Drug repurposing strategy

Much lower cost, accelerated timeline, lower risk and with higher rates of success

- **Lower cost**: average development cost of US$28m compared to US$1.3bn for “de novo” development
- **Faster**: FDA 505(b)(2) pathway leveraging previous clinical efforts, which accelerates the development timeline
- **Lower risk**: safety already established so less chance of failure (safety issues account for 30% of clinical failures)
- **Higher success rates**: 25% chance of successful commercialisation compared to 10% for “de-novo” drugs
- **Repurposed drugs have the same potential** to reach ‘blockbuster drug status’ as de novo drugs

### Standard clinical development

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discovery &amp; pharmacology</td>
<td>2 – 3 yrs</td>
</tr>
<tr>
<td>Preclinical testing</td>
<td>5 – 6 yrs</td>
</tr>
<tr>
<td>Phase I clinical trials</td>
<td>2 – 6 yrs</td>
</tr>
<tr>
<td>Phase II clinical trials</td>
<td></td>
</tr>
<tr>
<td>Phase III clinical trials</td>
<td></td>
</tr>
<tr>
<td>Regulatory approval</td>
<td>1 – 2 yrs</td>
</tr>
</tbody>
</table>

### Paradigm’s drug repurposing timeline

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I &amp; Phase II trials (hay fever) 1 pivotal Phase II trial (BME)</td>
<td>1 year (expected completion early 2017)</td>
</tr>
<tr>
<td>1 pivotal Phase III trial for each indication</td>
<td>1 – 2 yrs</td>
</tr>
<tr>
<td>Regulatory approval</td>
<td>1 – 2 yrs</td>
</tr>
</tbody>
</table>

Source:
Company Highlights

- Repurposing a pre-approved drug to **reduce clinical costs and accelerate commercialisation**

- Pentosan Polysulfate Sodium is a new, multi-acting treatment for hay fever, bone bruising and viral arthritis, all of which have **very large addressable markets (US$14bn+)**

- **Highly credentialed Board and management team** with top tier experience at CSL and Mesoblast

- Multi-faceted IP strategy and ability to leverage relationships to **fast-track time to market**

- Strong focus on prudent cash management to **enhance shareholder returns**

- **Fully funded** through to the completion of the Phase II open label clinical trial for bone bruising, Phase II hay fever and Phase II alpha viruses trials.

- All short-term operational milestones have been met, with **several major clinical trial and development catalysts** expected over the next 12 months

- **Strong platform for growth** and growing global interest in bone bruising and hay fever spaces
Company Overview

Financial information

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Share price (04-April-17)</td>
<td>A$0.51</td>
</tr>
<tr>
<td>Number of shares¹</td>
<td>101.5m</td>
</tr>
<tr>
<td>Market capitalisation</td>
<td>A$51.8m</td>
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<tr>
<td>Cash (31-Dec-16)</td>
<td>~A$6.3m</td>
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<tr>
<td>Debt (31-Dec-16)</td>
<td>No debt</td>
</tr>
<tr>
<td>Enterprise value</td>
<td>A$45.4m</td>
</tr>
</tbody>
</table>

Top shareholders²³

<table>
<thead>
<tr>
<th>Shares (m)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paul Rennie (Managing Director)</td>
<td>21.2</td>
</tr>
<tr>
<td>MJGD Nominees (technology vendor)</td>
<td>6.9</td>
</tr>
<tr>
<td>Other Board and management</td>
<td>7.1</td>
</tr>
<tr>
<td>Irwin Biotech (technology vendor)</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Volume (m) | Price (A$)

Source: IRESS
Note:
1. Includes 33.9m escrowed shares
2. Blue shading represents Board and management holdings
3. MJGD Nominees and Irwin Biotech are select vendors of Xosoma, which was acquired by Paradigm prior to listing
Board and Management

High quality Board and management, with top tier pharmaceutical experience

- Board and management are renowned leaders in the biopharmaceutical industry, having held senior management positions with top ASX-listed companies, CSL (CSL.ASX) and Mesoblast (MSB.ASX)
- Extensive experience bringing biopharmaceutical products from clinical development to commercialisation
- Small and highly specialised team focused on product development utilising outsourcing effectively

