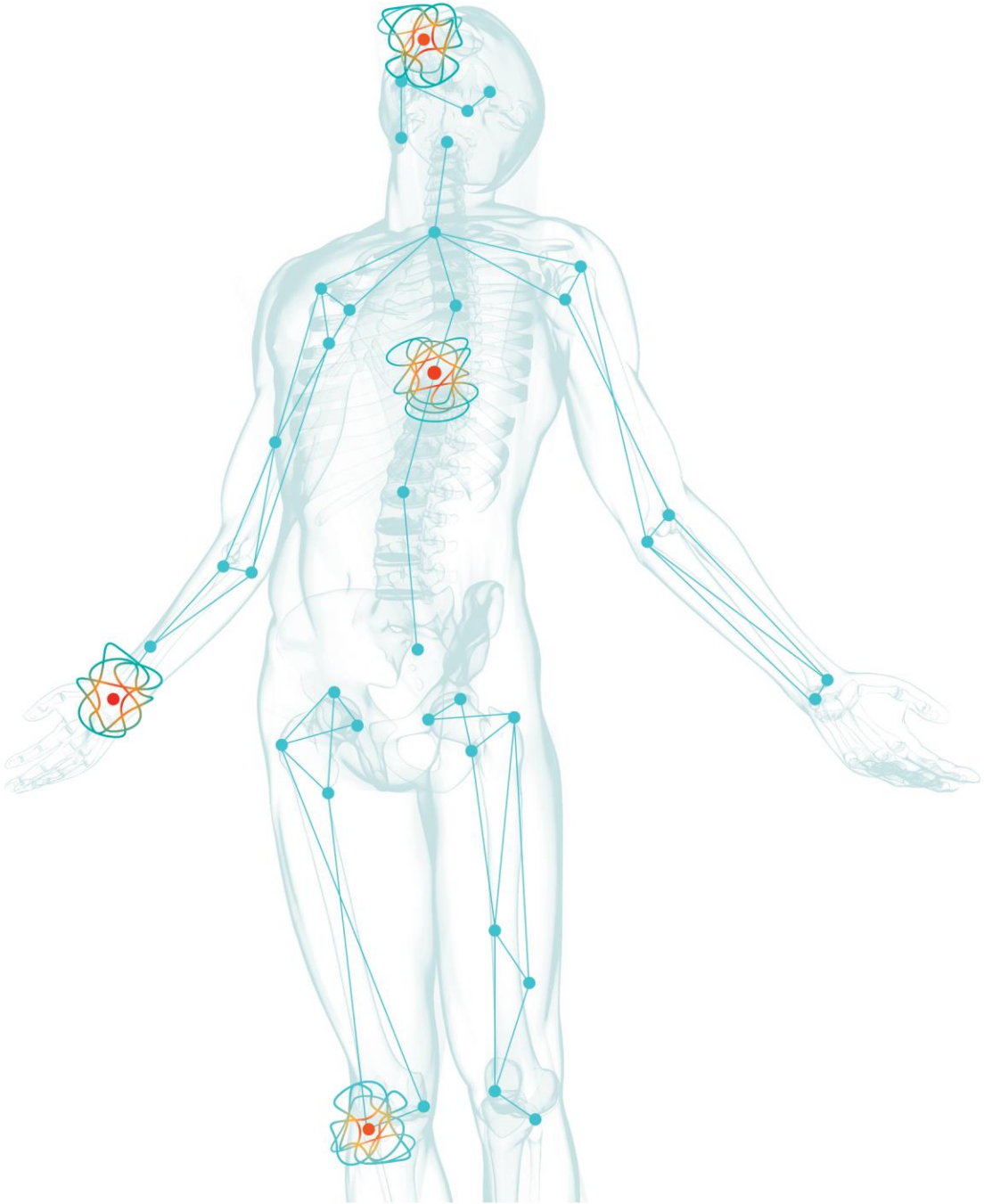
paradigm
BIOPHARMA

AGM

Paul Rennie, CEO & MD

30 November, 2016



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]

