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PARADIGM BIOPHARMACEUTICALS LTD (PAR.ASX)

RESEARCH NOTE
7 June 2016

RECOMMENDATION
Buy – Initiation of Coverage

PRICE
$0.30

TARGET PRICE
$0.96

RISK
High (Speculative)

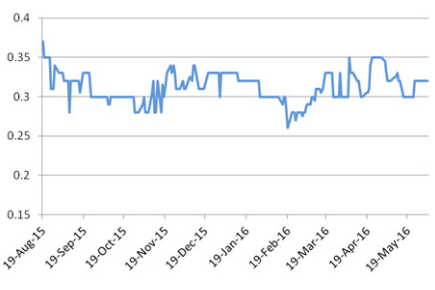
BRIEF COMPANY DESCRIPTION

Paradigm Biopharmaceuticals listed on the ASX in August 2015, is focused on repurposing pentosan polysulphate sodium (PPS) for new orthopedic and respiratory applications. Pentosan Polysufate Sodium was developed in Germany in 1949 and has established anti-inflammatory and anti-thrombotic properties. It has been in use for over 60 years and as such its safety profile has been firmly established. The Company addresses conditions that start with and are sustained by inflammation. Lead clinical indications involve treating injury that results in bone marrow edema (BME) and the allergic inflammatory response in allergic rhinitis (AR), which is commonly known as 'Hay Fever'. The combined markets for these indications are well in excess of US$13.5B.

COMPANY DATA (07.06.2016)

ASX Code	PAR.ASX
Market Capitalisation (fully diluted)	~$28.1m
Enterprise Value	~$24m
Shares on Issue	~87.5m
12 Month High/Low	$0.40/0.25
Ave Monthly Turnover	~0.487m
Cash – Mar 2016	~A$4.1m

12 MONTH SHARE PRICE



Paradigm Biopharmaceuticals – Reduced Risk without Reduced Reward

Baker Young Stockbrokers recently met with the Australian Biotechnology company, Paradigm Biopharmaceuticals Ltd ('Paradigm' or 'PAR') management to discuss the Company's repurposing of the existing drug Pentosan Polysulfate Sodium (PPS) for treating Hay fever (Allergic Rhinitis) and Bone Bruising (Bone Marrow Edema).

By repurposing an existing drug with a well known and established safety profile Paradigm is significantly reducing the risk and cost of bringing the drug to market for other uses. Trial costs are greatly reduced and trial result timelines (price catalysts) are significantly brought forward all without diminishing the end potential payoff. Coupled with the multi-billion dollar target market potential (combined US$13.5B) we believe there is a very real potential for a circa billion-dollar partnering transaction to be executed between Paradigm and a global pharmaceutical company leading up to/ upon conclusion of the upcoming Hay fever and/or BME trials – expected early CY2017.

We initiate coverage of Paradigm with a BUY recommendation and we value PAR $0.96 per share which is derived from using a combination of probability weighted DCF methodology ($1.06) and peer group valuation ($0.87 implied PAR share price). Our target price of $0.96 per share sits in the midpoint of our valuation range.

Repurposing an existing drug – Pentosan Polysulfate Sodium (PPS) greatly improves chances of clinical success

Repurposed drugs have a 2.5 times better chance of being successfully commercialised compared to "de novo" (new drugs)[1]. With over 60 years of global sales, PPS has a host of human data and an excellent safety profile. This well know safety profile should lead to a significantly lower cost of development, reduced clinical trial timelines and a reduced risk of clinical failure. It is this primary factor, which distinguishes Paradigm from the majority of biotechnology companies on the ASX.

Targeting very large addressable markets in excess of US$13.5B+

PPS is set to be a new, multi-acting treatment for bone marrow edema (estimated >US$2.5B market)[2], a condition currently with no effective treatment and allergic rhinitis – Hay fever (>US$11B[3] market), a widespread condition currently treated by largely ineffective antihistamines and perceived harmful corticosteroids. There is also great potential for other disease states involving inflammation such as Chronic obstructive pulmonary disease (COPD) and Asthma to be treated with PPS thus opening up new markets and increasing the potential value of the compound.

