ASX RELEASE

SHAREHOLDER UPDATE

16 March 2016, Melbourne, Australia: Paradigm Biopharmaceuticals Limited (ASX: PAR) is an Australian Biopharmaceutical company focused on repurposing Pentosan Polysulfate Sodium (PPS) as a potential new treatment for Bone Marrow Edema (BME) and respiratory diseases like Allergic Rhinitis (AR), also known as hay fever. PPS is a well-established, anti-clotting and anti-inflammatory agent that has been used for over 60 years and has a solid safety and efficacy profile

INVESTMENT HIGHLIGHTS

- Repurposing a pre-approved drug to reduce clinical costs and accelerate commercialisation
- Pentosan Polysulfate Sodium is a new, multi-acting treatment for bone marrow edema and allergic rhinitis, both of which have very large addressable markets (US$13.5bn+)
- 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 open label clinical trial for BME
- All short-term operational milestones have been met, with several major clinical trial and development catalysts expected over the next 6-12 months
- Strong platform for growth and growing global interest in BME and AR spaces

NEAR TERM MILESTONES

- Paradigm will assess and release to market as required, the results of the open label clinical trial to investigate the role of PPS in acute ACL injuries using ZILOSUL® as it is being conducted
- Potential to accelerate ZILUSOL®'s regulatory pathway by using interim analysis to move forward to the closed label Phase II(b) clinical trial as early as 3Q 2016
- Results of the animal intranasal toxicology study investigating the role of PPS in respiratory diseases expected in 2Q 2016
- Phase I safety study investigating the role of intranasal PPS in respiratory diseases in humans expected to commence in 3Q 2016

Managing Director Paul Rennie said: *"We are very pleased to have met all our planned milestones from the IPO to date. We enrolled our first participant with an acute ACL injury in the open label clinical trial at the Box Hill Sportsmed Biologic medical clinic in Melbourne. Pleasingly we also initiated a second clinical trial site at Southern Orthopaedics in Adelaide. The next 12 months represents an exciting period for Paradigm as we assess data from the ZILOSUL® open label clinical trial and initiate the RHINOSUL® Phase I safety study."*

For more information, please contact:

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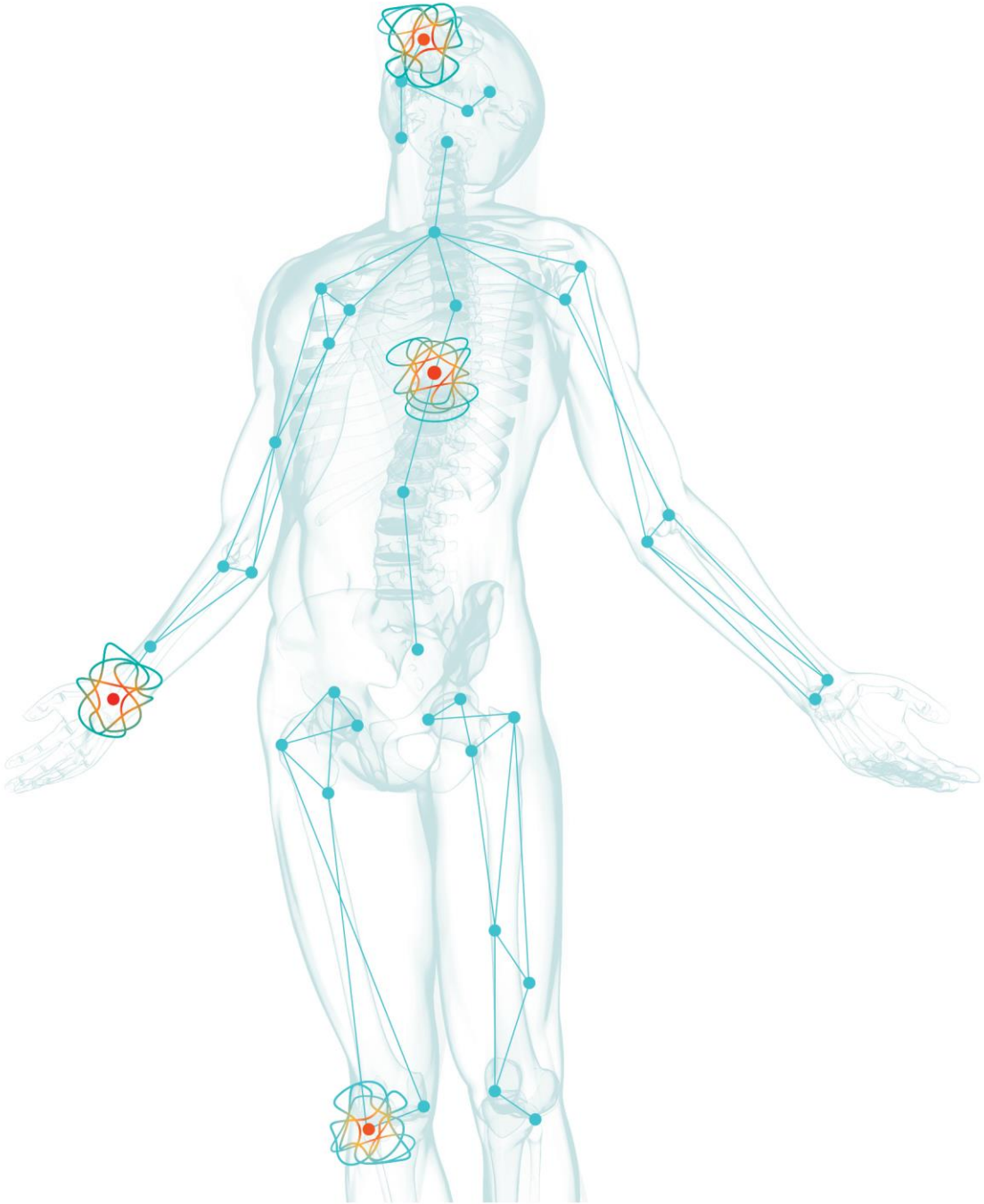
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paradigm
BIOPHARMA

