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\(^1\)
- **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\(^1\))
- **Higher success rates**: 25% chance of successful commercialisation compared to 10% for “de-novo” drugs\(^1\)
- **Repurposed drugs have the same potential** to reach ‘blockbuster drug status’ as de novo drugs

**Standard clinical development\(^{1,2}\)**

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

**Paradigm’s drug repurposing timeline**

<table>
<thead>
<tr>
<th>Process</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I &amp; Phase II trials (hay fever)</td>
<td>1 year</td>
</tr>
<tr>
<td>1 pivotal Phase II trial (BME)</td>
<td></td>
</tr>
<tr>
<td>1 pivotal Phase III trial for each indication</td>
<td>1 – 2 years</td>
</tr>
<tr>
<td>Regulatory approval</td>
<td>1 – 2 years</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

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Share price (09-Mar-17)</td>
<td>A$0.45</td>
</tr>
<tr>
<td>Number of shares¹</td>
<td>101.5m</td>
</tr>
<tr>
<td>Market capitalisation</td>
<td>A$45.6m</td>
</tr>
<tr>
<td>Cash (31-Dec-16)</td>
<td>~A$6.3m</td>
</tr>
<tr>
<td>(inc ~$1.3m R&amp;D Tax Rebate)</td>
<td></td>
</tr>
<tr>
<td>Debt (31-Dec-16)</td>
<td>No debt</td>
</tr>
<tr>
<td>Enterprise value</td>
<td>A$39.3m</td>
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</table>

### Top shareholders²,³

<table>
<thead>
<tr>
<th>Top shareholder</th>
<th>Shares (m)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paul Rennie <em>(Managing Director)</em></td>
<td>21.2</td>
<td>21.1%</td>
</tr>
<tr>
<td>MJGD Nominees <em>(technology vendor)</em></td>
<td>6.9</td>
<td>6.9%</td>
</tr>
<tr>
<td>Other Board and management</td>
<td>7.1</td>
<td>7.1%</td>
</tr>
<tr>
<td>Irwin Biotech <em>(technology vendor)</em></td>
<td>6.3</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

### Volume (m)

![Volume Graph](image)

### Price (cents)

![Price Graph](image)

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
Hay Fever: The Market for RHINOSUL®

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>✓¹</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>
<td></td>
<td></td>
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</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


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

ABSTRACT

The Th2 cytokines are key mediators in allergic rhinitis. Pentosan Polysulphate Sodium (PPS) has been shown to reduce allergen-induced Th2 cytokine production in vitro, but it remains to be determined if PPS reduces Th2 cytokine production in vivo.

BACKGROUND

The Th2 cytokines are believed to be important immunopathological drivers of allergic rhinitis. In a recent study, we found that PPS significantly reduced allergen-induced Th2 cytokine production in vivo.

RESULTS

PPS has shown strong binding affinity to IL-4, IL-6, and IL-13.

CONCLUSIONS

Conclusions:

- The Th2 cytokine binding site of PPS is similar to that of theophylline.
- Binding of PPS to Th2 cytokines translates into reduced allergic inflammation.
- Topical administration of PPS to the nasal mucosa has a broad anti-inflammatory action on late-phase allergic responses.
- The fact that PPS has also been demonstrated to reduce mast cell degranulation responses further enhances PPS as a potential broad-spectrum drug for allergic and inflammatory disorders.
- Since recent data suggest that topical administration of PPS is well-tolerated and safe in humans, further efficacy studies in the clinic are highly warranted.

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>100 mg/ml or placebo</td>
<td></td>
<td></td>
<td></td>
<td>100 mg/ml or placebo</td>
</tr>
<tr>
<td>200 mg/ml or placebo</td>
<td></td>
<td></td>
<td></td>
<td>200 mg/ml or placebo</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 to be treated by March 31
- Results due late Q2 CY17 / early Q3 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></td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
</tr>
<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>
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<td></td>
</tr>
<tr>
<td>Ethics approval for Phase II trial</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Phase II placebo-controlled allergen challenge study</td>
<td></td>
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</table>

Investor Presentation 09 March, 2017
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 bruising¹,²,³

US$1,750 potential price per ZILOSUL® treatment

US$2.5+ BILLION ZILOSUL® 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></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethics approval for pilot trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 2 open label clinical trial (n=40)</td>
<td></td>
<td></td>
<td></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>
<td></td>
</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

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

Matthew J Sampson1,*, Margie Kobbum2, Ravi Krishnan3, Michael Nganga4 and Jegan Krishnan5

1Benson 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, 517 Flinders Lane, Melbourne, Victoria, Australia 3000
4Flinders University, Bedford Park, Bedford Park, South Australia, Australia 5042

Corresponding Author: Jegan Krishnan; Email: jegan@krishnan.com.au
In Life Clinical Trial
Osteoarthritis & Bone Marrow Edema

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

Lara I. Naumen, Susan-Fox Yu, Kuo-Ching Sheng, Wai-Kong Chau, Mark R. Fontana, Richard Bucala, Somch Mahalagam

Institute for Glycomics, Griffith University, Gold Coast, QLD, Australia; School of Medical Science and UQ-IHR Health Institute, Griffith University, Gold Coast, QLD.