Highly experienced board and management team that have delivered large licensing transactions

Paradigm's board and senior management have held positions with top ASX listed companies, CSL (CSL.ASX) and Mesoblast (MSB.ASX) and were part of the team that executed the US$1.7B Cephalon partnership. We have confidence in the small, but highly regarded PAR team and their ability to bring biopharmaceutical products from clinical development to commercialisation.

Pre-clinical and clinical data indicates PPS could be very effective treatment in humans with BME and Hay fever

Paradigm's compound RHINOSUL® (PPS in Hay fever) has been shown in preclinical models to have both anti-histamine and anti-inflammatory effects, making it a potential fist in class non-steroid based treatment for hay fever.

Multiple share price catalysts expected over the coming 12 months

Over the next 12 months Paradigm will have numerous major clinical milestones, namely Hay fever Phase I results, pivotal phase II results, BME Phase II ongoing and interim results and a Peer Review Publication for Hay fever. This newsflow will be complemented by the Company's reporting on operations, IP and other programs.

Potential to fast-track BME Clinical Study

Paradigm has commenced its Phase II(a) open label study of PPS for the treatment of Bone Marrow Edema. Interim results are due late CY2016 and if compelling results are returned, the Company can elect to complete the study early and fast-track to a blinded Phase II(b) study. We anticipate at this point there would be significant partner/license interest.

Recent Transactions highlight big pharma interest in respiratory and BME spaces

Generic drug maker Mylan NV (MYL.O) acquired Meda AB (MEDAa.ST) in a US$7.2 billion cash-and-stock deal that was a 92% premium to last close. One of Meda's main drugs was Dymista® which is RHINOSUL®'s closest comparative product.

1. Khanaoure A, Chuki P & De Sousa A (2014) Ind J Appl Res 4: 462-466. Drug Repositioning: Old Drugs for New Indications
2. Paradigm Company Presentation 16/03/2016
3. Visiongain: Allergic Rhinitis Drugs Market Forecast 2015-2025: Future Prospects for Companies in Antihistamines, Corticosteroids, Immunotherapy & Vaccines &Paradigm Company Presentation

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(All dollars referred to in this report are in Australian dollars unless otherwise stated)

10 Reasons to Invest in Paradigm Biopharma

Repurposing an existing drug with excellent safety profile greatly improves chances of clinical success. With over 60 years of global sales, PPS has a host of human data available and an excellent safety profile. This will greatly reduce the risk of clinical failure.

Paradigm is targeting Bone Marrow Edema, a condition with no effective treatment. PPS has the opportunity to be 'first in class' for treating BME, a US$2.5B market and potentially much larger when you take into account other forms of bone bruising. There are very strong links between BME being left untreated and early onset of osteoarthritis indicating that PPS may one day be a treatment for the prevention of OA resulting from traumatic injury.

An experienced board and management team that are industry leaders, having held senior management positions with top ASX listed companies, CSL (CSL.ASX) and Mesoblast (MSB.ASX). The Paradigm board/management has the ability to bring biopharmaceutical products from clinical development to commercialisation and the proven track record of transacting with big pharma.

Targeting very large addressable markets in excess of US$13.5bn+ will attract big pharma interest should PPS be a new, multi-acting treatment for bone marrow edema, a condition currently with no effective treatment and allergic rhinitis (hay fever), a widespread condition currently treated by largely ineffective antihistamines and perceived harmful corticosteroids.

Short and inexpensive trials means Paradigm is fully funded to the completion of Phase II(a) and Phase I & II(a) for BME and Hay fever respectively. After successfully raising A$8.0m during its Initial Public Offering in August 2015 Paradigm is fully funded to the completion of pivotal trials, strongly positioning the Company for partnering discussions. Shorter/Cheaper trials result in less dilution, which means far greater shareholder returns in the event of successful licensing.

