PARADIGM BIOPHARMACEUTICALS LIMITED

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PARADIGM'S (ASX: PAR) FIRST FDA IND IS CLEARED WITHIN THE 30-DAY REVIEW PERIOD.

KEY HIGHLIGHTS

- **Paradigm's first expanded access IND cleared by the US FDA.**
- **FDA Clearance means validation of Paradigm's safety data, the finished product's quality and confirmation of an unmet medical need.**
- **Paradigm's future submissions include;**
  - **TGA Provisional Approval (Australia),**
  - **Pre-IND meeting Phase 3 for osteoarthritis (US FDA) and**
  - **Pre-IND for Phase 2/3 for the rare disease mucopolysaccharidosis (US FDA), all expected by end of Q4 CY2019.**

Paradigm Biopharmaceuticals Ltd (ASX: PAR) Paradigm is pleased to report that its first Investigational New Drug (IND) application (Filed 7 August 2019) has been cleared by the US FDA within the 30-day review period.

The FDA IND application must contain information in three broad areas:

- **Non-clinical Pharmacology and Toxicology Studies** - Preclinical data to permit an assessment as to whether the product is reasonably safe for initial testing in humans. Also included are any previous experience with the drug in humans (often foreign use i.e. outside the USA).
- **Manufacturing Information** - Information pertaining to the composition, manufacturing process of finished product, stability, and controls used for manufacturing the drug substance and the drug product. This information is assessed to ensure that the company can adequately produce and supply consistent batches of the drug.
- **Clinical Protocols and Investigator Information** - Detailed protocols for proposed clinical studies to assess whether the initial-phase trials will expose subjects to unnecessary risks. Also, information on the qualifications of clinical investigators--professionals (generally physicians) who oversee the administration of the experimental compound to assess whether they are qualified to fulfil their duties under the expanded access program.[1]

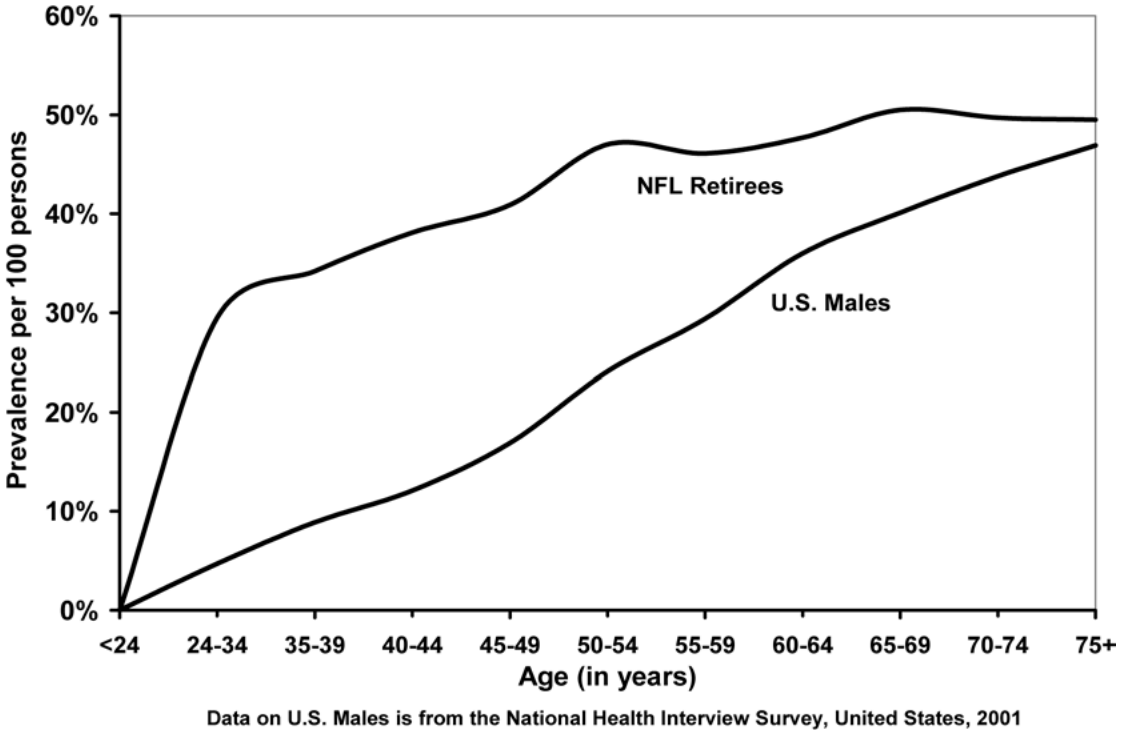
Paradigm submitted an Expanded Access Investigational new drug application (IND) for pentosan polysulfate sodium (PPS) for the treatment of approximately 10 patients with pain associated with knee osteoarthritis (OA) with concurrent bone marrow lesions where patients have failed to respond to standard of care.

