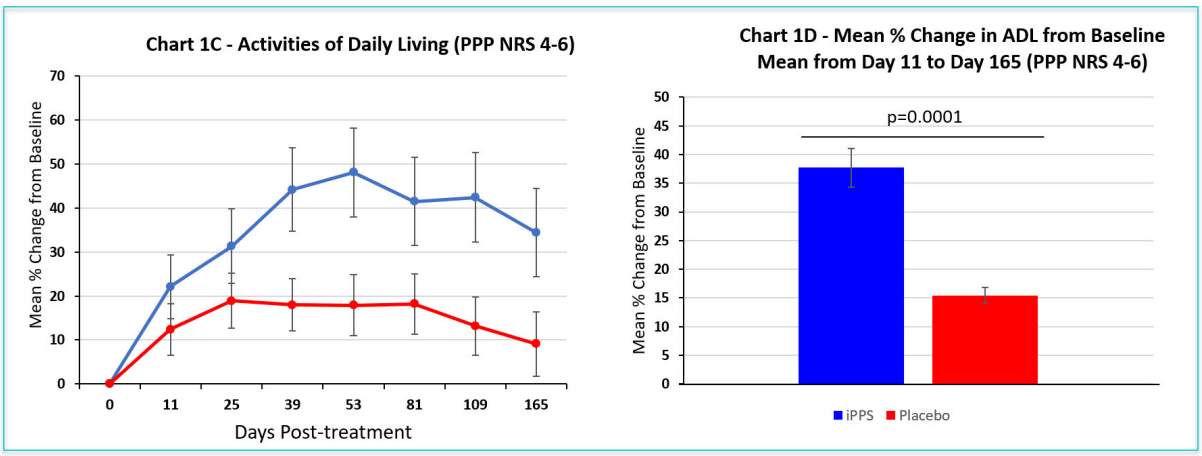
- Improved knee function (Activities of Daily Living or ADL) showed improved physical function to Day 165 in subjects treated with injectable pentosan polysulfate sodium (iPPS) compared to placebo. The mean % change of ADL of iPPS (39.6%) versus placebo (26.6%) was statistically significant (p=0.0061).
- Pain reduction to 6 months (reduction in KOOS pain score from baseline to Day 165). The mean change in KOOS pain score demonstrated a clinically effective outcome at Day 165. This means the pain reducing effects of iPPS are durable over a 6 month period.
- At Day 165 the proportion of subjects receiving iPPS with a greater than 50% reduction in KOOS pain score is clinically meaningful and statistically significant (p=0.0469) over placebo; and
- Objective data of reduction in BML Grade, Size and Volume in the iPPS groups as measured on MRI. The objective data end-point measuring Bone Marrow Edema Lesion (BML) Grade by MRI demonstrated that the number of subjects receiving iPPS treatment had a clinically meaningful reduction in the Grade of their BML compared to placebo. The iPPS group's reduction was also statistically significant over placebo (P=0.03).

Importantly, a reduction of BML Grade, Size and Volume on MRI highlights the potential of iPPS to slow the progression of the disease.

Improved Knee Function (Activities of Daily Living) to Day 165:

- The key functional secondary end-point of Activities of Daily Living (ADL) showed improved physical function to Day 165 in subjects treated with injectable pentosan polysulfate sodium (iPPS) compared to placebo. See Charts 1A and 1C.
- The mean % change of ADL of iPPS (39.6%) versus placebo (26.6%) was statistically significant (p=0.0061). See Charts 1B and 1D.