Potential to disrupt the dissatisfied hay fever market. Over half of patients are dissatisfied with available hay fever medications, with 60% indicating they would be very interest in new treatments. With the potential be an effective treatment in a growing US$11 billion market, RHINOSUL® may become a very interesting proposition for big pharma.

Multi-faceted IP strategy which covers manufacturing, formulation and delivery patents protects Paradigm from competition. Exclusive rights to the only FDA-approved version of PPS (bene pharmaChem) for human use ensure protection of Paradigm's position.

Management/Board own ~33% of the company and are very much aligned with shareholders. Having Management/Board own such a meaningful position as this means they will always act in the best interest of shareholders, this has been shown by their prudent cash management and efficient use of shareholders funds.

Arguably one of the best risk-reward plays in the ASX listed biotechnology sector. Paradigm's small market capitalisation compared to the potential payout of a successful licensing deal makes the Company a unique and desirable risk/reward investment opportunity.

Several major clinical trial and product development catalysts expected over the next 1-12 months. These news events will spark investor interest, de-risk the company and create momentum for the share price coming up to the pivotal clinical results from the Phase II Hay fever Trial and the Phase II BME Trial.

Contents

Company Overview

Paradigm Biopharmaceuticals listed on the ASX in August 2015 and is focussed on repurposing pentosan polysulphate sodium (PPS) for new orthopaedic and respiratory applications. PPS was developed in Germany in 1949 and has established anti-inflammatory and anti-thrombotic properties. It has been in use for over 60 years and as such its safety profile has been firmly established. The Company addresses conditions that start with and are sustained by inflammation. Lead clinical indications involve treating injury that results in bone marrow edema (BME) and the allergic inflammatory response in allergic rhinitis (AR), which is commonly known as 'Hay Fever'.

Given the pitfalls, time and costs involved in new drug (De Novo) development repurposing existing registered drugs has become more popular over recent times. From 2007-09, 30-40% of drugs or biologics that were approved or launched for the first time in the US were either drugs repurposed for new indications, reformulations or new combinations of existing drugs.

Paradigm's core business revolves around the repurposing of PPS for a number of indications unrelated to its already approved uses. These are:

First target indications:

- Bone marrow edema (**ZILOSUL® - PPS for bone bruising**) – currently in clinical trial
- Allergic rhinitis (**RHINOSUL® – PPS for hay fever**) – about to enter clinical trial

Secondary indications:

- Asthma
- Chronic obstructive pulmonary disease (COPD) (conditions of the lungs which cause air flow through them to be reduced)

Primary PPS Indications

- Bone Marrow Edema - Zilosul®
- Hay Fever - Rhinosul®.

About Pentosan Polysulphate Sodium (PPS)

The oral formulation of PPS, manufactured by Bene PharmaChem ("Bene"), was approved by the US FDA in 1996 for the treatment of interstitial cystitis, commonly known as painful bladder syndrome, where it is sold under the brand name Elmiron® by Janssen Pharmaceuticals. It is also an approved anti-thrombotic (blood clot dissolving) agent in certain, predominantly European, countries. The patents covering the oral formulation expired in 2010. Although due to the extremely complex manufacturing process, no generic competition has been formulated, suggesting other companies are unable to manufacture or source PPS to the approved standard. It is believed that the biological activity of a sample of PPS is tied to and varies according to the set of polysaccharides (xylose chains) and the degree of suphatation of the actual PPS sample. Since this is tied to the manufacturing method, the method used to create the PPS with consistent, well characterised content and biological activity, already deemed acceptable by the US FDA, is a key component of the company's IP of its product.

The Company also has a proprietary platform technology based on exosomes. Exosomes are unique small bodies secreted by human cells and are thought to be responsible for part /all the regenerative characteristics of stem cells. The Company plans to continue further development of exosomes in line with its other programs as potential mono therapies or in combination with PPS, however due to the early stage of this program we will expand on this platform technology in the future once it has progressed further.