Investor presentation

Paul Rennie, CEO

16 March 2016



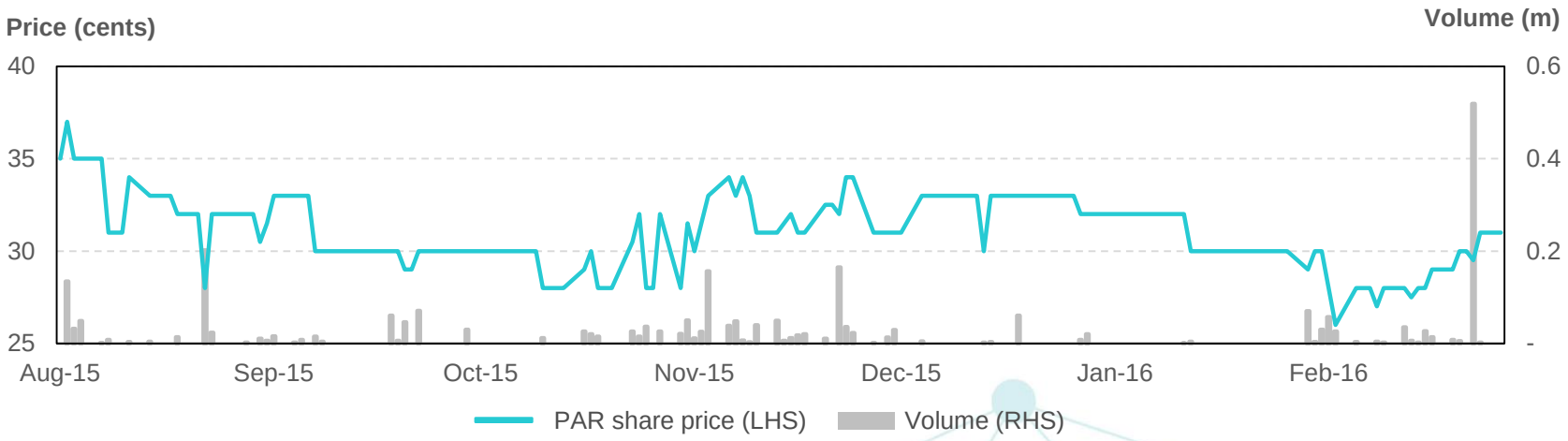
Company highlights

- Repurposing a pre-approved drug to **reduce clinical costs and accelerate commercialisation**
- Pentosan Polysulfate Sodium is a new, multi-acting treatment for bone marrow edema and allergic rhinitis, both of which have **very large addressable markets (US$13.5bn+)**
- **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 open label clinical trial for BME
- All short-term operational milestones have been met, **with several major clinical trial and development catalysts** expected over the next 6-12 months
- **Strong platform for growth** and growing global interest in BME and AR spaces