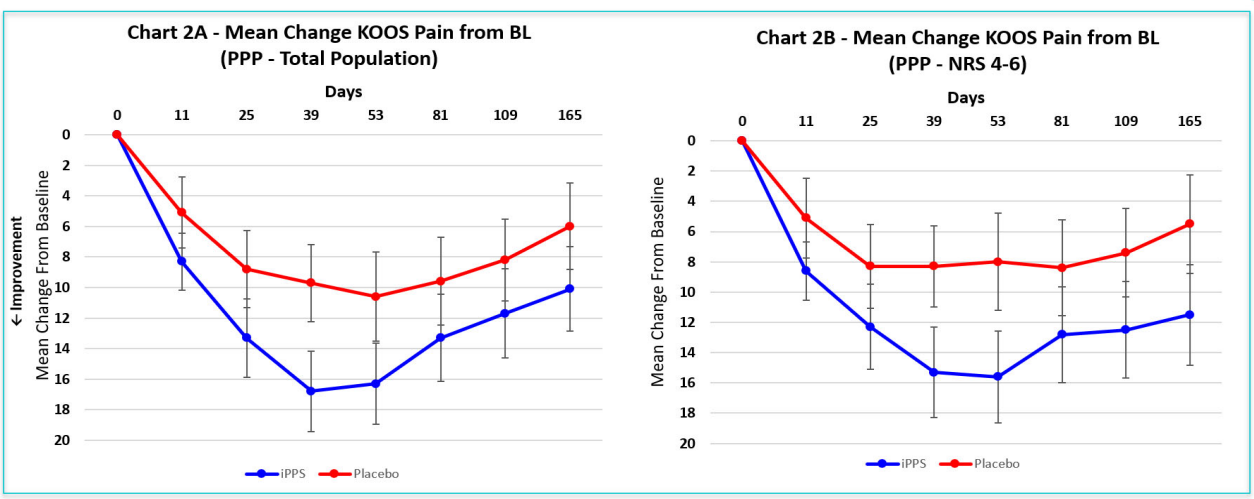




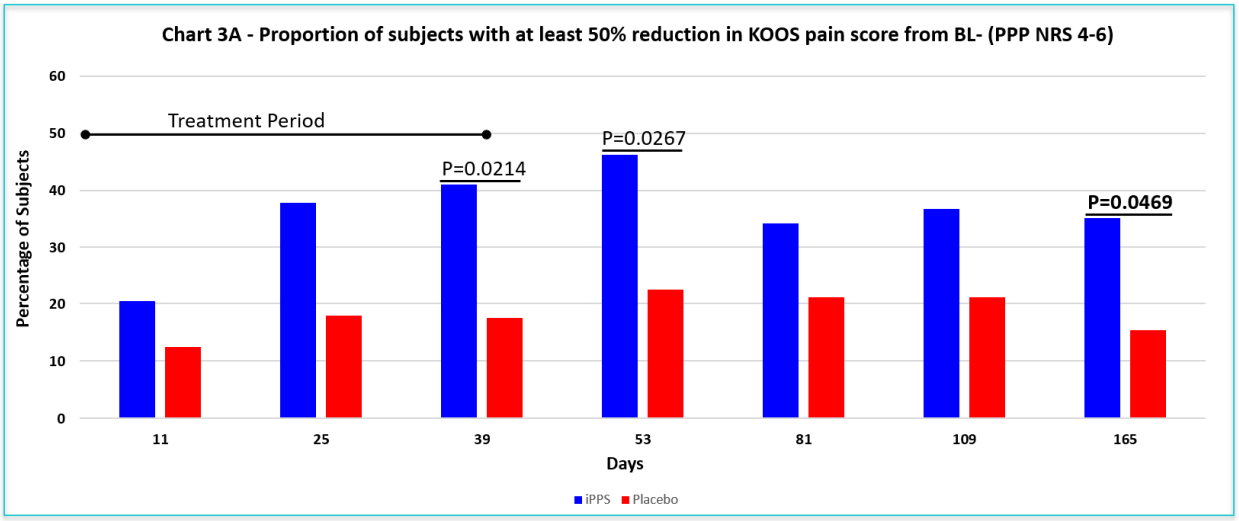
These data suggest that iPPS improves physical function as assessed by the ADL in subjects and these changes are concomitant with the observed clinically meaningful and statistically significant improvement in the Patient Global Impression of Change (PGIC) and reduction in knee pain as previously reported.

Pain Reduction for 6 Months (KOOS pain score to Day 165):

- The mean change in KOOS pain score demonstrated a clinically effective outcome at Day 165. **This means the pain reducing effects of iPPS are durable over a 6 month period.** See Charts 2A and 2B.



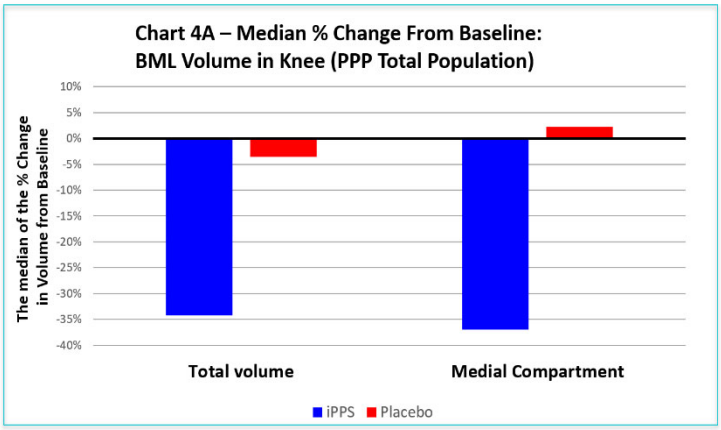
- At Day 165 the proportion of subjects receiving iPPS with a greater than 50% reduction in KOOS pain score is clinically meaningful and statistically significant (p=0.0469) over placebo. See Chart 3A.