Regional Approval for PPS

The injectable form of PPS has been sold in Germany since 1949, approved for the prevention of thrombeombolism and the treatment of acute blood vessel occlusions. It is the injectable formulation (intramuscular) that Paradigm will employ for the treatment of Bone Marrow Edema.

The injectable formulation of PPS is not presently approved for human use (approved for veterinary use to treat osteoarthritis) in Australia. The safety profile of the injectable form is proven, being approved for use in numerous countries, including four of the prevalent pharmaceutical markets, being Germany, Spain, Italy and France. Since approval, there have been in excess of 100 million injectable doses administered.

The Oral formulation of PPS is approved by the TGA in Australia and FDA in the United States and is sold under the name Elmiron, by Janssen Pharmaceuticals, for the treatment of interstitial cystitis (painful bladder syndrome).

Paradigm is the first Company to formulate PPS into a nasal spray form and will require a short phase I safety and tolerability clinical trial. The nasal spray form has been formulated to standard, enabling PPS to be finely dispersed in a stable manner. Importantly, the nasal spray form can be manufactured to either be preservative free or contain preservatives to suit individual markets.

The injectable form of PPS has been sold in Germany since 1949.

Since approval, there have been in excess of 100 million injectable doses of PPS administered.

Paradigm is the first Company to formulate PPS into a spray form.

Why Repurpose Compounds?

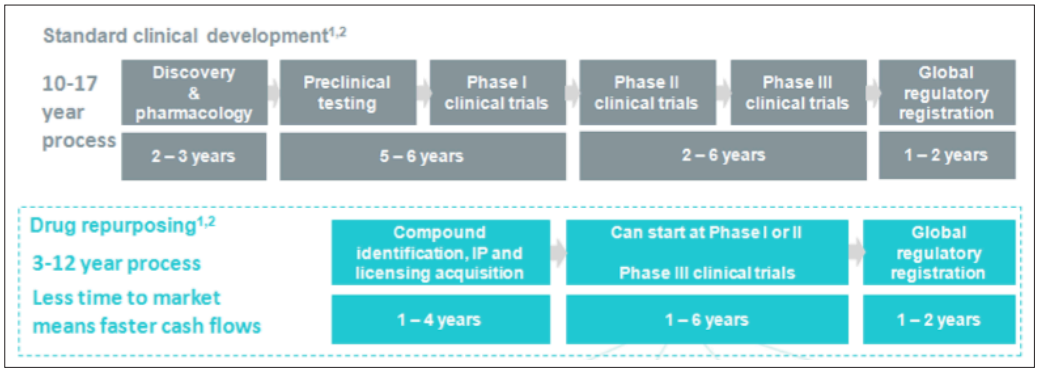
The quote of Dr Stephen Naylor & Judge M. Schonfeld rings true for the global pharmaceutical industry: "The pharmaceutical industry is still beleaguered by escalating costs, stagnant productivity and protracted timelines as it struggles to bring therapeutic drugs to market. This situation has been compounded by a ravenous generic drug sector, and patients that have morphed into a discerning consumer population."[4]

Value and challenges of Drug Repurposing/Repositioning/Rescue ("DRPx")

There are a number of substantial benefits of utilising a DRPx strategy in comparison to conventional de novo drug development programs, which result in a greater chance of clinical success, in a reduced timeframe for a fraction of the traditional capital outlay. The most prevalent benefits include:

I. **Cost Savings** – It is suggested by Dr Aris Persidis, President and co-founder of Biovista Inc, that the cost "to relaunch a repositioned drug averages US$8.4 million."[5] This figure is at the low end of the spectrum, relatable to line extension DRPx cases, thus may be multiplied to a high case of US$100-300 million if the DRPx drug has to undergo complex Phase II and Phase III clinical trials. This figure represents a fraction of the average de novo drug development cost of US1.778 billion.[6]

II. **Time Savings** – Repurposing a compound dramatically reduces the clinical approval process due to the established clinical data that accompanies it. The average cycle time of a DRPx drug is approximately 3-12 years, considerably less than de novo drug development at 10-17 years.[7]



The pharmaceutical industry is still beleaguered by escalating costs, stagnant productivity and protracted timelines as it struggles to bring therapeutic drugs to market.