Company overview

Financial information	
Share price (14-Mar-16)	A$0.31
Number of shares[1]	87.6m
Market capitalisation	**A$27.2m**
Cash (31-Dec-15)	A$5.3m
Debt (31-Dec-15)	No debt
Enterprise value	**A$21.9m**

Top shareholders[2,3]	Shares (m)	%
Paul Rennie *(Managing Director)*	21.2	24.2%
MJGD Nominees *(Xosoma vendor)*	7.1	8.1%
Other Board and management	7.1	8.1%
Irwin Biotech *(Xosoma vendor)*	6.8	7.8%



Source: IRESS
Note:
1. Includes 54.3m escrowed shares, where the escrow date for 0.9m shares is 8-May-16, 19.5m shares is 7-Aug-16 and 33.9m is 18-Aug-17
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

Operational milestones

Paradigm has met all short term deliverables since IPO

18-Aug-15 — Initial public offering

- ✓ Paradigm lists on the ASX raising A$8.0m at A$0.35 offer price

26-Aug-15 — BME patent

- ✓ Paradigm secures US patent to use PPS for treatment of BME
- ✓ More recently secured patent in Japan

23-Nov-15 — BME clinical trial approved

- ✓ Ethics approval granted from the Human Research Ethics committee

3-Dec-15 — Elite athlete successfully treated with ZILOSUL®

- ✓ Athlete had an unresolved orthopaedic condition
- ✓ 6 intramuscular injections over a 3 week period

15-Dec-15 — Respiratory patent

- ✓ Secured European patent to use PPS to treat respiratory diseases

25-Feb-16 — First patient enrolled for BME trial

- ✓ Open label pilot trial to determine the safety and tolerability of ZILOSUL® in patients with a BME lesion

Board and management

Highly 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))

Senior management

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)

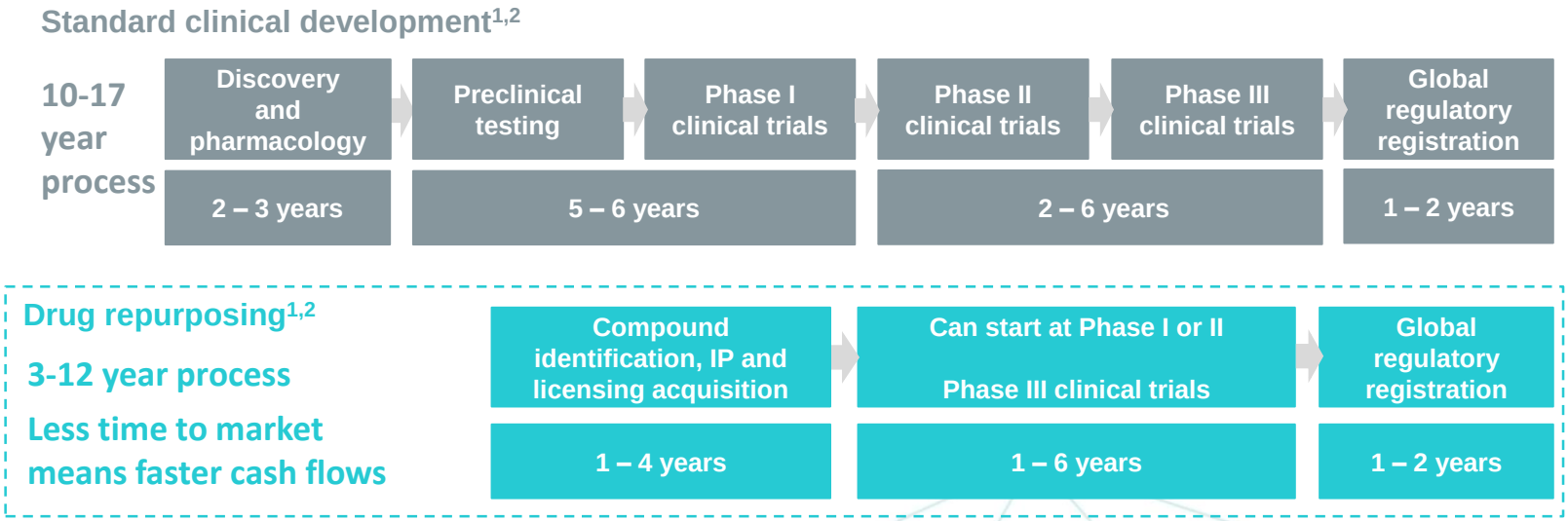
Dr Keith Williams – VP Business Development
- Founder & CEO of Proteome Systems, extensive relationships with major biotech & engineering companies