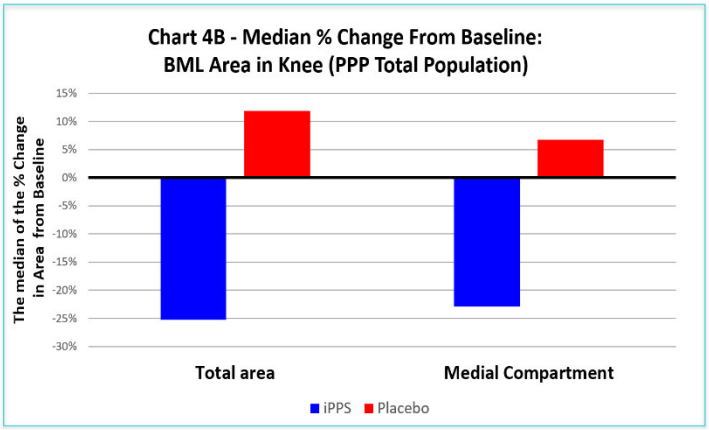


These results demonstrate iPPS achieves a clinically meaningful, statistically significant and durable pain reduction to Day 165.

Objective MRI Data – Total Population (PPP) at Day 53:

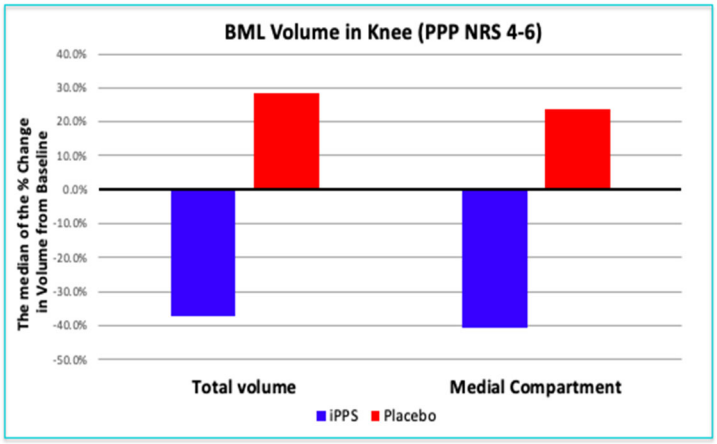
- The objective data end-point measuring Bone Marrow Edema Lesion (BML) Grade by MRI demonstrated that the number of subjects receiving iPPS treatment had a clinically meaningful reduction in the Grade of their BML compared to placebo. The iPPS group's reduction was also statistically significant over placebo (P=0.03).
- iPPS treatment also reduced BML Volume compared to placebo. iPPS:(-)34.2% vs placebo: (-) 3.6%. See Chart 4A.
- iPPS treatment reduced BML Area by (-)25.3% in contrast to a (+)11.9% increase in the placebo group. See Chart 4B.

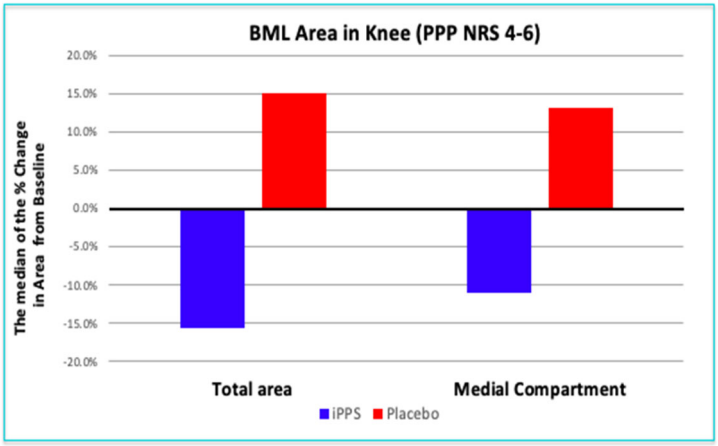




Objective MRI Data – PPP NRS 4-6 Stratum at Day 53:

- iPPS treatment reduced BML Volume by (-)37.3% in contrast to an increase of (+)28.5% in the placebo. See Chart 5A.
- iPPS treatment reduced BML Area by (-)15.6% in contrast to an increase of (+)15.2%, in the placebo group. See Chart 5B.