Repurposing reduces the cost of development by approximately ~90%.

The average cycle time of a DRPx drug is approximately 3-12 years, considerably less than de novo drug development at 10-17 years.

Figure 1.
Standard Drug Development vs Drug Repurposing

Source: PAR Company Presentation

III. **Risk/Productivity** – The attrition rate of conventional de novo drug drugs is a staggering ~95%. The leading factor of the high attrition rate is due to a compound's lack of safety (~45% failure in Phase I) and efficacy (65% failure rates in Phase II).[8] As a result of the high attrition, there is an increased pressure on the drug pipeline, which negatively affects the productivity/focus of pharmaceutical companies.

IV. **Higher Success Rates** – As DRPx drugs have been either been approved or shown to be safe in late stage trials, they can enter the clinical cycle at the efficacy stage, therefore the failure rate is significantly decreased, promoting the chances of a successful launch. Approximately 25% of DRPx drugs successfully make it from Phase II to launch, in comparison to only 10% for conventional de novo drugs.

V. **Market Potential** – The market potential for a DRPx drug is subject to the same market forces as a conventional de novo drug, such as, market need, patient acceptance, market strategy and intellectual property position.[9] Therefore a DRPx drug has the same potential to reach 'blockbuster drug status' as a de novo drug. A recent example of a DRPx blockbuster drug is dimethyl fumarate (brand name Tecfidera) from Biogen IDEC. It was approved for a new indication to treat multiple sclerosis (MS) in 2013 and achieved revenue sales of >$2.5 billion worldwide in 2014. This represented ~30% of total revenues for Biogen IDEC last year

VI. **Intellectual Property** – Utilising a DRPx strategy can help elongate a drugs patent life, thus prolonging product lifecycle and reducing the 'patent cliff' effect.

Approximately 25% of DRPx drugs successfully make it from Phase II to launch, in comparison to only 10% for conventional de novo drugs.

Repurposed drugs have the same potential to reach 'blockbuster drug status' as a de novo drug.

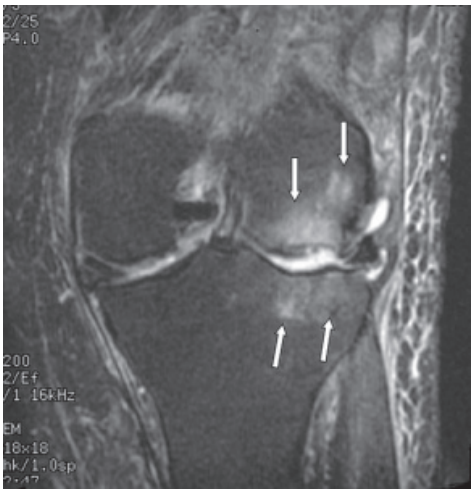
4. Therapeutic Drug Repurposing: repositioning and rescure. Winter 14 by Dr Stephen Naylor & Judge M. Schonfeld.
5. Persidis, A. The Benefits of Drug Repositioning. Drug Discov. World Spring Edition: 9-12 (2011).
6. http://www.ddw-online.com/drug-discovery/p274232-therapeutic-drug-repurposing:-repositioning-and-rescue-winter-14.html
7. Source: PAR Company Presentation
8. Paul, SM et al. How to Improve R&D Productivity: the Pharmaceutical Industry's Grand Challenge. Nature Reviews: Drug Discovery, 9, 203-214 (2010).
9. Persidis, A. The Benefits of Drug Repositioning. Drug Discov. World Spring Edition: 9-12 (2011).