Dr Claire Kaufman – Respiratory Operations Manager
- Extensive experience with pre-clinical and clinical immunology research and therapeutic trials, as well as using PPS in clinical veterinary practice

Focus on drug repurposing

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

- **Lower cost:** average development cost of US$8-41m compared to US$1.3bn for “de novo” development[1,3]
- **Faster:** leverages the value of 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]
- **Addressable markets and expected returns** for repurposed drugs are equivalent to those of new drug indications



Source:
1. Khanaoure A, Chuki P & De Sousa A (2014) Ind J Appl Res 4: 462-466. Drug Repositioning: Old Drugs for New Indications
2. Ashurn T & Thor K (2004): 673-683, Nature Reviews Drug Discovery 3
3. Estimated cost of US$8.4m to relaunch a repositioned drug while estimated cost of US$41.3m to reformulate an existing drug in the original indication

Repurposing Pentosan Polysulfate Sodium

Biologically PPS is an ideal drug to treat the issues associated with BME and AR

Existing applications

- Deep vein thrombosis
- Interstitial cystitis or painful bladder syndrome

✓ PPS has well established biological characteristics

- Anti-inflammatory
- Anti-clotting (first developed to treat blood clots)
- Anti-histamine
- Long history of safe use in humans (60 years)
- First approved by the FDA > 30 years ago

Repurposed applications

- BME treatment via ZILOSUL® - *refer to slides 8-11*
- AR treatment via RHINOSUL® - *refer to slides 12-14*

✓ PPS addresses multiple aspects of BME and AR

	BME	AR
Inflammation	✓	✓
Necrosis (premature cell death)	✓	na
Cartilage degeneration	✓	na
Blood clotting	✓	na
Histamine release	na	✓

PPS has a unique combination of biological characteristics that make it ideally suited to BME and AR treatments

Bone Marrow Edema (BME)

Injuries related to BME are a significant burden on health care expenditure

What is BME (bone bruising)?

- Disorder causing excess fluid build-up inside bone, typically at the end of long bones

Why focus on BME?

- **Clinical condition that presently has no regulatory approved pharmaceutical therapeutic options**
- Chronic health impacts associated with untreated BME
  - 10x greater likelihood of developing osteoarthritis (OA)
- Very large potential market
  - **Worldwide hip & knee surgical implant market is US$16.7bn, will be US$33bn by 2022[1]**
  - Current focus is on acute knee injuries but potential for ZILOSUL® to treat other major joints (ankle, shoulder, elbow, hip, etc.) and chronic injuries (BME case study)

Addressable market based on acute traumatic injuries:

1.4 MILLION

KNEE & ANKLE

INJURIES ASSOCIATED WITH BME[1,2,3]

US$1,750

POTENTIAL COST PER ZILOSUL® TREATMENT

US$2.5 BILLION

ZILOSUL® MARKET IN USA

(Excludes shoulder, elbow and hip injuries as well as chronic injuries)