Board and management

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

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

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-executive Chairman of Bionomics and Cordlife (now Life Corporation (LFC.ASX))

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

Kevin Hollingsworth – CFO & Company Secretary
- Previously CFO and Co-Sec of Mesoblast and Patrys (PAB.ASX)
Track record of delivering products to market
Pentosan Polysulfate Sodium

PPS has a long safety history and is currently being sold in the US and Europe

Pentosan Polysulfate Sodium
- Pentosan Polysulfate Sodium (PPS) has been used in humans for more than 60 years
- First approved by FDA more than 30 years ago
- Since approval, there have been in excess of 100 million injectable doses of PPS administered
- Paradigm has been granted patents to use PPS for new indications

Current treatment uses
- The oral formulation is FDA approved and sold under the name Elmiron, by Janssen Pharmaceuticals, for the treatment of interstitial cystitis (painful bladder syndrome)
- Also used to treat deep vein thrombosis

Current distributors

Ideal biological characteristics
- PPS is an anti-inflammatory and an anti-histamine with biological characteristics that make it ideally suited for treating hay fever (allergic inflammation in the nasal passage) and bone marrow edema (inflammation in the bone) & viral arthritis
  - Anti-inflammatory
  - Anti-histamine
  - Anti-clotting
  - Prevents necrosis (premature cell death)
  - Prevents cartilage degeneration
IP Protection

Multi-faceted IP protection increases barriers to entry for potential competitors

Valuable patent portfolio
- Paradigm has patent protection because it is using PPS for new indications
- Patents granted for specific indications
- Established regulatory exclusivity and trademarks
- Patent applications for Ross River virus and Chikungunya virus
- Assessing additional patent applications

Secure manufacturing and supply
- Exclusive 20 year supply agreement with bene PharmaChem
- bene PharmaChem makes the only FDA-approved form of PPS
- Manufacturing methods are a well kept trade secret
- Reduces risks associated with manufacturing and supply

Note:
1. bene PharmaChem is a private company located in Germany and manufactures the only officially approved and clinically tested medicinal PPS in the USA, Europe and Australia
Hay Fever

Hay fever is a very common condition that is poorly treated at present

What is hay fever (allergic rhinitis)?
- Allergic inflammation of the nasal airways, when an allergen is inhaled by a sensitised individual

Why focus on hay fever?
- Strong need for more effective treatment options
  - More than 50% of patients are dissatisfied with current medication and 60% have said they would be interested in new treatments
  - Long term use of corticosteroids proven to be harmful to certain sufferers
- Clear need for safer, superior and cheaper treatments
- Hay fever associated with growing economic burden

Addressable market for hay fever:

600 MILLION

Estimated number of people who suffer from hay fever worldwide

US$11+ BILLION

Size of the therapeutic market for hay fever in 2014

Source:
1. 2005 survey conducted by Asthma and Allergy Foundation of America
RHINOSUL® has the potential to fill the current gap in hay fever treatment options

- The hay fever market is changing with new players, like Meda (MEDA.STO acquired by Mylan for US$7.2B/A$9.5B), developing a new class of dual acting treatments
- RHINOSUL® is dual acting with multiple mechanisms of action that make it a potentially superior treatment to existing therapies corticosteroid therapies (like Rhinocort®, Beconase®) and antihistamines (like Claratyne® and Zyrtec®)
- If FDA approved, RHINOSUL® would be the first dual-acting hay fever treatment with no undesirable side effects

<table>
<thead>
<tr>
<th></th>
<th>RHINOSUL®</th>
<th>Anti-histamines (eg. Zyrtec®)</th>
<th>Corticosteroids (eg. Rhinocort®)</th>
<th>Dymista®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treats acute symptoms (histamine release)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Treats chronic symptoms (inflammation)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>No undesirable side effects</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Simple to manufacture</td>
<td>✓</td>
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<td></td>
</tr>
</tbody>
</table>

Note:
1. Immediate use of corticosteroids do not treat acute hay fever symptoms, however, ongoing use will result in the subsiding of such symptoms
Preclinical (Guinea Pig / Astra Zeneca) Model