Accepted: Department of Immunology, Yale University School of Medicine, New Haven, Connecticut, USA.

Abstract

Arthrogenic alphavirus 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 has become a circulating illness in the United States. The hallmark of alphavirus disease is crippling pain and inflammation of the joints, a similar immunopathology to rheumatoid arthritis. The use of glucos 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 polysulphate (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 qPCR, and immunohistochemistry studies (IHC). 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 glucosaminoglycans as a new class of treatment for infectious arthritis.

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 polysulphate (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 R T I C L E

Pentosan polysulphate is an anti-inflammatory glucosaminoglycan that can alleviate the symptoms of rheumatoid arthritis by reducing joint pain and swelling. In the past year, CHIKV has spread to the Americas, with approximately 1 million cases reported. Pentosan polysulphate (PPS) is an anti-inflammatory glucosaminoglycan approved for the treatment of cystitis. Our study shows that PPS can alleviate symptoms of alphavirus-induced arthritis, suggesting its potential for repurposing in the treatment of alphavirus-induced arthritis.

Received: 1 January 2015. Accepted: 18 May 2015

Accepted manuscript published: 27 May 2015

Griffith University

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>
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<td></td>
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</tr>
<tr>
<td>Proof of concept study under SAS (n=5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Design and Ethics approval for Phase II Trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Commence Phase 2 Clinical Trial Ross River</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Commence Phase 2 Clinical Trial Chikungunya</strong></td>
<td></td>
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</tbody>
</table>
Enhancing Shareholder Returns

Strong ongoing focus on prudent cash management

- Paradigm maintains a highly specialised and nimble team through effective outsourcing
- Paradigm’s focus is to use cash for clinical development rather than administration and overheads

- Paradigm’s clinical and R&D expenditure is significantly higher than industry average
- This expenditure is also eligible for the R&D tax refund

<table>
<thead>
<tr>
<th>Expenditure ratios</th>
<th>Paradigm</th>
<th>ASX-listed health care companies</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D expenditure (inc IP etc) / total operating expenditure (%)</td>
<td>78%</td>
<td>29%</td>
</tr>
<tr>
<td>Staff, marketing &amp; advertising expenditure / total operating expenditure (%)</td>
<td>9%</td>
<td>35%</td>
</tr>
</tbody>
</table>

- Paradigm’s staff, marketing and advertising expenditure is significantly lower than industry average
- Clear alignment of interests and strong focus on shareholder returns

Source: IRESS, company filings
Note:
1. Total operating expenditure is exclusive of “interest and other costs of finance” and “income taxes paid”
2. ASX-listed health care universe figures are reflective of companies that reported quarterly cash flows via an Appendix 4C for the quarter ending 31 March 2015
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>291</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>250</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>120</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>125</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>45</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 09 March 2017, exchange rates of AUDGBP 1.62 and AUDUSD 0.7515
2. Based on BME addressable market size, excludes CRPS addressable market due to lack of available information and thus likely underestates true market size
3. Only includes the market size for COPD which is US$12b+, 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>Acquirer</th>
<th>Deal value (US$)</th>
<th>Relevance</th>
</tr>
</thead>
</table>
| Jun-16| Afferent          | $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              | $7.2Bn            | - Meda’s third biggest product is Dymista®, which is a dual acting AR product                                                            |
| Dec-15| Takeda            | $575m            | - Acquired Takeda’s respiratory business only  
  - Acquisition includes expanded rights to roflumilast, used to treat COPD                                                             |
| Jul-14| Almirall          | $2.1Bn            | - Acquired Almirall’s respiratory products only  
  - Products focused on asthma and COPD                                                                                                 |
| May-13| 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

**BME TRIAL**
*Phase 2 trial*
- Open label trial anticipated to confirm efficacy together with optimal dosing of ZILOSUL® and clinical endpoints
- SAS results Peer Review Publication
- Potential to expand to OA and RA

**HAY FEVER**
*Initiating human trials*
- Publication of comparator study in “Allergy” expected in Q1 CY17
- Phase 2 ‘allergen challenge’ results in late Q2 CY17 / early Q3 CY17
- Potential interest from Big Pharma up to and after release of Phase 2 results

**ALPHAVIRUSES AND OTHER MULTIPLE USES**
*Multiple indications available*
- Initiation of Ross River Virus/CHIKV Phase 2 clinical trials
- BME for PPS to treat other joints (hips, ankles, shoulders and elbows) & RA
- Further potential indications in other respiratory diseases

**CORPORATE OPPORTUNITIES**
*Potential partners*
- Demonstrated interest from major pharmaceuticals companies in treatments for BME, Hay fever and Alpha Virus’
- Partnership with world-class manufacturers

**EXPANSION**
*Market share*
- Expansion of BME market beyond acute injury therapy
- Respiratory expansion of PPS for allergic asthma (AA) and chronic obstructive pulmonary disease (COPD)
- Develop new IP (Alphavirus)
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