10-17 year process

Discovery & pharmacology	Preclinical testing	Phase I clinical trials	Phase II clinical trials	Phase III clinical trials	Regulatory approval
2 – 3 years	5 – 6 years		2 – 6 years		1 – 2 years

Paradigm’s drug repurposing timeline

3-5 year process to approval, potential for cash flow in 2017 if a partnering opportunity is secured

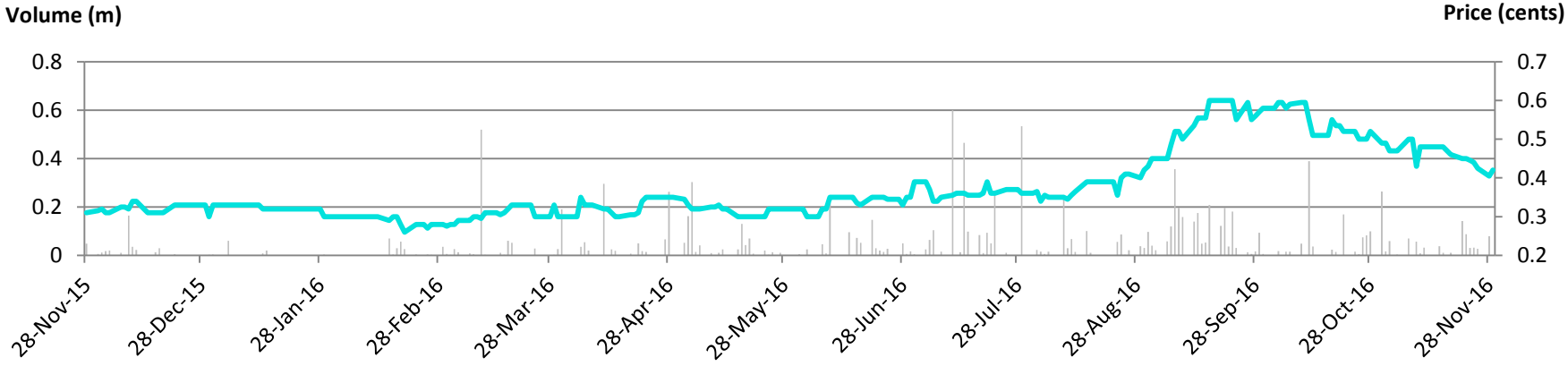
Phase I & Phase II trials (hay fever) 1 pivotal Phase II trial (BME)	1 pivotal Phase III trial for each indication	Regulatory approval
1 year (expected completion early 2017)	1 – 2 years	1 – 2 years

Source:
1. Khanaoure A, Chuki P & De Sousa A (2014)
2. Ashurn T & Thor K (2004)

Company Overview

Financial information	
Share price (29-Nov-16)	A$0.42
Number of shares[1]	100.3m
Market capitalisation	**A$42.1m**
Cash (30-Sept-16) Inc Placement (Not inc SPP & ~$1.2m R&D Tax Rebate)	~A$6.9m
Debt (30-Sept-16)	No debt
Enterprise value	**A$35.2m**

Top shareholders[2,3]	Shares (m)	%
Paul Rennie *(Managing Director)*	21.2[4]	21.1%
MJGD Nominees *(technology vendor)*	6.9	6.9%
Other Board and management	7.1	7.1%
Irwin Biotech *(technology vendor)*	6.3	6.3%



Source: IRESS

Note:

1. Includes 43.6m 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
4. Mr Paul Rennie subscribed for 416,666 ordinary shares ($0.48 per share) in the Oct 2016 Placement subject to shareholder approval

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 and executive VP of Mesoblast

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)