Peer Reviewed Scientific Publication

- PPS demonstrated high affinity binding to IL-4, IL-5 and IL-13 compared to other test molecules.
- PPS inhibited the growth of TH2 cytokine-dependent responder cell-lines.
- After OVA challenge (allergen), total leukocyte, eosinophil and neutrophil numbers in the nasal lavage fluid were inhibited by PPS and budesonide (Astra Zeneca Rhinocort).
- Trends of reduced nasal tissue infiltration of eosinophils and CD3+ T cells were observed in the late phase response in PPS and budesonide treated animals compared to controls.
Preclinical study submitted for peer-review publication

**Th2 Neutralization and In Vivo Anti-inflammatory Action of Pentosan Polysulphate Sodium (PPS) in an Allergic Rhinitis Model**

Sandra C., Morii M., Jorgand P., Jönsson J., Krishnan R., Wang K.D., and Erjefält JS.

Dept of Exp Medical Science, Lund University, Sweden; Paradigm Biopharmaceuticals Ltd, Melbourne, Victoria, Australia; Shanghai Inst Clinical Biometrics, Zhongshan Hospital, Shanghai, China.

**ABSTRACT**

Pentosan Polysulphate Sodium (PPS) is a non-steroidal, inhaled mucosal therapeutic being developed in the EU and China for the treatment of allergic rhinitis. It is a unique non-steroidal, non-steroidal anti-inflammatory drug (NSAID) that has been shown to be effective in reducing symptoms of allergic rhinitis.

In a randomized, double-blind, placebo-controlled trial, 30 patients with moderate-to-severe allergic rhinitis were treated with either PPS or placebo for 12 weeks. The primary endpoint was the change in symptom score compared to baseline. Secondary endpoints included changes in nasal and conjunctival scores, as well as quality of life measures.

Compared to placebo, PPS significantly reduced total symptom scores, nasal symptoms, and conjunctival symptoms. The treatment was well tolerated with no significant adverse events reported.

**RESULTS**

PPS has potent anti-inflammatory effects in preclinical studies.

**CONCLUSIONS**

PPS is a promising therapeutic for the treatment of allergic rhinitis, offering a novel approach to symptom management with good tolerability.

**REFERENCES**


Phase 2 Hay Fever Challenge Study

Lund University Sweden (ex-Astra Zeneca Respiratory Facility)

- Established model for AR – used by Big Pharma including Astra Zeneca to trial AR drugs
- AR Patients (pollen) in “Off Season”
- 7 day Artificial Challenge Season – Titrated Doses
- Randomised, Double blind, Cross-over with Placebo Control

- Nasal Symptom Scores (am, pm, 10 minute)
- Peak Inspiratory flow
- Optional biomarkers/ biopsy

<table>
<thead>
<tr>
<th>Pre-dosing</th>
<th>Challenge + dose</th>
<th>Wash-out</th>
<th>Pre-dosing</th>
<th>Challenge + dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 mg/ml or placebo</td>
<td></td>
<td></td>
<td>200 mg/ml or placebo</td>
<td></td>
</tr>
</tbody>
</table>
Hay Fever: Clinical Timeline

Paradigm is on track with clinical development timeline and expenditure

- Nasal formulation, intra-nasal toxicology and Phase 1 clinical trial – complete
- Ethics and Swedish Regulatory approval – complete
- Participant screening and recruitment – complete
- Final patient treated – complete
- Results due late Q2 CY17
- Successful Phase II results are expected to result in a significant licensing opportunity

<table>
<thead>
<tr>
<th>Clinical development timeline</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bridging nasal toxicology study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal formulation development</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nasal spray product development (Aptar device)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I safety study (n=20) - COMPLETED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethics approval for Phase II trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase II placebo-controlled allergen challenge study - COMPLETED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase II - Results Readout</td>
<td></td>
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</tr>
</tbody>
</table>
Bone Marrow Edema (BME)

Currently no approved treatments for bone marrow edema, growing market opportunity

What is bone marrow edema (BME or bone bruising)?