Source:
1. Winter Green Research (2016), Hip and Knee Orthopaedic Surgical Implants Market Shares, Strategies, and Forecasts, Worldwide, 2016 to 2022
2. Based on 200k ACL injuries per annum, with 80% being associated with BME – Niall D, et al. (2004) and Friedberg R, et al. (2016)
3. Based on 1m meniscal injuries per annum, with 80% assumed as being associated with BME – Jones C, et al. (2012)
4. Based on 600k ankle injuries per annum, with 80% assumed as being associated with BME – Waterman B, et al. (2010)

BME: Comparative advantages of ZILOSUL®

Multi-acting treatment that addresses the underlying pathology of BME

- ZILOSUL® is the only therapy being used that addresses multiple pathways to treat BME
  - ZILOSUL® provides a more complete solution to BME
  - Competing treatments have failed to capture market share due to limited safety and efficacy profiles
- Paradigm has completed a proof of concept trial for ZILOSUL®
  - All 5 patients experienced complete resolution of BME and associated pain



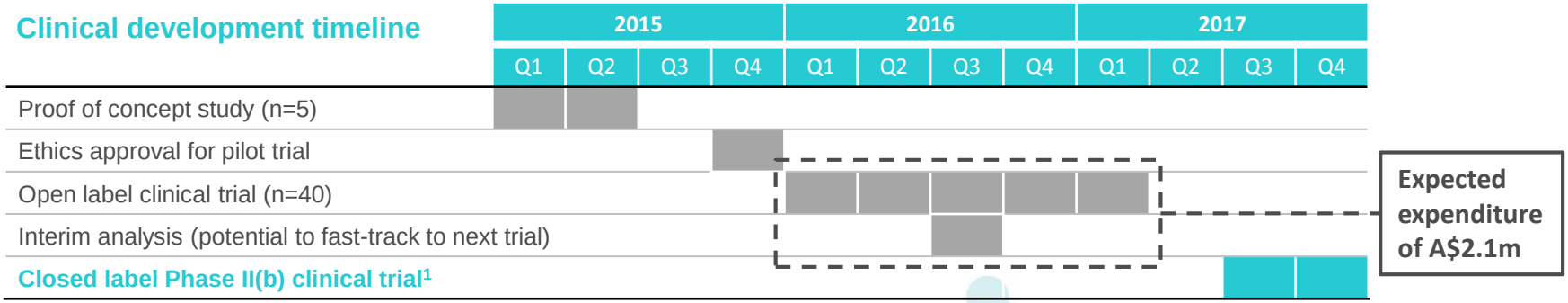
	ZILOSUL®	Iloprost®	Ibandronate®
Anti-inflammatory	✓	✓	
Fibrinolytic agent (anti-clotting)	✓	✓	
Prevents cell death and necrosis	✓		
Increase in cartilage synthesis	✓		
High safety profile	✓		✓
Hospitalisation not required	✓		
Not administered intravenously	✓		

BME: Clinical development program

Opportunity to further accelerate clinical trial development timeline

- **First patient enrolled in open label trial investigating the efficacy of ZILOSUL® in patients with a BME lesion due to a recent acute ACL injury**
  - Open label design means that dosage levels can be adjusted and optimised due to real time data transparency
- Commencement of Phase II(b) may be brought forward pending the results of interim analysis
- Clinical trial strategy aims to utilise the FDA 505(b)(2) regulatory pathway in the USA
  - **A single positive Phase III trial is sufficient for regulatory clearance and marketing approval**
- Paradigm fully funded from IPO until Q2 2017 to complete Phase II(a) open label clinical trial

Clinical development timeline



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

Elite athlete case study

Potential to open new market opportunities by treating chronic BME with ZILOSUL®

- Elite athlete in a major Australian sporting code successfully treated for a chronic orthopaedic injury by ZILOSUL®
- Robust results highlight the potential for market expansion as ZILOSUL® is used to treat both chronic and acute BME
- Treatment permitted under TGA's Special Access Scheme and consisted of 6 intramuscular injections over 3 weeks
- Patient experienced no adverse events and treatment was well tolerated

Pre-treatment wellbeing

- × Un-resolving bone marrow lesion
- × Fluid had to be drained from the knee at least once a week
- × Patient had undergone multiple unsuccessful therapeutic and surgical interventions

ZILOSUL®

Results

- ✓ Patient has not had to drain fluid from knee since the treatment in November 2015
- ✓ Encouraging result that significantly improved patient's well-being

	Pre treatment	Post treatment	Change
Pain	8.5 (very bad)	3.2 (mild)	↓ 62%
Joint function	69 (fair)	95 (excellent)	↑ 37%

Allergic Rhinitis (AR)

AR is a common condition that is inadequately treated with quality of life impacts

What is AR (hay fever)?