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

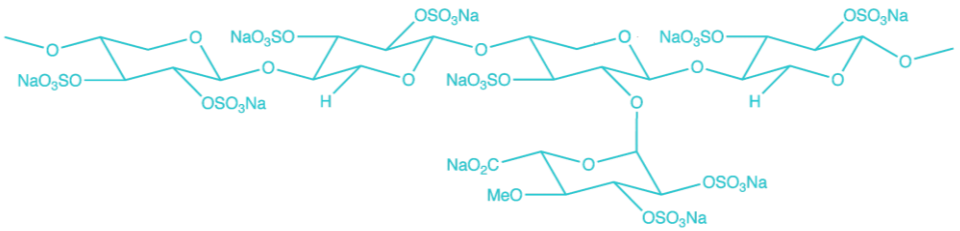
- The oral formulation is FDA approved and sold under the name Elmiron, by Janssen Pharmaceuticals, for the treatment of interstitial cystitis (painful bladder syndrome)
- Also used to treat deep vein thrombosis

Current distributors

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

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

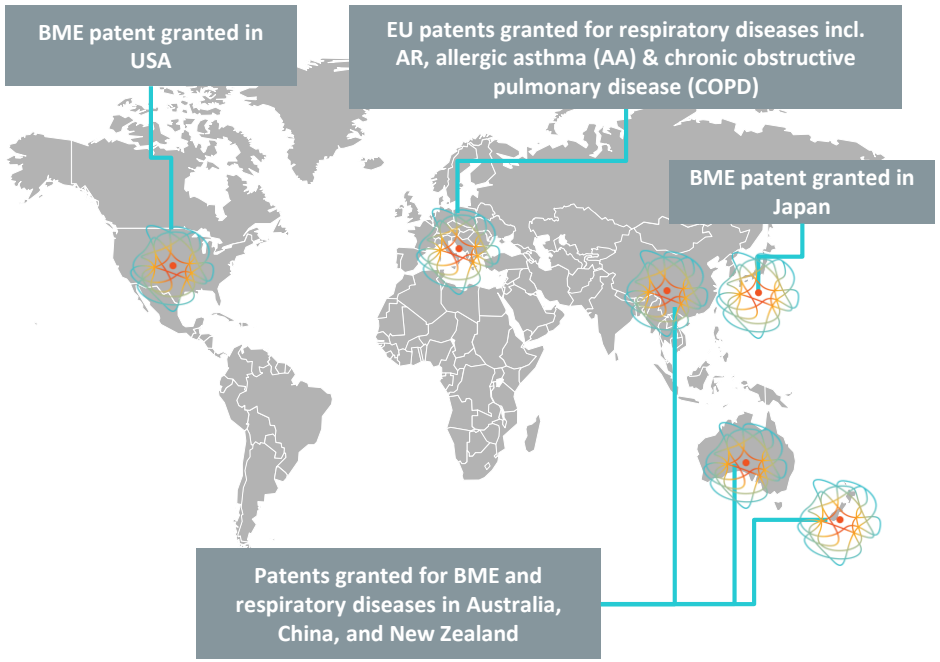
Multi-faceted IP protection increases barriers to entry for potential competitors

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

Secure manufacturing and supply

- Exclusive 20 year supply agreement with bene PharmaChem[1]
- 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

The AGM – the Company Scoreboard



Company Scoreboard – Milestones achieved for 2016

Milestones Achieved
1. US Patent granted for treatment of Bone Marrow Edema with PPS;
2. Ethics Approval for Open Label Pilot Phase 2 Bone Marrow Edema clinical trial;
3. 1st Patient treated under the Open Label Pilot Bone Marrow Edema trial;
4. 1st Patient treated under the TGA's Category B Special Access Scheme for Bone Marrow Edema;
5. Finalize Nasal Formulation for Allergic Rhinitis;
6. ✕ Peer review scientific publication of preclinical Allergic Rhinitis study;
7. Ethics Approval for Phase 1 clinical trial Allergic Rhinitis;
8. ✕ 1st Patient treated with PPS Nasal Spray;
9. Granted Allergic Rhinitis patent in at least one major market, USA, Japan or Europe.