These objective MRI data, of large reductions in BML Grade, Volume and Area, signals potential of disease regression of osteoarthritis in subjects treated with iPPS.

These objective MRI data also support the subjective data of the clinically meaningful and significant outcomes of reduced pain, improved Patient Global Impression of Change (PGIC, p=0.0062) and Activities of Daily Living (ADL) in subjects treated with iPPS.

Compared with BMLs that stay the same, enlarging BMLs are strongly associated with increased cartilage loss, pain, joint destruction and increased risk of joint replacement.

MUCOPOLYSACCHARIDOSIS (MPS) – ADVANCING TO PHASE 2/3

Paradigm Biopharmaceuticals Ltd announced on 14th February 2019 that it had conducted a satellite meeting on 3-4th February at the "World Symposium 2019, 15th Annual Research Meeting on Lysosomal Disease Research" in Orlando, USA to discuss plans for its upcoming

randomised double-blind placebo-controlled multicentred multinational Phase 2/3 Mucopolysaccharidosis (MPS) clinical trial.

MPS is a progressive rare disease that has a severe unmet need. The current standards of care are not adequate in treating pain associated with joint inflammation and musculoskeletal issues and **these drugs currently equate to a market size of around US$1.4b per annum.**

There is a growing collection of data which support iPPS as a potential treatment for MPS.

1. **Professors Schuchman and Calogera (Mt Sinai) defined the rationale for iPPS in human clinical trials.** Their pioneering pre-clinical work on the effects of iPPS in animal models of MPS demonstrated that iPPS was able to:
   - reduce the levels of Glycosaminoglycans (GAGs), which accumulate as a result of enzyme deficiency in cells and tissues leading to joint pain and dysfunction; and
   - inhibit the inflammatory responses due to TLR-4 signalling by the accumulated GAGs.

2. **Paradigm/Hennermann et al. Phase 2a open label study (n=4)** had promising results which warrant further studies. The conclusions of this trial were:
   - iPPS treatment was well tolerated (safe), resulting in a significant reduction of urinary GAG excretion (Chart 6) and in an improvement of joint/mobility and pain (Chart 7) above any beyond ongoing/existing ERT treatment.

Chart 6 – Urinary GAG excretion

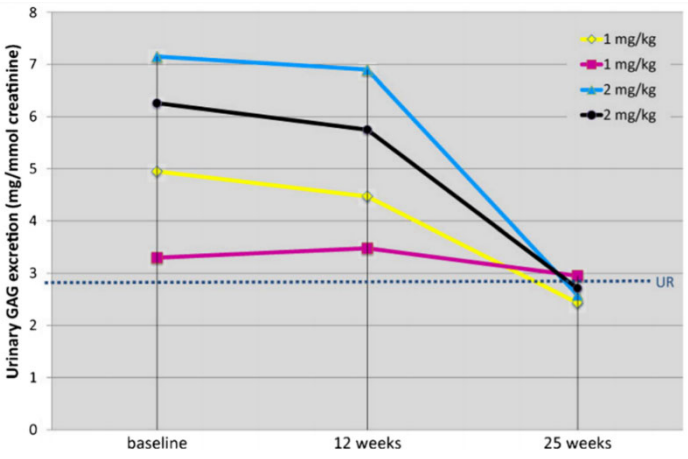
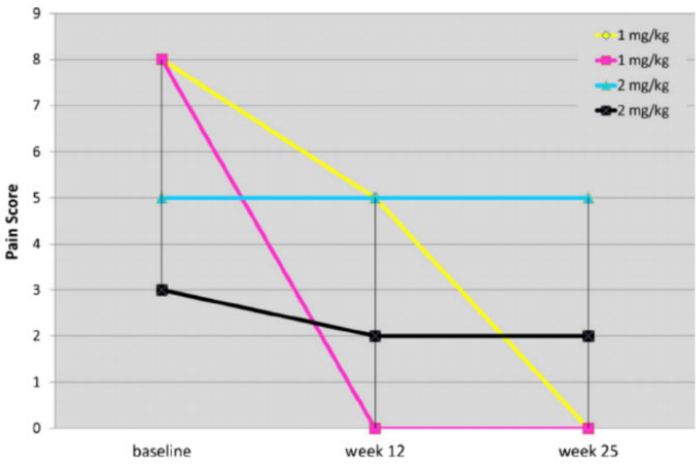


Chart 7 – Pain Score



3. **The findings presented by Dr Furujo at the WORLD Symposium further demonstrate that iPPS could have a positive impact on pain and physical function in patients suffering from MPS**
   - The results below show that there was a reduction in the inflammatory markers (Graph 8) and urinary GAG levels (Graph 9) with no serious adverse events.
   - The preliminary findings of this open label study were encouraging, demonstrating a reduction in the inflammatory markers and urinary GAG levels with visible signs of improved joint function and pain reduction.