- Allergic inflammation of the nasal airways, when an allergen is inhaled by a sensitised individual

Why focus on AR?

- Strong need for more effective treatment options
  - >50% of patients dissatisfied with current medication[1]
  - Long term use may be harmful to certain sufferers
- Clear need for safer, superior and cheaper treatments
- Growing economic burden (missed days at work, school)
- Swedish study (2016) indicated the size of the AR market may be significantly underestimated in current literature
  - **Total cost of AR in Sweden (population 9.5 million) is estimated to be US$1.4 billion annually[2]**
  - Potential implications for value of global market

Addressable market for allergic rhinitis / hay fever:

600 MILLION

NUMBER OF PEOPLE WHO SUFFER FROM AR WORLDWIDE[3]

US$11 BILLION+

SIZE OF THE THERAPEUTIC MARKET FOR AR IN 2014[4]

Source:
1. 2005 survey conducted by Asthma and Allergy Foundation of America, found >50% patients were dissatisfied with current medication; 60% indicated they were interested in new treatments
2. Cardell L, et al. (2016) Primary Care Respiratory Medicine 26. TOTALL: high cost of allergic rhinitis—a national Swedish population-based questionnaire study
3. Mullol J, et al. (2008) J Investig Allergol Clin Immunol 18: 327-334. Allergic Rhinitis and its Impact on Asthma Update: The Perspective from Spain
4. Visiongain: Allergic Rhinitis Drugs Market Forecast 2015-2025: Future Prospects for Companies in Antihistamines, Corticosteroids, Immunotherapy & Vaccines

AR: Comparative advantages of RHINOSUL®

RHINOSUL® has the potential to fill the current gap in AR treatment options

- RHINOSUL® has multiple mechanisms of action making it a potentially superior treatment to existing therapies
- **Meda (MEDA.STO, A$8.7bn market cap) manufacture the only commercialised new class of dual acting treatment – Dymista®**
  - Dymista® has been widely praised as a dual-acting treatment but has a number of undesirable side effects
- Paradigm's RHINOSUL® is a candidate for a new class of dual-acting treatments, revolutionising an old market
  - The first ever potential dual-acting treatment with no undesirable side effects for AR, if FDA approval is achieved



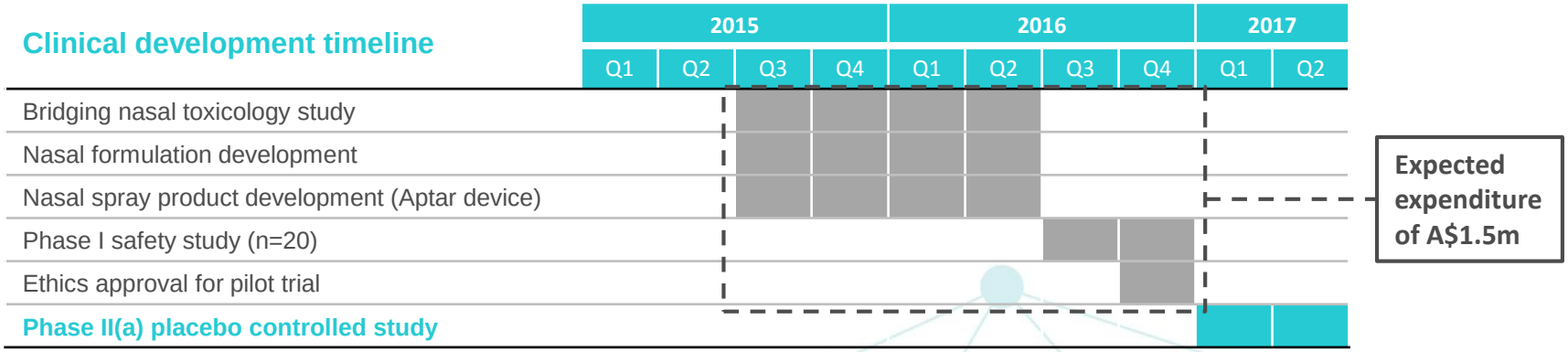
	RHINOSUL®	Anti-histamines	Corticosteroids	Dymista®
Treats acute phase symptoms (histamine mediation)	✓	✓	✓[1]	✓
Treats chronic phase symptoms (tissue inflammation)	✓		✓	✓
No undesirable side effects	✓			
Anti-inflammatory	✓		✓	✓
Simple to manufacture	✓			