Company Scoreboard – Bonus Runs: Additional Milestones Achieved

Additional Milestones Achieved
New acute injury BME clinical trial centre initiated. Ten BME patients treated under Therapeutic Goods Administration (TGA) Special Access Scheme (SAS). This has created interest in two pilot clinical trials (1) BME in patients with osteoarthritis and (2) BME in newly diagnosed rheumatoid arthritis.
New IP acquired from Griffith University (PPS to treat viral arthritis arising from Alphavirus Infections).
Ten Ross River Virus patients treated under TGA SAS. Ross River and Chikungunya clinical trial preparation has commenced.
Over subscribed capital raise ($6.2M) and R&D Tax ($1.25M).
Publication drafted for BME case report.
R&D undertook DD on and feasibility on four new projects



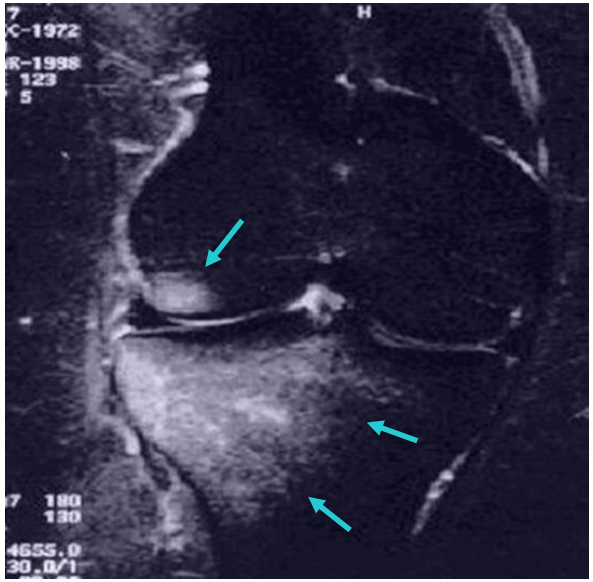


Bone Marrow Edema (BME)

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® 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:

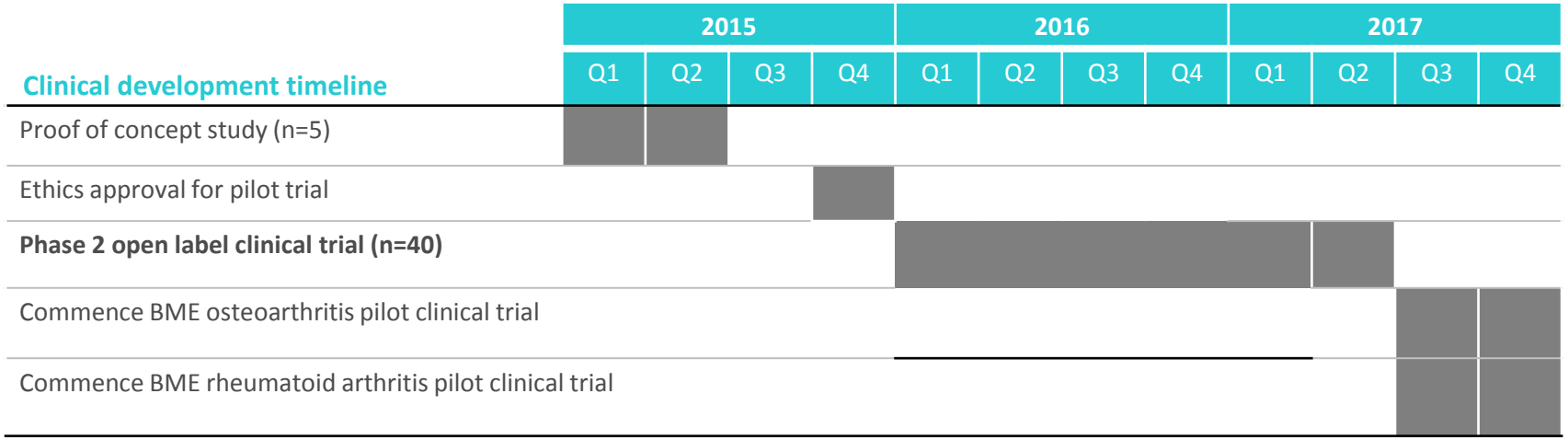
1. Based on 200k ACL injuries per annum, with 80% being associated with BME – Niall D, et al. (2004) and Friedberg R, et al. (2016)
2. Based on 1m meniscal injuries per annum, with 80% assumed as being associated with BME – Jones C, et al. (2012)
3. Based on 600k ankle injuries per annum, with 80% assumed 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 treated under the Phase 2 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.**



