PARADIGM BIOPHARMACEUTICALS LIMITED

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COMPANY UPDATE & PROGRESS REPORT

KEY HIGHLIGHTS

- **During FY2019 Paradigm successfully met the primary endpoints in its Phase 2 double blinded placebo controlled clinical trials in both Osteoarthritis (OA) and Ross River virus (RRV).**
- **Company now fully funded (A$78m end of June 2019) and on track to file pre-IND meeting packages for Investigational New Drug (IND) applications with US FDA in leading indications of osteoarthritis (OA) and the Orphan Indication - Mucopolysaccharidosis (MPS). Post successful Phase 3 trials, both OA and MPS have the potential to be blockbuster (>US$1billion revenue per year) commercial opportunities for Paradigm.**
- **Company is focusing on value creating commercial opportunities that will either generate potential revenue from early sales of finished product or through partnering/commercial transactions.**
- **Multiple confidentiality agreements (CA) have been signed and discussions are progressing with potential partners for both OA and MPS.**
- **Based on the strength of the Ross River trial data, the Company intends to enter into discussions with US Department of Defense and other potential partners for potential further development of iPPS in alphavirus infections.**
- **Good Manufacturing Practice (GMP) manufacturing campaign successfully completed, providing supply of iPPS to be used in forthcoming pivotal phase 3 trials, TGA special access scheme (SAS) and expanded access program (EAP) for treatment of ex-NFL players.**
- **Paradigm expects to file initial submission for Provisional Approval with the Australian TGA which, if approved, would provide potential first revenue and sales in Australia.**
- **Signed Employment Agreements with 5 new staff members to create a global clinical and regulatory team to execute Paradigm's clinical programs and undertake our filings with the US FDA and other Regulatory Agencies in CY 2019.**
- **Paradigm's absolute focus is on the clinical development and commercialization of iPPS for the indications of osteoarthritis, the orphan indication of MPS and Alphavirus infections such as RRV and CHIKV.**

Paradigm Biopharmaceuticals Ltd (ASX: PAR) Paradigm is pleased to report that after a very successful FY2019, the company is now moving forward on several fronts concurrently in order to further progress the development and potential commercialisation of the drug (iPPS) for 3 indications (Osteoarthritis (OA), Mucopolysaccharidosis (MPS), Ross River virus (RRV)). This update seeks to provide a comprehensive update to shareholders about the timeline for regulatory submissions ahead in CY2019 along with a detailed description about the experienced new staff working on the filings.

Osteoarthritis (OA) – Commercial Partnerships - Ongoing

Paradigm has now moved through a critical value inflection point by successfully passing both its primary and secondary endpoints from its phase 2b trial in OA. As a result, the company has now signed several confidentiality agreements (CA) and will continue negotiations with potential partners, while still progressing towards its IND filings and potential start of the pivotal phase 3 trial.

These potential partnerships or deals could potentially unlock significant value for shareholders and further de-risk upcoming clinical trials should any partnership develop. Paradigm has valuable intellectual property (IP), patent protections, real world evidence (RWE) and exclusivity of supply of PPS from benePharma Chem. Any potential transaction or partnership discussion will need to be assessed and valued against the potential size of the revenue that could be earned in in any country, region or the whole world that any potential transaction or partnership may cover.

As such the company wants to assure shareholders that the experienced Paradigm Board will only consider partnerships or transactions that reflect the potential revenue opportunities the company would capture post any successful phase 3 trial. Any such discussions will take time to progress towards terms and extensive due diligence by all parties will need to be undertaken. The company will keep shareholders updated should any commercial arrangements be entered.

Anti-Nerve Growth Factor (NGF) – iPPS Method of Action (MOA) – Q3 2019 (July/Aug)
The indication of OA has a significant unmet clinical need that is not being successfully addressed from current treatments. Billions of dollars have been spent in the development of a potential chemical compounds or biological agents that could reduce pain, improve joint function and ideally, reverse the progression of the disease.

The novel multi-billion-dollar NGF drugs that were being developed by big pharma companies had been seen as the potential next breakthrough treatment of OA outside traditional drugs.