Note:
1. Immediate use of corticosteroids do not treat acute AR symptoms, however, ongoing use will result in the subsiding of such symptoms

AR: Clinical development program

Paradigm is on track with clinical development timeline and expenditure

- Paradigm is developing RHINOSUL®, the first intra-nasally applied PPS product to be used humans
  - For this new route of administration, Paradigm has conducted a bridging nasal toxicology study
  - To be followed by a Phase I (safety/tolerability) and Phase II(a) allergen challenge study
- First enrolment for Phase II(a) placebo controlled allergen challenge study estimated for 1Q 2017
- **Established large scale manufacturing capabilities through partnership with MoNo chem-pharm GmbH**
- **Successful product developed in nasal PPS formulation with Aptar nasal spray device technology**



Valuable IP portfolio

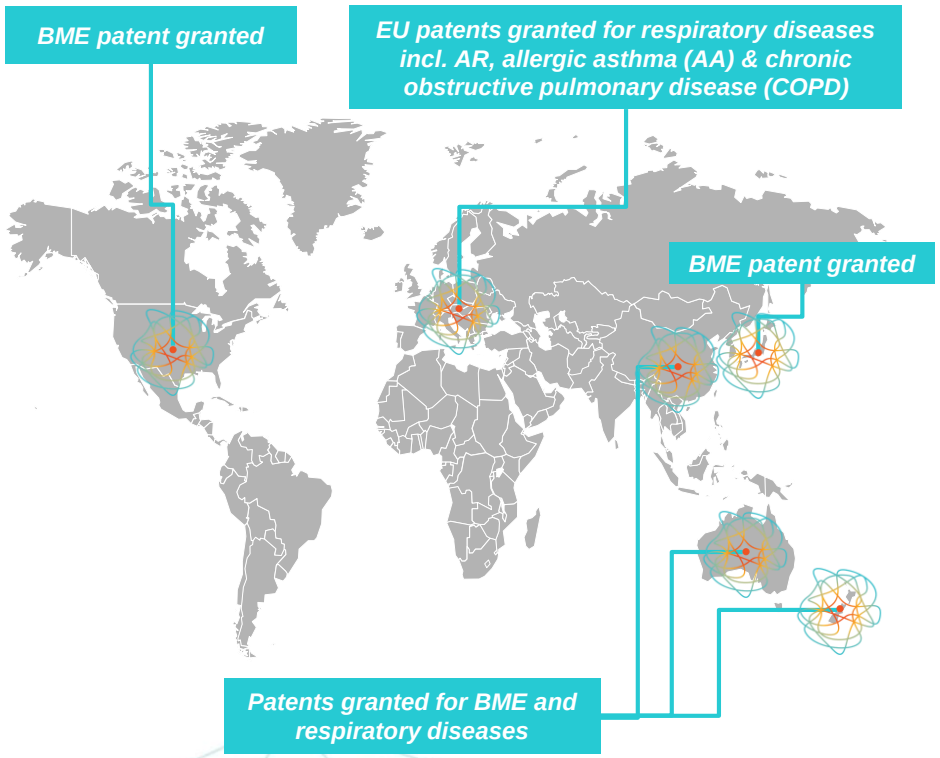
Multi-faceted IP protection increases barriers to entry for potential competitors

Valuable patent portfolio

- Disease specific patents secured in a growing number of geographic regions
- Likely to attain reformulation patents for alternative PPS delivery methods in humans
- Established regulatory exclusivity and trademarks