Note:
1. Closed label, randomised, double blind, placebo controlled trial commences in Q3 2017, expected to be completed in 12-24 months after commencement

Company Scoreboard – BME Milestones for 2017

BME Milestones for 2017
Close-out open-labelled acute BME study Q2 2017
Commence pilot randomised, double-blind placebo-controlled osteoarthritis study (total n=20)
Commence pilot randomised, double-blind placebo-controlled rheumatoid arthritis study (total n=20)



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**[1]
  - 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:



Estimated number of people who suffer from hay fever worldwide[2]

US$11+ BILLION

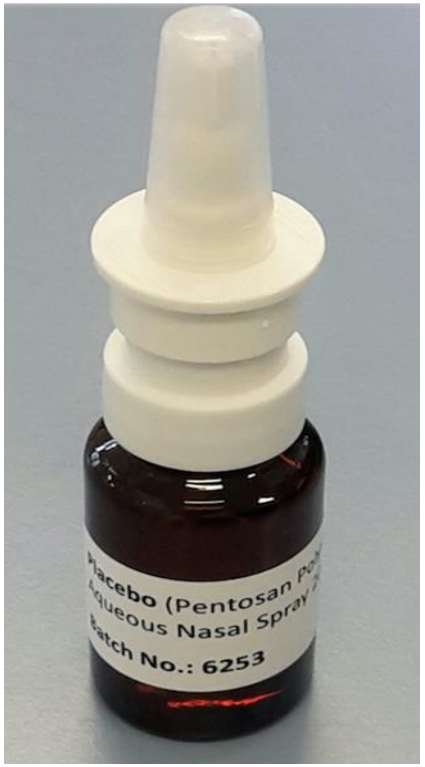
size of the therapeutic market for hay fever in 2014[3]

Source:
1. 2005 survey conducted by Asthma and Allergy Foundation of America
2. Mullol J, et al. (2008)
3. Visiongain: Allergic Rhinitis Drugs Market Forecast 2015-2025

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.**
- **Participant screening and recruitment has commenced.**
- **Successful Phase II results are expected to result in a significant licensing opportunity**