Chart 8 Inflammatory Markers

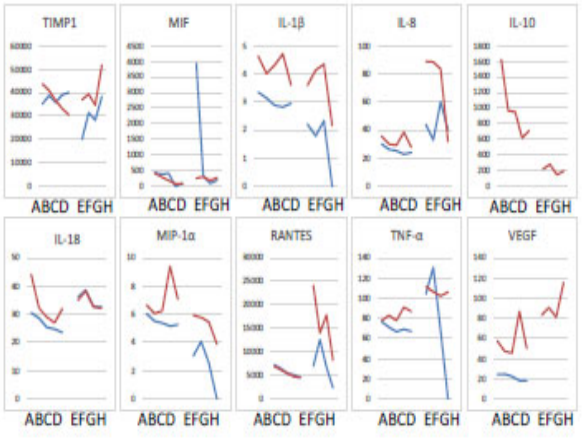
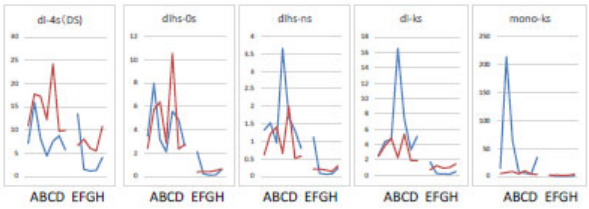


Chart 9 Urinary GAG Levels



PLACEMENT AND ENTITLEMENT OFFER

On 15th April 2019 Paradigm announced a $77.9m capital raise, comprising the $51.6m Placement to professional and sophisticated investors across Australia, Asia, the UK and the USA, including some existing shareholders, and a $26.3m underwritten institutional and retail entitlement offer.

As announced on the 17th of April 2019, the Institutional Entitlement Offer and Placement were successfully executed, raising approximately $61.3m, with the remaining ~$16.6m expected to be received over the coming weeks via the retail entitlement offer (underwritten by Bell Potter Securities).

The funds raised under the Offer are anticipated to fund the Company's osteoarthritis (OA) and mucopolysaccharidosis (MPS) programs through to the end of their respective pivotal phase 3 clinical trials, new drug applications, working capital, costs of offer, further preclinical studies and possibly further intellectual property acquisitions.

THE OSTEOARTHRITIS MARKET

OA also remains the most common form of joint disease globally. In the US alone, it affects over 30 million adults, while in Australia, arthritis affects around 3 million people. In both countries, the condition is a leading cause of pain and disability among the elderly and a cause of life-years lost due to disability.[1]

The demand for a new effective treatment is significantly amplified by the opioid epidemic throughout the United States ("US"). Every day, more than 115 people in the US die after overdosing on opioids.[2] The misuse of, and addiction to opioids is a serious national crisis that affects public health as well as social and economic welfare. The Centers for Disease Control and Prevention estimates that the total "economic burden" of prescription opioid misuse

[1] https://www.cdc.gov/arthritis/basics/osteoarthritis.htm
[2] CDC/NCHS, National Vital Statistics System, Mortality. CDC Wonder, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wonder.cdc.gov.

alone in the United States is $78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement.[3]

ABOUT PARADIGM BIOPHARMACEUTICALS LTD

Paradigm Biopharmaceuticals Limited (ASX: PAR) is an ASX-listed biotechnology company focused on repurposing Pentosan Polysulfate Sodium (iPPS), an FDA approved drug that has a long track record of safely treating inflammation over 60 years.

On 18 December 2018 the Company announced the successful results from their phase 2b randomised, double blind, placebo controlled multicentre trial, investigating subjects with osteoarthritis and concurrent bone marrow edema lesions (n=112). 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 iPPS treatment.

The Company is aiming to achieve Fast-Track designation and begin a phase 3 trial in the US in CY2019, both these initiatives are expected to attract significant big pharma interest.

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. MPS is classified as an Orphan Indication/Designation in the US/EU and provides Paradigm the opportunity to serve a US$1.4bn p.a. market that is in desperate need of new cost-effective treatments.

