Corporate Factsheet

Paradigm Biopharma Ltd

Paradigm Biopharmaceuticals Limited

Paradigm Biopharmaceuticals Ltd ('Paradigm' or 'the Company, ASX: PAR) listed on the ASX in August 2015. Paradigm has a focused, multidisciplinary management team with broad fundamental experience in taking drugs through clinical trials.

Paradigm's out-sourcing model allows the Company to work with leading experts in pharmaceutical and clinical development, while maintaining a lean operational structure. This means the Company can allocate a significantly higher proportion of funding to research and development.

Repurposing Pentosan Polysulfate Sodium

Paradigm's focus is on repurposing pentosan polysulfate sodium (PPS), an FDA approved drug that has been used to treat various diseases since the 1960s.

PPS is manufactured in Germany as a semi-synthetic compound made from European beech trees, and shares structural similarities with glycosaminoglycans (GAGs) and heparin. These complex carbohydrates have a modulatory role in the body, via interactions with proteins involved with inflammation.

Biological characteristics of PPS:

- Anti-inflammatory
- Anti-histamine
- Anti-clotting
- Prevents necrosis (premature cell death)
- Prevents cartilage degeneration

Paradigm leverages substantial knowledge, expertise and accumulated safety and manufacturing data.

Advantages of Repurposing

- **Lower cost:** average development cost of US$28m compared to US$1.3bn for "de-novo" development.
- **Faster:** FDA 505(b)(2) pathway for repurposed drugs accelerates the development timeline.
- **Lower risk:** safety already established, therefore less chance of failure (safety issues account for 30% failures).
- **Higher success rates:** 25% chance of success compared to 10% for "de-novo" drugs.

Clinical Development

Paradigm's robust programme of clinical development is currently focussed on the treatment of **inflammatory diseases**, including **orthopaedic conditions, respiratory conditions, heart failure, and the debilitating arthritis associated with arthritogenic alphaviruses** (Ross River virus and chikungunya). The Company is developing therapeutics that are able to modulate the unchecked propagation of inflammation in multiple pathways, without damaging healthy responses and causing undesirable side effects. Additionally Paradigm hold a novel peptide, **'IL-1RA'** which has established safety (Phase 1/2) and is a potential treatment for auto-immune diseases.

Corporate Snapshot

ASX Code		PAR
Share Price (26 Sept 2017)		A$0.39
52 week high/low		A$0.72 / A$0.23
Market Capitalisation		~A$39.7m
Cash (30 June 2017) (Inc R&D rebate ~A$1.8m)		~A$4.4m
Shares on Issue		~101.9m
Options		~6.7m
Top Shareholders	Shares (m)	%
Paul Rennie (CEO & MD)	21.5	21.1%
Other Board and Management	7.1	7.0%
MJGD Nominees (vendor)	6.9	6.8%
Irwin Biotech (vendor)	6.3	6.2%

Clinical Programs

Orthopaedic

Indication	▪ **Bone marrow edema (BME); and** ▪ **Osteoarthritis (OA) associated with BME**
Rational	▪ There is no effective treatment for BME and OA ▪ Opioid abuse resulting from mismanagement of pain is a major problem in the US
Market	**BME from Injury** ▪ **US$2.5bn+** opportunity in US[1] ▪ 1.4m BME, knee & ankle injuries p.a. in US[2,3] **Osteoarthritis** ▪ Therapeutics to treat OA - **~US$5.5bn+** ▪ Cost to US Economy – **US$128bn+**[4]
Pre-clinical	▪ Successful preclinical studies warranted a Phase 2 clinical trial
Phase 2a	▪ Open label clinical trial ▪ Investigating safety, tolerability and efficacy of ZILOSUL® in patients with a BME from a recent ACL injury ▪ **Close out of study expected Q3 CY2017**
Special Access Scheme	▪ 30 additional patients treated under the TGA SAS scheme. ▪ Very positive clinical signals from BME patients with osteoarthritis (OA) and rheumatoid arthritis (RA) - improved pain and knee/joint function
Phase 2b	▪ Plan to enter Phase 2b placebo controlled (n = 100) clinical trial for OA with BME ▪ Duration of clinical trial – 12-24 months ▪ Success in Phase 2b will present a Big Pharma partnering opportunity

Viral Arthritis – Alphavirus

Indication(s)	▪ **Alphaviruses – Including Ross River virus (RRv) and Chikungunya (CHIKV).** ▪ mosquito-transmitted arthritogenic alphaviruses that cause epidemics of severe musculoskeletal disease

1.. Based on US$1,750 treatment cost for 1.4m injuries 2. Jones C, et al. (2012) 3. Waterman B, et al. (2010) 4. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September

Viral Arthritis – Alphavirus continued

Rational	▪ No effective treatment, with sufferers left incapacitated ▪ Symptoms can persist for several years
Market	▪ Severe outbreak of Ross River in Australia over the past 6 months ▪ 1.7m reported cases of CHIKV in the Americas[5]
Pre-clinical	▪ PPS significantly alleviated the severity of disease and reduced both the inflammatory response and the loss of articular cartilage
Special Access Scheme	▪ 30 patients treated under SAS, demonstrated tolerability and potential clinical effects
Phase 2	▪ Phase 2 clinical trials for RRV commenced Q3 CY2017 ▪ Primary end point – Efficacy
Partnering	▪ Interest from the US Department of Defence for CHIKV indication ▪ Potential early revenue from RRv treatment sales into APAC region