Paradigm have completed studies that are due to be published on the mechanism of action (MoA) of iPPS on NGF and the MOA for pain reduction in symptomatic OA. These results are expected to be published in Q3 CY19 (July/Aug). The data will demonstrate iPPS has pharmaceutical activity to reduce the level of NGF produced by bone cells thereby reducing pain in people with osteoarthritis.

The company is confident these unique and peer reviewed studies will provide further evidence around the MOA that iPPS has in the treatment of OA without the significant adverse events seen in the novel Anti-NGF compounds.

The below table reflects some of the deals done within these novel biological Anti-NGF drugs and other potential OA drugs.

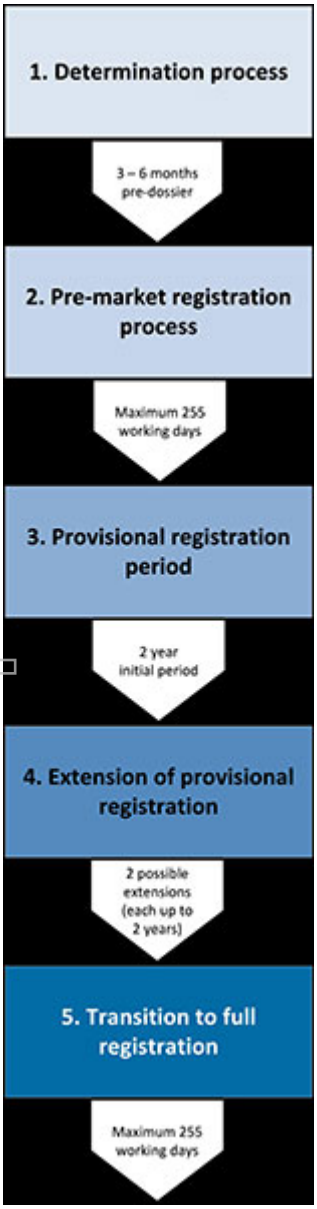
DEALS – GLOBAL BIG PHARMA INTEREST IN OA

Safety Issues

Recent transactions highlight big pharma interest in OA

COMPANIES	COMPOUND	REGION	UPFRONT	TOTAL VALUE	STATUS
Pfizer / Lilly	Anti-NGF	Global	US$200m	US$1.8bn	Phase 3
REGENERON / teva	Anti-NGF	Global	US$250m	US$1.25bn	Phase 3
flexion / SANOFI	Corticosteroid	Global	Take-over*	US$1.0bn*	Commercialised
AMGEN / janssen	Anti-NGF	Global (ex Japan)	US$50m	US$435m	Discontinued
	GLOBAL AVERAGE		**US$166m**	**US$1.12bn**	
Galapagos / SERVIER	ADAMTS-5 Inhibitor	EU	Unknown	US$346m	Phase 1
TissueGene, Inc. / Mitsubishi Tanabe Pharma	Gene therapy	Japan	US$24m**	US$434m**	Handed Back
TissueGene, Inc. / mundipharma	Gene therapy	Japan	US$27m	US$591m	Phase 3
REGENERON / Mitsubishi Tanabe Pharma	Anti-NGF	Asia	US$55m	US$325m	Phase 3
	REGIONAL AVERAGE		**US$35m**	**US$424m**	

Sources: Bloomberg, company filings; *Sanofi-Flexion take-over rumoured – Fierce Biotech; **Mitsubishi handed back rights to TissueGene who executed deal with MundiPharma



Expanded Access Program – Ex NFL Players – Q3 CY19 (July/Aug)

Submission of FDA IND Phase 2/3 & SAS Program - MPS - Q3 CY19 (Sept)
The company is also progressing its IND filing for MPS which is expected to be the next submission following the EAP submission to the FDA. The company has been in extensive discussions with key opinion leaders and clinicians on the submission for the final pivotal phase 2/3 trial design.

Paradigm also has identified several potential patients who may be eligible for treatment under the TGA SAS program within Australia. This would allow the company to see additional real-world evidence prior to any trial result and give valuable data as to the efficacy and safety of treatment of this rare disease.