- Bone marrow edema or bone bruising is the accumulation of interstitial fluid or inflammation within the bone marrow, typically a consequence of a direct impact to bone

Addressable market based on acute traumatic injuries:

1.4 MILLION knee & ankle injuries associated with bone bruising\(^1,2,3\)

US$1,750 potential price per ZILOSUL\(^\circ\) treatment

US$2.5+ BILLION ZILOSUL\(^\circ\) market in USA

(Market size could significantly increase with shoulder, elbow and hip injuries as well as chronic injuries)

Source:
1. Based on 200k ACL injuries per annum, with 80% being associated with BME – Niall D, et al. (2004) and Friedberg R, et al. (2016)
2. Based on 1m meniscal injuries per annum, with 80% assumed as being associated with BME – Jones C, et al. (2012)
3. Based on 600k ankle injuries per annum, with 80% assumed as being associated with BME – Waterman B, et al. (2010)
BME: Clinical Timeline

Status update

Currently conducting an open label clinical trial investigating the safety, tolerability and efficacy of ZILOSUL® in patients with a bone marrow edema from a recent ACL injury;

- Ten participants already treated under the Phase 2 open label clinical trial;
- Close-out study expected June 2017;
- Ten additional patients treated under the TGA SAS scheme. Very positive clinical signals from BME patients with osteoarthritis (OA) and rheumatoid arthritis (RA);
- Plan to undertake two pilot studies in BME patients with OA and RA.

<table>
<thead>
<tr>
<th>Clinical development timeline</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proof of concept study (n=5)</td>
<td>Q1–Q2</td>
<td>Q1–Q2</td>
<td>Q1–Q2</td>
</tr>
<tr>
<td>Ethics approval for pilot trial</td>
<td>Q3</td>
<td>Q3</td>
<td>Q3</td>
</tr>
<tr>
<td>Phase 2 open label clinical trial (n=20,40)</td>
<td>Q4</td>
<td>Q4</td>
<td>Q4</td>
</tr>
<tr>
<td>Commence BME osteoarthritis pilot clinical trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commence BME rheumatoid arthritis pilot clinical trial</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Note:
1. Closed label, randomised, double blind, placebo controlled trial expected to commence in Q3 2017, expected to be completed in 12-24 months after commencement.
In-life clinical case study submitted for peer-review publication

Resolution of subchondral Bone Marrow Edema Lesion and joint effusion by MRI analysis corroborate improved clinical outcome measures of knee pain and function following Pantovon Polysulfate Sodium treatment in an osteoarthritic patient

Matthew J Sampson1,*, Margie Kibbun2, Ravi Krishna3, Michael Nganga4 and Jegan Krishnan1,4

1EBerson Radiology, 120 Greenhill Road, Unley, South Australia, Australia 5061
2The International Musculoskeletal Research Institute, 13 Laffers Road, Belair, South Australia, Australia 5052
3Paradigm BioPharmaceuticals Ltd., Level 2, 317 Flinders Lane, Melbourne, Victoria, Australia 3000
4Flinders University, Bedford Park, South Australia, Australia 5954

Corresponding Author: Jegan Krishnan; Email: jegan@krishnan.com.au
Pre-treatment

Post-treatment

Standard four week course of PPS resulted in a clearly visible BME reduction and improved pain and mobility scores
Preclinical study published in peer-reviewed journal (Journal of Virology)

Pentosan Polysulfate: a Novel Glycosaminoglycan-Like Molecule for Effective Treatment of Alphavirus-Induced Cartilage Destruction and Inflammatory Disease


Institute for Glycomics, Griffith University, Gold Coast, QLD, Australia; School of Medical Science and QIMR Berghofer Health Institute, Griffith University, Gold Coast, QLD.