Heart Failure

Indication	**Chronic Heart Failure and Cardiac Remodelling**
Rational	▪ 5 year mortality rate > 50% ▪ Need for new effective treatments to stabilise & reverse heart degeneration
Market	▪ Heart failure affects 5.7m+ Americans costing **US$31bn+** in annual healthcare costs[5] ▪ Global Heart failure drug sales are approximately **~US$18.1bn** p.a[7]
Pre-clinical	Demonstrated: ▪ improved systolic function of the heart; ▪ potential to stop or reverse disease progression in heart failure.
Phase 2/Pilot	▪ 24 Patient Pilot study 2018/19 followed by Phase 2b clinical trial ▪ Primary end point – Efficacy

IL-1RA Peptide

What is it?	▪ A novel IL-1RA peptide antagonist (“**IP1510**”), consists of D-amino acids with reversed peptide sequence (a retro-inverso peptide)
Safety:	▪ Safety and efficacy confirmed in Phase 1/2 Clinical Trial (n:26) - Cancer cachexia
Potential Indications:	▪ Inflammatory bowel disease (“IBD”) ▪ Cancer-related cachexia ▪ Ulcerative colitis ▪ Distal colitis ▪ Crohn's disease
IBD Market:	▪ Global IBD drug sales set to reach US$9.3Bn by 2019[8]

Share Price Catalysts

- **Phase 2 open label results readout for BME – Q3 CY2017**
- SAS results peer review publication (BME)
- Demonstrated interest from major pharmaceuticals companies in treatments for BME, Hay fever and Alpha Virus’
- Potential to expand to Osteoarthritis and Rheumatoid Arthritis
- Initiation of Heart Failure Phase 2 clinical trial

Global Interest in Respiratory, Heart Failure and BME

Galápagos

Osteoarthritis
- Galapagos licensed GLPG1972 a potential disease-modifying oral therapy for osteoarthritis to Servier for **US$346m in 2017**

Protagonist Therapeutics

Inflammatory Bowel Disease (IBD)
- Protagonist Therapeutics licensed PTG-200 an oral interleukin-23 receptor antagonist for IBD to **Janssen for US$990m in 2017**

TissueGene, Inc. Cell Technologies

Osteoarthritis
- TissueGene, Inc. Licensed the rights for its degenerative osteoarthritis drug ‘Invossa’ to **Japan's Mitsubishi Tanabe Pharma for US$434m in 2016**

Knee Creations

Bone Marrow Edema
- Zimmer Biomet acquired Knee Creations for its Subchondroplasty procedure, designed to treat BME
- Amount undisclosed in 2013

Cardioxyl Pharmaceuticals

Heart Failure
- Bristol-Myers Squibb acquired Cardioxyl for **US$300m** upfront + **US$1.8bn** in milestones payments in 2015

Board and Management

Graeme Kaufman – Non-executive Chairman
- Broad experience in development and commercialisation of pharmaceutical drugs, previously CFO at CSL Ltd (ASX:CSL), executive VP of Mesoblast (ASX: MSB) and Chairman of Bionomics (ASX:BNO)

Paul Rennie – Managing Director
- Extensive experience in drug development and commercialisation, previously COO & Executive VP, New Product Development of Mesoblast (ASX:MSB)

John Gaffney – Non-executive Director
- 30+ years experience as a lawyer, previously Director of Patrys (PAB.ASX)

Christopher Fullerton – Non-executive Director
- Chartered Accounting and investment banking expertise, previously Non-ex Chairman of Bionomics and Cordlife

Dr Ravi Krishnan – Chief Scientific Officer
- Significant experience in experimental pathology and investigating novel compounds with immune modulatory effects and anti-inflammatory properties, ex MSB

5. Simon, Fabrice et al. “Chikungunya Virus Infection.” Current Infectious Disease Reports 13.3 (2011): 218–228. PMC. Web. 10 Oct. 2016 6. Division for Heart Disease and Stroke Prevention – Heart Failure Factsheet (2016) 7. Sales of six leading compounds – Statins $13.2bn (Research and Markets - Global Statin Market 2015-2016), Clopidogrel bisulphate $1.8bn, Beta-blockers $1.55bn, Ace inhibitors 0.47bn, Aspirin $0.54bn, Vitamin K antagonist $0.5bn (www.pharmacompass.com) 7. K Ramsauer et al. J Infect Dis 214 (suppl 5), S500-S505. 2016 Dec 15, 8 https://www.visiongain.com/Press_Release/932/The-World-Market-For-Inflammatory-Bowel-Disease-Medicines-will-reach-9-3-billion-in-2019 8. Vision Gain - The World market for IBD mecicines will reach 9.3 billion in 2019