Ross River/Chikungunya – US Department of Defense – Ongoing CY19/20
Paradigm recently announced the company met the primary end point in its Phase 2a double blind placebo controlled clinical trial in participants with Ross River virus (RRV). The secondary endpoints demonstrated that iPPS reduced RRV symptoms compared to placebo with 72.7% of subjects in the iPPS group showing near remission of the disease in contrast to 14.3% of subjects in the placebo group. These positive results from the pilot study along with

The Department of Defense and FDA have an agreement to advance the development and availability of medical products to help save the lives of American military personnel. This collaboration allows the treatment of American military personnel with safe drugs that are not yet approved through traditional pathways required by the FDA (i.e. Pivotal Phase 3 trials).

Preclinical work[1] undertaken by the company on Chikungunya (CHIKV) (a closely related alphavirus to RRV) will result in further discussions with the Department of Defence (DoD). CHIKV is a prevalent disease in areas such as Puerto Rico and the Caribbean affecting thousands of US military personnel [2]. The disease can be severe and render them unable to serve their country.
Paradigm plans to explore this expedited pathway to market with the DoD that could result in commercial sales to the DoD, a larger trial in military CHIKV patients or other potential partnership arrangements.

GMP Manufacturing – Commercial Quantities – Imminent (July 2019)
Good Manufacturing Practice (GMP) compliance is a mandatory global manufacturing standard for any drug product manufacturer. Compliance with GMP is audited by the national authorities, and only companies that have successfully passed compliance inspections by these agencies are then authorised and licensed for the manufacture and sale of pharmaceutical products. This regulatory approach ensures consistent quality, safety and efficacy of medicines supplied to the public.

Paradigm contracted Siegfried Hameln a leader of pharmaceutical drug manufacturing to develop GMP production of Zilosul®, Paradigm's drug using iPPS to treat OA. A manufacturing process has been successfully established to provide commercial quantities of Zilosul®, and drug product from these production runs will be used in the upcoming pivotal phase 3 trials.

Paradigm has also conducted relevant stability and material compatibility studies and has compiled the necessary information that will need to be provided to regulators for the forthcoming IND submissions. Commercial quantities will also be available to continue the TGA SAS program in Australia and file for EAP within the USA to treat ex-NFL players.

Paradigm's New Hires
NY Based Chief Medical Officer.
Paradigm's CMO has overseen a number of IND submissions to the US FDA and we are pleased she has joined Paradigm to oversee Paradigm's ambitious program of three IND submissions for Paradigm in CY2019 and CY2020. Our CMO will oversee the effective management of Paradigm's Clinical Trials. Our CMO has overseen over 16 IND Filings with the US FDA and has a deep understanding of the process and also good working relationship with the staff at the US FDA. Our CMO has also overseen the submission and clearance of at least 8 Phase 3 clinical trials.

Sharon Charles – Global Head of Clinical Development
Sharon is a seasoned Biotech / Pharmaceutical industry corporate leader with breadth and depth of 29 years' experience in the healthcare sector across global geographies (Asia Pacific, North America, Europe) and has held a number of roles traversing strategic clinical development, corporate leadership, medical affairs, sales/marketing, and business development. Sharon is a strong advocate for the Australian biotech and pharmaceutical R&D and is involved in a number of industry and government strategic think-tanks. Sharon has a strong track record in leading teams and achieving corporate growth, building corporate infrastructure and developing world-class products and services.

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[1] J Virol. 2015 Aug;89(15):8063-76. doi: 10.1128/JVI.00224-15. Epub 2015 May 27.
Pentosan Polysulfate: a Novel Glycosaminoglycan-Like Molecule for Effective Treatment of Alphavirus-Induced Cartilage Destruction and Inflammatory Disease.

[2] https://www.ncbi.nlm.nih.gov/pubmed/26505074 Chikungunya infection in DoD healthcare beneficiaries following the 2013 introduction of the virus into the Western Hemisphere, 1 January 2014 to 28 February 2015.

https://www.darpa.mil/about-us/timeline/chikv-challenge

Sharon has extensive experience in overseeing US FDA-regulated Expanded Access Programs (EAPs), global clinical development programs and real-world and reimbursement programs across numerous therapeutic disease areas including orphan / rare diseases. Paradigm is pleased Sharon is overseeing our therapeutic development and orphan drug program for Paradigm.