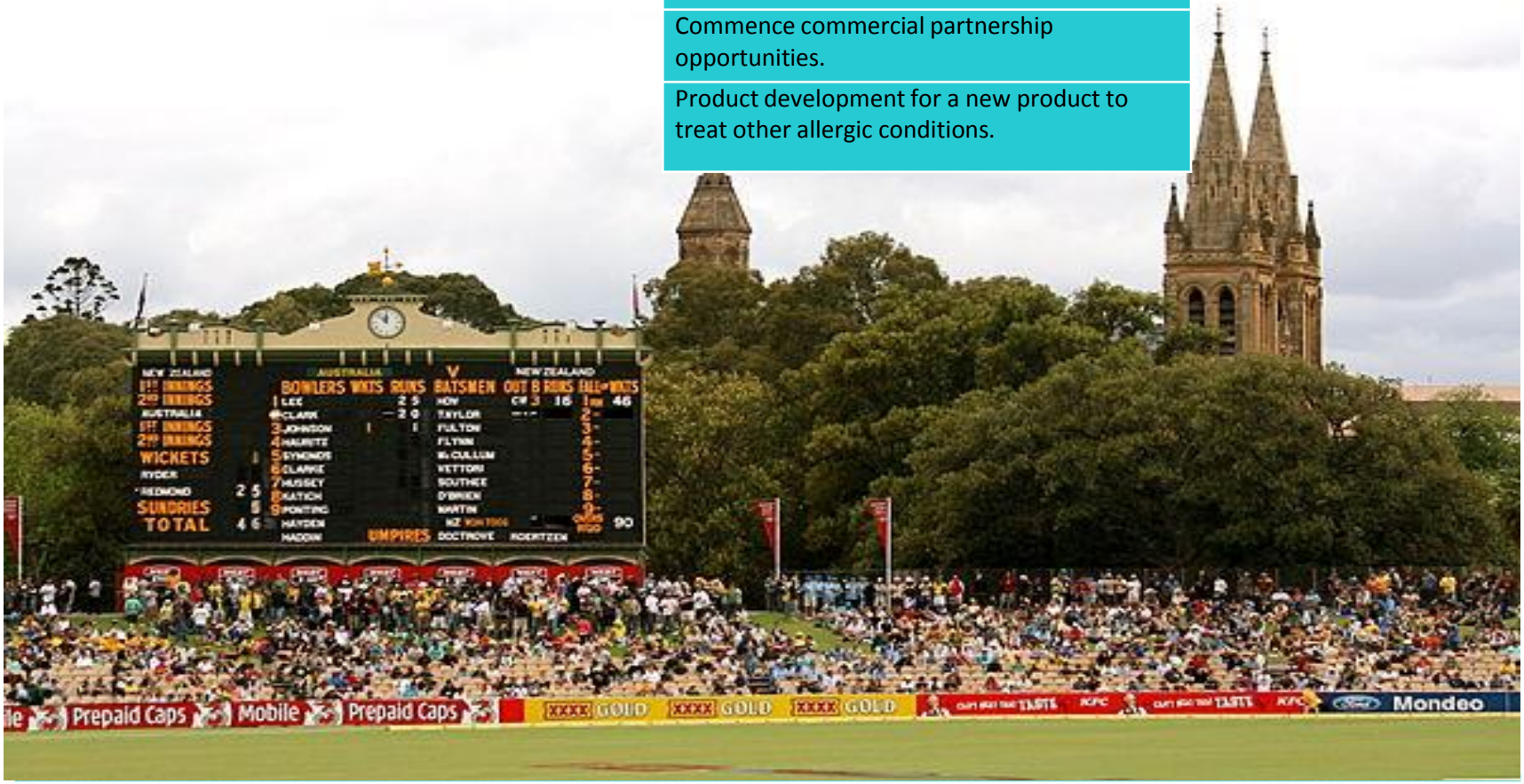
paradigm BIOPHARMA

Clinical development timeline

	2015				2016				2017	
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2
Bridging nasal toxicology study			■	■	■	■				
Nasal formulation development			■	■	■	■				
Nasal spray product development (Aptar device)			■	■	■	■				
Phase I safety study (n=20) - COMPLETED						■	■			
Ethics approval for Phase II trial							■			
Phase II placebo-controlled allergen challenge study								■	■	■

Company Scoreboard – Respiratory Milestones for 2017.

Respiratory Milestones for 2017
Complete Phase 2 clinical trial with read-out Q3 2017.
Commence commercial partnership opportunities.
Product development for a new product to treat other allergic conditions.



Viral Arthritis – Alphavirus

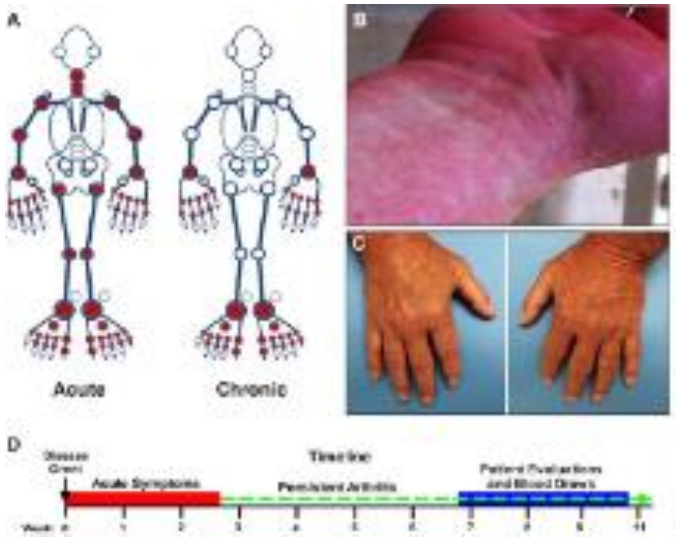
No approved treatment for severely debilitating virus infection

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

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 SeidelNews Corp Australia Network



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

Viral Arthritis – Alphavirus

Global emergence of Alphaviruses that cause arthritis in humans.