Industrial manufacturing involves bene pharmaChem's products

- The only FDA-approved form of PPS from bene pharmaChem[1]
- bene pharmaChem's manufacturing methods are a well kept trade secret making it a key component of Paradigm's IP
- Partnership mitigates the risk associated with manufacturing and supply expansion common to conventional drug developers



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

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

Peer	Ticker and exchange	Market cap (A$m)[1]	Rationale	Clinical stage of key product	Addressable market size
Medical Developments International	MVP.ASX	272	Developing new markets and applications for Penthrox, recent focus on respiratory diseases, significant IP in manufacturing process	Commercialisation	US$1.5bn+
starpharma	SPL.ASX	235	Commercialising an old technology of synthetic branching polymers (dendrimers), with lead product VivaGel in Phase III trials	Phase III & commercialisation	US$3bn+
verona pharma	VRP.LN	71	Focused on commercialising an old compound, RPL554, for respiratory diseases, with dual inhibition of key enzymes	Phase I/II(a)	US$12bn+ (COPD only)
paradigm BIOPHARMA	PAR.ASX	27	Focused on the clinical development of PPS as a multi-target treatment for complex conditions, such as BME and AR	Phase II(a)	US$13.5bn+

Source: Bloomberg, company filings
Note:
1. Market data as at 14 March 2016, exchange rate of GBPAUD of 1.91
2. Includes AR market of US$11bn+ and BME market of US$2.5bn+, 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

- Mylan's recent takeover offer of Meda was at a 92% premium to last close, with Dymista® being RHINOSUL®'s closest comparative product
- AstraZeneca's transactions highlight the potential value attributed to respiratory business units

Date ↓	Target	Acquirer	Deal value (US$m)	Relevance
Feb-16	MEDA	Mylan	7,200	▪ Meda's third biggest product is Dymista®, which is a dual acting AR product ▪ Transaction not yet complete
Dec-15	Takeda	AstraZeneca	575	▪ Acquired Takeda's respiratory business only ▪ Acquisition includes expanded rights to roflumilast, used to treat COPD
Jul-14	Almirall	AstraZeneca	2,100	▪ Acquired Almirall's respiratory products only ▪ Products focused on asthma and COPD
May-13	Knee Creations	ZIMMER BIOMET	Undisclosed	▪ Zimmer Biomet acquired Knee Creations for its Subchondroplasty procedure, designed to treat BME

Source: Bloomberg, company filings

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
- Evidenced by Paradigm's clinical and R&D expenditure as a ratio of total operating expenditure being significantly higher than the industry average for the quarter ending 31 December 15[1,2]
  - Clinical expenditure eligible for the Australian Government R&D tax refund leading to further cost minimisation
- Paradigm's staff, marketing and advertising expenditure as a ratio of total operating expenditure was significantly lower than the industry average for the quarter ending 31 December 15[1,2]
  - Clear alignment of interests drives strong focus on shareholder returns

Expenditure ratios	paradigm BIOPHARMA	ASX-listed health care universe	Difference
R&D expenditure / total operating expenditure (%)	**67%**	35%	*+32%* ✓
Staff, marketing & advertising expenditure / total operating expenditure (%)	**7%**	32%	*-25%* ✓

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 December 2015

Share price catalysts

Focused effort on compressing the BME and AR clinical development timelines

BME TRIAL
Phase II(a) trial

- Open label trial anticipated to confirm efficacy together with optimal dosing of ZILOSUL® and clinical endpoints
- Potential to bring forward closed label Phase II(b) clinical trial to 3Q 2016

AR TRIAL
Initiating human trials

- Phase I trial planned for 3Q 2016 with analysis to follow
- First enrolment for Phase II(a) trial expected in 1Q 2017

MULTIPLE USES
Multiple indications available

- Potential for PPS to treat other joints (hips, ankles, shoulders and elbows)
- Further potential indications in other respiratory diseases
- Second generation versions of PPS under investigation

CORPORATE OPPORTUNITIES
Potential partners

- Demonstrated interest from major pharmaceuticals companies in treatments for BME and AR
- Value accretive partnership with world-class manufacturers

EXPANSION
Market share

- Expansion of BME market beyond acute orthopaedic therapy
- Respiratory expansion of PPS for AA and COPD
- Preliminary stage review of novel IP

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