PARADIGM BIOPHARMACEUTICALS LIMITED

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PARADIGM PROVIDES REGULATORY FILING UPDATE

KEY HIGHLIGHTS

- **Following the successful US FDA approval of the Expanded Access Programme (EAP) Paradigm reports that the Institutional Review Board (IRB) has also cleared the treatment of Dr Michel's 10 patients (ex-NFL players) under the EAP.**
- **Paradigm has submitted to the US FDA the osteoarthritis Pre-IND Meeting request.**
- **Paradigm has requested for a meeting for December 2019.**
- **In advance of the provisional approval meeting on 11 November 2019 Paradigm has already submitted briefing documents to the Australian Therapeutic Goods Administration (TGA).**
- **If Paradigm is successful in obtaining TGA Provisional approval, Paradigm would be permitted to market and sell Zilosul® for the treatment of osteoarthritis in Australia generating revenue as early as Q3 CY2020.**
- **Paradigm's preparation and submission of Scientific advice documents for a joint submission to the US FDA and European EMA for the rare disease mucopolysaccharidosis (MPS) are scheduled for submission Q1 CY2020.**

Paradigm Biopharmaceuticals Ltd (ASX: PAR) Paradigm is pleased to report the Institutional Review Board (IRB)[1] submission to treat the 10 patients (Ex NFL players) under the FDA approved EAP has also been cleared and approved".

Ex-NFL player Mitch Marrow CEO of Pro Players Elite Network (PPEN).

[1] **What is an Institutional Review Board (IRB)?** https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-boards-frequently-asked-questions

Commencement of patient treatment under the EAP. Following the IRB (IRBco.com)[2] approval of the EAP, Paradigm has now authorised the shipment of Zilosul® (pentosan polysulfate sodium (iPPS)) to treat Dr Michel's patients. Since the IRB approval has been granted, the shipment of the iPPS will be sent from Paradigm's pharmaceutical warehouse in Europe to North America with first patient scheduled to be treated in December 2019 and all ten patients treated by end of Q1 CY2020.

What is the IRB? "Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects" [3].

The US FDA pre-IND OA meeting process. Paradigm has filed the Pre-Investigational New Drug Meeting r(pre-IND) request with the FDA. Paradigm has requested a meeting before end of year, we expect to receive communication back from the FDA before end of October on the acceptance of proposed dates or alternative dates proposed by the FDA. In the Pre-IND meeting Paradigm will discuss its clinical, pre-clinical and CMC (Manufacturing) data with the US FDA. The FDA will provide input during this meeting on Paradigm's data package and Paradigm will comply with the regulator's request in order to meet the requirements for a successful IND filing to enable the Phase 3 trial and marketing authorisation for NDA filing subsequently.

EMA OA Scientific Advice meeting: Paradigm is also preparing for a Scientific Advice meeting the European Medicines Agency (EMA). Paradigm plans to submit the filing late December or early Jan 2020. This is the same approach as the FDA pre-IND meeting where Paradigm is presenting its OA program to the regulators to ensure clinical, pre-clinical and CMC packages contain all the necessary information and data to cover any EMA requirements also to ensure easier Clinical trial application (CTA Process) and marketing authorisation filings at subsequent dates (MAA Process).

The TGA provisional approval process. The Provisional approval process is a new 'expedited' regulatory review procedure for promising new therapeutic products[4]. The provisional approval pathway allows sponsors to apply for provisional registration on the Australian Register of Therapeutic Goods (ARTG) for certain promising new medicines in diseases that are determined to be serious. OARSI has defined osteoarthritis to be a serious disease.
"The trends in osteoarthritis Years Lived with Disease (YLD) from 1990 to 2013 showed a 75% increase, the third most rapidly rising condition associated with disability, just behind diabetes at 135% and dementia at 84%. The most recent update of the Global Burden of Disease figures, (GBD 2013) estimated that 242 million people were living in the world with symptomatic and activity limiting OA of the hip and/or knee, accounting for 13 million YLDs. These figures are likely to be an underestimate of the true global burden of OA, as these

[2] http://irbco.com/

[3] **https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-boards-frequently-asked-questions**

[4] https://www.tga.gov.au/provisional-approval-pathway-prescription-medicines

rates only consider hip and knee OA, and not OA at other sites"[5]. Paradigm submitted the meeting request for the Provisional approval on 29th August 2019 and was granted a meeting date of 11th November 2019 by TGA. The key objective of this meeting is for Paradigm to present its iPPS program to the TGA for the OA indication, and that it meets the criteria for unmet need. If Paradigm is successful in obtaining TGA Provisional approval, Paradigm would be permitted to market and sell Zilosul® for the treatment of osteoarthritis in Australia generating revenue as early as Q3 CY2020.

Rare Disease MPS Pre-IND submission.
Paradigm has strategically decided to submit a joint Pre-IND application to FDA and EMA for its Rare Disease MPS in place of its previous proposal of submitting a single submission to the US FDA. Paradigm has concurred with its KOLs that the joint meeting would facilitate the review of the orphan and paediatric requirements for the study proposal. In addition, the joint meeting would enable a collaborative discussion with both regulators on the study design and concurrence of the clinical program for both regions therefore expediting the process. Paradigm will submit the request to both regulators for a Joint meeting before Q4 CY2019.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said:
"Paradigm has made excellent progress with the filing of a number of submissions to the regulatory authorities in the USA, Europe and Australia.

The FDA Approval of the EAP was a very significant milestone for Paradigm and also an external validation of the safety data. The IRB Approval is another important validation, and this now clears the way forward for Dr Michel to commence the treatment of the first patient which is scheduled for Dec 2019.

The briefing pack to support the US FDA pre-IND meeting has been prepared and is pending submission upon FDA's confirmation of the meeting date. This is another important milestone with the date of the osteoarthritis OA meeting requested to be Q4 CY 2019.

Paradigm's regulatory team is also having discussions with the European Medicines Agency (EMA) re our lead clinical program – osteoarthritis.

All of these regulatory submissions are evidence of Paradigm's progression to commercialising iPPS for the global market of more than 200 million OA sufferers[6] and Paradigm's regulatory and clinical expertise to file applications with regulatory authorities in the USA, EU and Australia".

About injectable PPS (iPPS)
Injectable PPS (iPPS) is not currently registered in Australia, but it is was previously registered in four of the seven major global pharmaceutical markets. In those European markets, iPPS is registered as an antithrombotic agent. In Australia, iPPS for human use is not currently available for sale.

Zilosul® is a registered Trademark of Paradigm Biopharmaceuticals Ltd (ASX: PAR).

[5] https://www.oarsi.org/sites/default/files/docs/2016/oarsi_white_paper_oa-serious-disease.pdf

[6] Ibid.

To learn more please visit: www.paradigmbiopharma.com

For more information, please contact

CORPORATE ENQUIRES

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