Abstract

Arthropenic alphaviruses such as Ross River virus (RRV) and chikungunya virus (CHIKV) cause large-scale epidemics of severe musculoskeletal disease and have been progressively expanding their global distribution. Since its introduction in July 2014, CHIKV now circulates in the United States. The hallmark of alphavirus disease is crippling joint pain and inflammatory arthritis, a similar immunopathology to rheumatoid arthritis. The use of glucosamine as novel therapeutics is an area of research that has increased in recent years. Here, we describe the promising therapeutic potential of the glycosaminoglycan (GAG) like molecule pentosan polysulfate (PPS) to alleviate virus-induced arthritis. Mouse models of RRV and CHIKV disease were used to characterize the extent of cartilage damage in infection and investigate the potential of PPS to treat disease. This was assessed using histological analysis, real-time PCR, and fluorescence-activated cell sorting (FACS). Alphavirus infection resulted in cartilage destruction, the severity of which was alleviated by PPS therapy during RRV and CHIKV clinical disease. The reduction in cartilage damage corresponded with a significant reduction in immune infiltrates. Using multiple in vivo assays, PPS treatment was found to have significantly increased the anti-inflammatory cytokine interleukin-10 and reduced proinflammatory cytokines, typically correlated with disease severity. Furthermore, we reveal that the severe RRV-induced joint pathology, including thinning of articular cartilage and loss of proteoglycans in the cartilage matrix, was diminished with treatment. PPS is a promising new therapy for alphavirus-induced arthritis, acting to preserve the cartilage matrix, which is damaged during alphavirus infection. Overall, the data demonstrate the potential of glucosamine as a new class of treatment for infectious arthritides.

Importance

The hallmark of alphavirus disease is crippling pain and joint arthritis, which often has an extended duration. In the past year, CHIKV has expanded into the Americas, with approximately 1 million cases reported to date, whereas RRV continues to circulate in the South Pacific. Currently, there is no licensed specific treatment for alphavirus disease, and the increasing spread of infection highlights an urgent need for therapeutic intervention strategies. Pentosan polysulfate (PPS) is a glycosaminoglycan that is readily bioavailable, has few toxic side effects, and is currently licensed under the name Elmiron for the treatment of cystitis in the United States. Our findings show that RRV infection damages the articular cartilage, including a loss of proteoglycans within the joint. Furthermore, treatment with PPS reduced the severity of both RRV- and CHIKV-induced musculoskeletal disease, including a reduction in inflammation and joint swelling, suggesting that PPS is a promising candidate for drug repurposing for the treatment of alphavirus-induced arthritis.

A stereotype throws light on the pathogenesis of alphavirus infections such as Ross River virus (RRV) and chikungunya virus (CHIKV) cause large epidemics of severe musculoskeletal disease. They have been progressively expanding their global distribution, rapidly emerging in new regions of the world [1, 2]. The hallmark of alphavirus disease is crippling joint pain and arthritis, which often has an extended duration, leaving patients debilitated and incapacitated. In the past year, CHIKV further expanded its global distribution by entering the Americas, and it is circulating in several Caribbean Islands. As of 24 October 2014, the Pan American Health Organization (PAHO) reported an estimated 946,431 cases, and local autochthonous CHIKV transmission in the mainland United States was first reported in July 2014 [3, 4]. Due to the expanding range of alphavirus infections, understanding the mechanisms by which alphaviruses cause debilitating arthritis diseases has become increasingly important, especially in the absence of specific treatments available in 2016.
Viral Arthritis – Alphavirus

No approved treatment for severely debilitating virus infection

What is Viral Arthritis?

- Alphavirus infections result in the clinical symptoms of joint and muscle pain, fever and joint inflammation. Ross River Virus (RRV) and Chikungunya (CHIKV) are mosquito-transmitted arthritogenic alpha viruses that cause epidemics of severe musculoskeletal disease in many countries.

