ASX RELEASE

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# Paradigm achieves 100% recruitment in Phase 2b Osteoarthritis Trial

**Highlights:**

- 100% recruitment of trial participants in Paradigm's Phase 2b randomised double-blind placebo-controlled clinical trial in knee osteoarthritis and concurrent subchondral bone marrow lesions.
- Paradigm expects to report the results of this pivotal Phase 2b clinical trial in knee osteoarthritis by late Q4 CY2018.
- In parallel to the Phase 2b osteoarthritis trial, Doctors have treated or are treating over 370 osteoarthritis patients through the TGA Special Access Scheme.
- Paradigm has reported that there is a consistent pain reduction of 50% on average on the 75 patients reported under the TGA SAS – more results from SAS patients will be reported on over the coming months.
- Osteoarthritis is a blockbuster indication, poorly treated by current therapies.
- Demand for an effective non-addictive alternative pain treatment amplified by the Opioid Epidemic currently devastating the United States.
- US FDA is encouraging the development of new pain treatment options that don't have the addictive features of opioids.

**Paradigm Biopharmaceuticals Ltd (ASX: PAR)** is pleased to announce that it has achieved a major commercial milestone by recruitment of 100% of participants in its phase 2b randomised double-blind placebo-controlled clinical trial. The primary outcome of the trial is to evaluate the effects of injectable pentosan polysulfate sodium (iPPS) on knee pain in participants with knee osteoarthritis and subchondral bone marrow lesions (BMLs) as assessed by the Knee injury and Osteoarthritis Outcome Score (KOOS) Pain subscale. Secondary outcomes include changes in KOOS joint symptom score of the knee and MRI changes to Bone Marrow Edema Lesion volume.

The trial was conducted in 6 sites in Queensland, Victoria, South Australia and Western Australia. The recruitment was supported by strong media coverage and public referral from patients treated by their doctors via the TGA Special Access Scheme. The rapid recruitment in this trial has reflected the inadequacy of current standard of care and the unmet need for effective treatment of osteoarthritis associated pain and dysfunction.

Paradigm's CEO, Mr Paul Rennie said that "the Paradigm clinical & regulatory team along with all the clinical trial recruitment and treatment centres have done an extraordinary job to conclude the recruitment of this Phase 2 clinical trial in just over 7 months. What further underlines the outstanding job is the Paradigm's second Phase 2a clinical study (Ross River virus) is also nearing completion of recruitment".

Paradigm is very pleased with the strong momentum that the clinical trial has been able to maintain. Injectable iPPS has the potential to be a 'break-through' in the treatment of osteoarthritis (OA), where

current therapies do not have adequate pain-relieving effects, provide no protection for the degenerating joint structures and are also associated with significant adverse side effects.

Throughout the rest of CY 2018, Paradigm will report on OA patients treated by their Doctor under the TGA SAS as data becomes available. This will occur on an ongoing basis over the coming months. As previously reported, this valuable SAS data adds to the growing body of Real World Evidence that will help support the Company's regulatory submissions for iPPS.

It is estimated that the size of the market of therapeutics to treat OA is US$5 billion per annum[1] and this figure could potentially be multiples higher if new, effective, patented treatments such a iPPS are commercialised.

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.[2]

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.[3] 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 alone in the United States is $78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment, and criminal justice involvement.[4]

Paradigm believes iPPS has the potential to receive Fast Track designation from the US Food and Drug Administration (FDA) which is greatly concerned about the opioid epidemic. In particular, the FDA Commissioner Scott Gottlieb was recently quoted as saying "The opioid epidemic continues to take an emotional, physical and financial toll on Americans. The U.S. Food and Drug Administration is committed to taking every possible step to address the many facets of this complex public health crisis" and furthermore "Our goal is to support more rational prescribing practices, ***as well as identify and encourage development of new treatment options that don't have the addictive features of opioids***."[5]

Fast Track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need. Filling an unmet medical need is defined by the FDA as providing a therapy where none exists or providing a therapy which may be potentially better than an available therapy.

Any drug being developed to treat or prevent a condition with no current therapy obviously is directed at an unmet need. If there are available therapies, a fast track drug must show some advantage over available therapy, such as avoiding serious side effects of an available therapy or an ability to address emerging or anticipated public health need.[6]

Paradigm's iPPS is neither an opioid nor a steroid and most importantly is non-addictive, thus has the potential to positively impact the opioid epidemic and treat OA pain.

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[1] National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.
[2] https://www.cdc.gov/arthritis/basics/osteoarthritis.htm
[3] CDC/NCHS, National Vital Statistics System, Mortality. CDC Wonder, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wonder.cdc.gov.
[4] Florence CS, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. *Med Care*. 2016;54(10):901-906. doi:10.1097/MLR.0000000000000625.
[5] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612779.htm
[6] https://www.fda.gov/ForPatients/Approvals/Fast/ucm405399.htm

**The results from this phase 2b clinical trial are expected in late Q4 CY2018.**

Click here for Clinical Trial Details:
https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373400&isReview=true

Recruitment is also progressing very well in Paradigm's second Phase 2 randomised, double-blind, placebo-controlled clinical trial which is investigating iPPS in alpha-viral (Ross River) arthralgia. Currently the alpha-virus Phase 2 clinical trial is over 80% recruited again with a read-out late Q4 CY 2018.

Click here for Clinical Trial Details:

https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372925&isReview=true

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