In parallel to its clinical programs, Paradigm is pursuing a Provisional Approval for iPPS for OA pain via the Australian Therapeutic Goods Administration (TGA), in addition to treating retired elite sportspeople and past NFL players via a US Expanded Access (Compassionate Use) program.

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 Q2/Q3CY2019.

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 timelines for new chemical entities or novel biologicals.

To learn more please visit: www.paradigmbiopharma.com

For more information, please contact

CORPORATE ENQUIRES

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Paradigm Biopharmaceuticals Ltd
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[3] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612779.htm

+Rule 4.7B

Appendix 4C

Quarterly report for entities subject to Listing Rule 4.7B

Introduced 31/03/00 Amended 30/09/01, 24/10/05, 17/12/10, 01/09/16

Name of entity

Paradigm Biopharmaceuticals Limited

ABN	**Quarter ended ("current quarter")**
94 169 346 963	31 March 2019

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(1,593)	(5,157)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(142)	(425)
	(f) administration and corporate costs	(226)	(675)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	15	26
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	2,319
1.8	Other (provide details if material)	-	-
1.9	**Net cash from / (used in) operating activities**	**(1,946)**	**(3,912)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire:		
	(a) property, plant and equipment	-	-
	(b) businesses (see item 10)	-	-
	(c) investments	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9 months) $A'000
	(d) intellectual property	(2)	(2)
	(e) other non-current assets	-	-
2.2	Proceeds from disposal of:		
	(a) property, plant and equipment	(4)	(4)
	(b) businesses (see item 10)	-	-
	(c) investments	-	-
	(d) intellectual property	-	-
	(e) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**(6)**	**(6)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of shares	50	9,100
3.2	Proceeds from issue of convertible notes	-	-
3.3	Proceeds from exercise of share options	49	1,085
3.4	Transaction costs related to issues of shares, convertible notes or options	(18)	(650)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**81**	**9,535**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of quarter/year to date	9,934	2,446
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,946)	(3,912)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(6)	(6)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	81	9,535

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9 months) $A'000**
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of quarter**	**8,063**	**8,063**

5.	**Reconciliation of cash and cash equivalents** at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	**Current quarter $A'000**	**Previous quarter $A'000**
5.1	Bank balances	8,063	8,063
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**8,063**	**8,063**

6.	**Payments to directors of the entity and their associates**	**Current quarter $A'000**
6.1	Aggregate amount of payments to these parties included in item 1.2	60
6.2	Aggregate amount of cash flow from loans to these parties included in item 2.3	-

6.3 Include below any explanation necessary to understand the transactions included in items 6.1 and 6.2

Payments to Chairman and Non-Executive Directors

7.	**Payments to related entities of the entity and their associates**	**Current quarter $A'000**
7.1	Aggregate amount of payments to these parties included in item 1.2	-
7.2	Aggregate amount of cash flow from loans to these parties included in item 2.3	-

7.3 Include below any explanation necessary to understand the transactions included in items 7.1 and 7.2

8.	**Financing facilities available** *Add notes as necessary for an understanding of the position*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
8.1	Loan facilities	NIL	NIL
8.2	Credit standby arrangements	NIL	NIL
8.3	Other (please specify)	NIL	NIL

8.4 Include below a description of each facility above, including the lender, interest rate and whether it is secured or unsecured. If any additional facilities have been entered into or are proposed to be entered into after quarter end, include details of those facilities as well.

9.	**Estimated cash outflows for next quarter**	**$A'000**
9.1	Research and development	2,750
9.2	Product manufacturing and operating costs	-
9.3	Advertising and marketing	-
9.4	Leased assets	-
9.5	Staff costs	195
9.6	Administration and corporate costs	223
9.7	Other (provide details if material)	-
9.8	**Total estimated cash outflows**	**3,168**

10.	**Acquisitions and disposals of business entities (items 2.1(b) and 2.2(b) above)**	**Acquisitions**	**Disposals**
10.1	Name of entity	N/A	N/A
10.2	Place of incorporation or registration	N/A	N/A
10.3	Consideration for acquisition or disposal	N/A	N/A
10.4	Total net assets	N/A	N/A
10.5	Nature of business	N/A	N/A

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

30 April 2019

Sign here: ..... Date: .....
Company secretary

Kevin Hollingsworth

Print name: .....

Notes

1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity that wishes to disclose additional information is encouraged to do so, in a note or notes included in or attached to this report.
2. If this quarterly report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.
3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.