Michelle Coffey – Global Head of Regulatory Affairs.
Michelle has over 23 years' global experience (North America, Brazil, Europe, ANZ, Asia, Japan, and Africa,) in the biotech/pharmaceutical industry. Michelle has extensive knowledge in global regulatory requirements for global phase 2, phase 3, phase 4 and post-approval products and has held many meetings with global regulators on complex topics concerning both novel and generic products in a variety of dosage forms including sterile products for injection.

Michelle has a wealth of experience in the areas of strategy, continuous improvement, quality compliance, regulatory, CMC and technical transfers and has held corporate leadership roles within the pharma industry with a key focus on regulatory strategy, quality and leading cross-functional teams to develop effective product strategy, to ensure submission timelines and global regulatory bodies requirements are met.

Michelle has global experience in the biopharmaceutical regulatory space, and Paradigm is pleased Michelle has joined our global team and her experience with the Japanese market will be very important to Paradigm. Michelle has been involved in 3 Phase 3 clinical trials, 2 global orphan applications and IND submissions.

Karla Knower – Associate Director of Regulatory Affairs.
A seasoned Regulatory Affairs professional, Karla has extensive knowhow in managing global Regulatory strategies and submissions for diverse product portfolios, specifically pharmaceutical, device, drug-device, and stem cell products. Karla's expertise spans across the progressive stages of product development, from R&D through to marketed products and life-cycle maintenance.

Throughout her career, Karla has delivered regulatory oversight on the conduct of Phase II, Phase III, and Pivotal Clinical trials both in the USA and in the Europe. It is through these processes that Karla's regulatory intelligence has broadened and strengthened to set up a solid foundation for well-considered, tactically planned regulatory filings for the advancement of clinical development plans.

Jill Forrest – Project Manager, Clinical Operations.
Jill has been working in the clinical research industry for nearly 20 years and has had roles ranging from study coordinating to CRA and Project management. Jill has worked in the hospital setting as well as large global pharmaceutical companies and both small and large CROs. Jill has recently worked on Paradigm's Phase 2b osteoarthritis clinical trial as a Clinical Research Consultant and she currently manages Paradigm's TGA SAS program. Jill has been actively involved in more than 40 clinical trials across varying therapeutic areas.

With these additions to the Paradigm team, we have consolidated and strengthened the depth of expertise that has driven the success of our clinical programs to date, deepened our expertise and relationships with global regulatory agencies, and are strongly positioned to execute Paradigm's clinical development strategy moving forward.

Summary Timelines for Value Inflexion Points:

- **File Expanded Access Program (EAP) for 10 EX-NFL players with US FDA Q3 CY 2019;**
- **File submission with the TGA for Provisional Approval Application of Zilosul® for treatment of osteoarthritis, Q3 CY 2019;**

- **Pre-IND meeting with US FDA Orphan Indication (MPS) Phase 2/3 clinical Trial Q3 CY 2019;**
- **Pre-IND Meeting with US FDA Osteoarthritis Phase 3 Clinical Trial Q4 CY 2019;**
- **Commercial Discussions – ongoing;**
- **Discussions with US DoD – ongoing.**

Q2 Milestones achieved:

- **Pain reduction Mechanism of Action (MoA) of iPPS in osteoarthritis complete and manuscript has been sent for peer review and publication.**
- **Reported on 205 patients treated by their Doctor under the TGA SAS with an average pain reduction of > 50% from baseline.**
- **Reported on the successful Phase 2a Ross River Clinical Trial.**
- **Employed 5 new Clinical and Regulatory Staff;**
- **Completed cGMP Manufacturing of Phase 3 product.**
- **Face-to-Face Meetings with Key Pharmaceutical Companies in Europe and Japan.**
- **Completed the successful capital raise which strengthened the shareholder register;**
- **Established a scientific advisory committee for Orphan indication for the rare disease Mucopolysaccharidosis (MPS).**

About injectable iPPS

Injectable PPS is not currently registered in Australia, but it is registered in four of the seven major global pharmaceutical markets. In those European markets, injectable PPS is registered as an antithrombotic agent. In Australia, injectable PPS for human use is not currently available for sale. Injectable PPS for human use is only available by inclusion into a Paradigm Sponsored clinical trial or via a treating physician applying for its use in patients via the TGA's SAS - Category B.

To learn more please visit: www.paradigmbiopharma.com

For more information, please contact

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