The physician treating the patients, under the IND, is an ex-NFL player with the Green Bay Packers. Since his retirement from the NFL, Dr Michels, has worked primarily with sportspeople such as retired NLF players.

A major risk factor for osteoarthritis is joint injury. Knee injury is a common injury amongst NFL players. In males under the age of 60, arthritis is over 3 times more prevalent in retired NFL players than in the general U.S. population. This excess of early-onset arthritis may be due to the high incidence of injury in football. The chart below demonstrates the prevalence of osteoarthritis

[1] https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application#FDA%20Guidances%20for%20Investigational%20New%20Drugs

compared to the general population but also highlights the early onset of the disease in retired football players. Osteoarthritis is a disease of the entire joint leading to the clinical symptoms of pain and joint stiffness. Paradigm's Phase 2b clinical trial demonstrated the drug injectable pentosan polysulfate sodium (iPPS) branded as Zilosul® was able to reduce pain and improve joint function compared to placebo. Paradigm's data also reported objective structural data (BML's (on MRI) and biomarkers (blood)) that Zilosul® can slow the progression of osteoarthritis. Retired NFL players are a sub-set of the general population and it is estimated that there are 33 million people in the USA diagnosed with osteoarthritis[2].



Data on U.S. Males is from the National Health Interview Survey, United States, 2001

Paradigm has undertaken the clinical development of a non-opioid pharmaceutical product (injectable pentosan Polysulphate (iPPS)) to treat the symptoms of degenerative 'early onset' osteoarthritis[3].Osteoarthritis is a major cause of disability for which there are currently no products registered to modify the course of the disease. This represents a major global unmet medical need. iPPS also addresses another unmet medical need - a safe and effective alternative to opioid based medications to treat chronic pain. Despite their remarkable physical traits, professional athletes have even felt the effects of painkiller misuse[4].

What is expanded access programme?
Expanded access, also called "compassionate use," provides a pathway for patients to gain access to investigational drugs, biologics, and medical devices used to diagnose, monitor, or treat patients with serious diseases or conditions for which there are no comparable or satisfactory therapy options available.

Mr. Paul Rennie, Paradigm's Chief Executive Officer said:
"We are very pleased to announce that Paradigm's Expanded Access IND has been cleared by the US FDA within the 30-day review period. This clearance demonstrates the need for effective and safe

[2] https://www.arthritis.org/Documents/Sections/About-Arthritis/arthritis-facts-stats-figures.pdf

[3] Golightly, Y.M., Marshall, S.W., Callahan, L.F., and Guskiewicz, K. (2009). Early-onset arthritis in retired National Football League players. Journal of physical activity & health 6, 638-643.
[4] Opioids: A Painful Problem for the NFL https://www.therecoveryvillage.com/opiate-addiction/related-topics/misuse-nfl/

therapies for the serious chronic disease of osteoarthritis. It also provides validation of the Paradigm dossier which contained information about our non-clinical and toxicology, our manufacturing and our clinical data and data about the previous human experience with the drug".

"FDA Clearance means validation of Paradigm's

- ***safety data,***
- ***the finished product's quality and***
- ***confirmation of an unmet medical need".***

"Paradigm has also been able to demonstrate it now has very experienced staff with regulatory, manufacturing and clinical expertise, which is important as we plan to have an additional two pre-IND submissions with the US FDA before the end of CY 2019".

"Dr Michels will be treating people with osteoarthritis who have failed to respond to standard of care medications. Paradigm now looks forward to the completion of the Expanded Access Programme and reporting on those results in the months ahead".

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 Trade Mark of Paradigm Biopharmaceuticals Ltd (ASX: PAR).

To learn more please visit: www.paradigmbiopharma.com

For more information, please contact

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