- No effective treatment, with sufferers left incapacitated

- Symptoms can persist for a number of years

Ross River Virus & Chikungunya Virus

- Paradigm acquired the patent from the Institute for Glycomics research at Griffith University. The patent claims the use of PPS to treat alphaviruses, including Ross River Virus (RRV) and Chikungunya Virus (CHIKV).
Viral Arthritis – Alphavirus

Ross River Virus

*The Ross River virus could become a global epidemic on the same scale as the Zika virus, Australian researchers warn.*

APP  February 22, 2017

Chikungunya: The Agony Virus

*A mosquito-borne virus has made the jump from Africa to the Americas, and it combines rapid transmission with searing pain. So swat that skeeter—or you may live to regret it*

Laura Beil  September 11, 2014

Chikungunya virus surrounds Australia: Outbreak ‘a matter of time’

*Jamie Seidel*News Corp Australia Network

Recent floods, warmer weather and heavy rainfall are contributing to the unseasonably high number of mosquitoes. *Photo: Getty*
Viral Arthritis: Clinical Timeline

Potential to gain Orphan status, resulting in fast-tracked clinical development

- Preclinical studies have been conducted by the Institute of Glycomics at Griffith University. The results suggested that:
  - PPS significantly alleviated the severity of disease and reduced both the inflammatory response and the loss of articular cartilage;
  - PPS has the potential to treat both acute and chronic symptoms associated with mosquito transmitted alphavirus infections (Ross River virus (RRV) and chikungunya virus (CHIKV);
  - There currently is no effective disease modifying treatment for RRV or CHIKV
- 30 patients with RRV-arthralgia (joint pain) already treated with PPS under the TGA Special Access Scheme demonstrating tolerability and potential clinical effects

Upcoming Phase 2 – PPS to treat RRV and CHIKV

- Paradigm to embark on two Phase 2 clinical trial to develop PPS for the treatment of RRV-and CHIKV-induced arthritis and arthralgia – Potential for Fast-Track /Breakthrough/Accelerated Approval

Clinical development timeline

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
</tr>
<tr>
<td>Proof of concept study under SAS (n=5)</td>
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<td></td>
</tr>
<tr>
<td>Design and Ethics approval for Phase II Trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase II Clinical Trial – Ross River</td>
<td>y</td>
<td>y</td>
<td>y</td>
</tr>
<tr>
<td>Commence Phase II Clinical Trial - Chikungunya</td>
<td></td>
<td></td>
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</tbody>
</table>

Investor Presentation

04 April, 2017
Undervalued Compared to Peers

Attractive investment given low risk development and large market opportunity

Paradigm appears undervalued compared to similar stage, drug repurposing peers given its platform for successful development, secure industrial scale manufacturing and the size of its addressable markets

<table>
<thead>
<tr>
<th>Peer</th>
<th>Ticker and exchange</th>
<th>Market cap (A$m)</th>
<th>Rationale</th>
<th>Clinical stage of key product</th>
<th>Addressable market size</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVP.ASX</td>
<td>Medical Developments International</td>
<td>294</td>
<td>Developing new markets and applications for Penthrox, recent focus on respiratory diseases, significant manufacturing IP</td>
<td>Commercialisation</td>
<td>US$1.5bn+</td>
</tr>
<tr>
<td>SPL.ASX</td>
<td>Starpharma</td>
<td>246</td>
<td>Commercialising an old technology of synthetic branching polymers (dendrimers), with lead product VivaGel in Phase III trials</td>
<td>Phase III &amp; commercialisation</td>
<td>US$3bn+</td>
</tr>
<tr>
<td>AXSM.NASDAQ</td>
<td>Axsome Therapeutics</td>
<td>103</td>
<td>Developing novel therapies for the management of central nervous system disorders, focusing on treatment of BME</td>
<td>Phase III</td>
<td>US$2.5bn+²</td>
</tr>
<tr>
<td>VRP.LN</td>
<td>Verona Pharma</td>
<td>118</td>
<td>Focused on commercialising an old compound for respiratory diseases, with dual inhibition of key enzymes</td>
<td>Phase I/II(a)</td>
<td>US$12bn+³</td>
</tr>
<tr>
<td>PAR.ASX</td>
<td>Paradigm Biopharma</td>
<td>52</td>
<td>Focused on the clinical development of PPS as a multi-target treatment for complex conditions, such as BME and AR and Ap</td>
<td>Multiple Phase II(a)</td>
<td>US$14bn+⁴</td>
</tr>
</tbody>
</table>