- *Lwande OW et al . Infect Ecol Epidemiol. 2015 Dec 18;5:29853. doi: 10.3402/iee.v5.29853.*

Pentosan Polysulphate: A Novel Glycosaminoglycan-Like Molecule for Effective Treatment of Alphavirus-Induced Cartilage Destruction and Inflammatory Disease.

- *Herrero LJ et al J Virol. 2015 Aug;89(15):8063-76. doi: 10.1128/JVI.00224-15.*

Chronic pain associated with the Chikungunya Fever: long lasting burden of an acute illness

- *de Andrade et al. BMC Infectious Diseases 2010, 10:31*

Persistent Arthralgia Associated with Chikungunya Virus: A Study of 88 Adult Patients on Reunion Island.

- *Borgherini G et al Clinical Infectious Diseases 2008; 47:469–75*

Chikungunya Virus-associated Long-term Arthralgia: A 36-month Prospective Longitudinal Study

- *Schilte C et al PLoS Negl Trop Dis 7(3): e2137. doi:10.1371*

Chikungunya Viral Arthritis in the United States : A Mimic of Seronegative Rheumatoid Arthritis

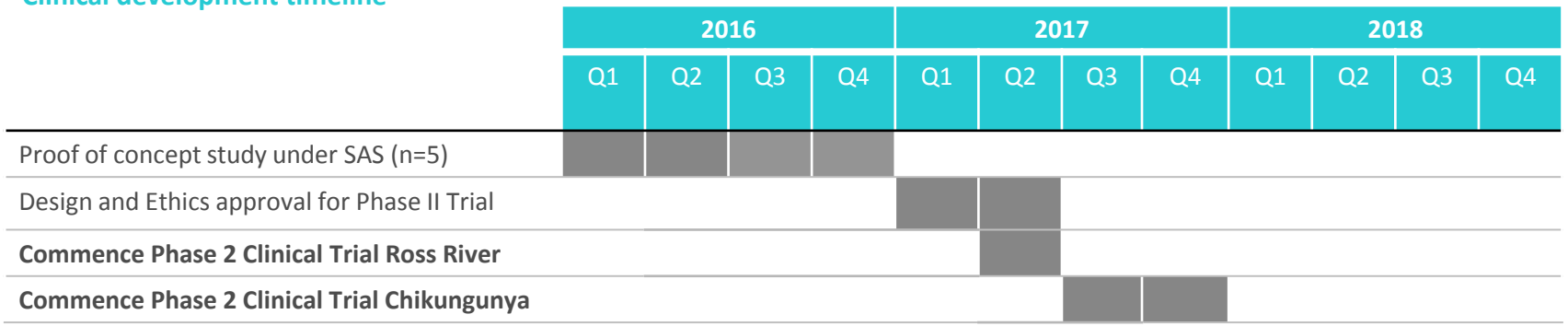
- *Milner J et al Arthritis & Rheumatology Vol. 67, No. 5, May 2015, pp 1214–1220 DOI 10.1002/art.39027*

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
- Five 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.

Clinical development timeline



Company Scoreboard – Alphavirus Milestones for 2017

Alphavirus Milestones for 2017
Commence Ross River Phase 2 clinical trial (Planning has commenced)
Commence Chikungunya Phase 2 clinical trial (Brazil) (Planning has commenced).



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

Expenditure ratios	paradigm BIOPHARMA	ASX-listed health care companies
R&D expenditure (inc IP etc) / total operating expenditure (%)	**78%**	29%
Staff, marketing & advertising expenditure / total operating expenditure (%)	**9%**	35%

✓ 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

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 ▪ Potential to expand to OA and RA
HAY FEVER *Initiating human trials*	▪ Publication of comparator study in "Allergy" expected in 2H 2016 ▪ Phase 2 'allergen challenge' trial to begin in Sweden in December 2016 ▪ 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, and hay fever ▪ 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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