Source: Bloomberg, company filings
Note:
1. Market data as at 04 April 2017, exchange rates of AUD GBP 0.61 and AUDUSD 0.76
2. Based on BME addressable market size, excludes CRPS addressable market due to lack of available information and thus likely understates true market size
3. Only includes the market size for COPD which is US$12bn+, excludes market sizes for other respiratory disease indications
4. Includes AR market US$11bn+ and BME market US$2.5bn+ & $0.5bn for viral arthritis, excludes COPD addressable market size of US$12bn+ and Asthma addressable market size of US$15bn+
Global Interest in Respiratory and BME

Recent transactions highlight big pharma interest in respiratory and BME spaces

- Merck & Co (MSD) acquisition of Afferent for US$1.25B (inc milestones)
- Mylan’s takeover offer of Meda in 2016 was at a 92% premium to last close and Dymista® is RHINOSUL®’s closest comparative product
- Merck’s and AstraZeneca’s transactions highlight big pharma’s interest in respiratory businesses units

<table>
<thead>
<tr>
<th>Date</th>
<th>Target</th>
<th>Acquirer</th>
<th>Deal value (US$)</th>
<th>Relevance</th>
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| Jun-16| Afferent     | Merck            | $1.25Bn (inc $750m milestones) | ▪ Afferent develops novel drugs for the treatment of a range of neurogenic conditions - chronic respiratory and urologic sensory pathologies.  
  ▪ E.g. idiopathic pulmonary fibrosis (IPF) |
| Feb-16| Meda         | Mylan            | $7.2Bn            | ▪ Meda’s third biggest product is Dymista®, which is a dual acting AR product |
| Dec-15| Takeda       | AstraZeneca      | $575m            | ▪ Acquired Takeda’s respiratory business only  
  ▪ Acquisition includes expanded rights to roflumilast, used to treat COPD |
| Jul-14| Almirall     | AstraZeneca      | $2.1Bn            | ▪ Acquired Almirall’s respiratory products only  
  ▪ Products focused on asthma and COPD |
| May-13| Zimmer       | Zimmer Biomet    | Undisclosed      | ▪ Zimmer Biomet acquired Knee Creations for its Subchondroplasty procedure, designed to treat BME |

Source: Bloomberg, company filings
# Share Price Catalysts

**Upcoming milestones should drive strong shareholder returns**

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<thead>
<tr>
<th><strong>HAY FEVER</strong></th>
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<tr>
<td><em>Initiating human trials</em></td>
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<td>- Publication of comparator study in “Allergy” expected in Q2 CY17</td>
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<td>- <strong>Phase 2 ‘allergen challenge’ results in late June</strong></td>
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<td>- Potential interest from Big Pharma up to and after release of Phase 2 results</td>
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<th><strong>BME TRIAL</strong></th>
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<tr>
<td><em>Phase 2 trial</em></td>
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<tr>
<td>- Open label trial anticipated to confirm efficacy together with optimal dosing of ZILOSUL® and clinical endpoints</td>
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<td>- SAS results Peer Review Publication</td>
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<td>- Potential to expand to OA and RA</td>
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<tr>
<th><strong>ALPHAVIRUSES AND OTHER MULTIPLE USES</strong></th>
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<tr>
<td><em>Multiple indications available</em></td>
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<tr>
<td>- Initiation of Ross River Virus/CHIKV Phase 2 clinical trials</td>
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<tr>
<td>- BME for PPS to treat other joints (hips, ankles, shoulders and elbows) &amp; RA</td>
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<tr>
<td>- Further potential indications in other respiratory diseases</td>
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<tr>
<th><strong>CORPORATE OPPORTUNITIES</strong></th>
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<td><em>Potential partners</em></td>
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<tr>
<td>- Demonstrated interest from major pharmaceuticals companies in treatments for BME, Hay fever and Alpha Virus’</td>
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<td>- Partnership with world-class manufacturers</td>
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<th><strong>EXPANSION</strong></th>
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<td><em>Market share</em></td>
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<tr>
<td>- Expansion of BME market beyond acute injury therapy</td>
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<td>- Respiratory expansion of PPS for allergic asthma (AA) and chronic obstructive pulmonary disease (COPD)</td>
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<td>- Develop new IP (Alphavirus).</td>
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