Bone Marrow Edema – What is BME (bone bruising)?

Bone Marrow Edema ("BME") commonly known as 'bone bruising' is the accumulation of interstitial fluid or inflammation within bone marrow structure (figure 2). With the development of magnetic resonance imaging (MRI), BME lesions are now easily identified and diagnosed. BME lesions are typically associated with or a consequence of a direct impact to the bone, bone fractures, ligament injury, bone tumours, invasive surgery, osteoarthritis or synovitis.

Among medical professionals it is accepted there are two distinct forms of BME:

1. Traumatic BME, such as a rupture of the anterior cruciate ligament of the knee (focus of Paradigm Phase II trial), which may resolve over a period of weeks to months[10].
2. Atraumatic BME, which occurs without trauma and may be associated with the rapid progression of osteoarthritis.[11]



There are two forms of BME:
1. Traumatic BME
2. Atraumatic BME

Figure 2.
MRI of Bone Marrow Edema – indicated by the arrows

Source: Company Reports and BYS

Why focus on BME? - No regulatory approved pharmaceutical therapeutic options

The presence of bone marrow edema results in severe and chronic pain in the affected area. Apart from prolonged rest and immobilisation of the affected joints/anatomical region there is currently no effective, regulatory approved, therapeutic treatment available for suffers.

The traditional treatment via rest and immobilisation may result in resolution of symptoms of pain & joint dysfunction and the normalisation in MRI within 6-18 months, although during this period the patient's quality of life is usually considerably diminished.[12]

Other treatments may include analgesics and anti-inflmmatories, physiotherapy and surgical treatment (core decompression). Analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) are usually prescribed to provide some relief for BME, although it is widely accepted that NSAIDs and corticosteroids have a detrimental side-effects on the metabolism of bone and cartilage. More importantly, all current treatment options are considered as symptomatic therapy since they have little or no effect on the underlying pathophysiology responsible for BME. No treatments are currently available that influence the underlying pathology.[13]

There is currently no effective, regulatory approved, therapeutic treatment available for BME suffers.

Acute impact injuries, Bone Marrow Lesions and BME

There is a substantial body of research demonstrating that BME lesions are associated with acute joint injury, cartilage loss and progressive joint degeneration, as evidenced by the following studies:

- Acute-impact joint injuries initiate a sequence of biologic events that cause the progressive joint degeneration that leads to a condition known as Post Traumatic Osteoarthritis (PTOA) (J Orthop Res 2011, 29:802–809).
- Joint injuries cause striking alterations in synovial fluid levels of compounds that may contribute to joint degeneration, including pro-inflammatory cytokines and mediators such as tumor necrosis factor alpha (TNF-a), interleukin (IL)-1, nitric oxide, and matrix metalloproteinases (MMPs) (Biorheology 2006, 43:517–521).
- Follow up of people who suffered knee ligamentous and meniscal injuries demonstrated that they had a 10-fold increased risk of OA as compared with those who did not have a joint injury (Sports Med 1999, 27:143–156) and (Arthritis Rheum 1998, 41:687–693).

There is a substantial body of research demonstrating that BME lesions are associated with acute joint injury, cartilage loss and progressive joint degeneration.

10. Meaney, Falko-Alexander Stichnoth, Clinical MR Imaging: A Practical Approach
11. rimm, J., et al., MRI of transient osteoporosis of the hip. Arch Orthop Trauma Surg, 1991. 110(2): p. 98-102.
12. Krause, R., et al., [The transitory bone marrow edema syndrome of the hip]. Z Orthop Ihre Grenzgeb, 2002. 140(3): p. 286-96.
13. Ibid.

Bone Marrow Edema – What is BME (bone bruising)? Continued

- Many patients with a torn ACL develop osteoarthritis of the knee irrespective of current treatment (BMJ 2013:346:f232 doi: 10.1136/bmj.f232).
- Many acute joint injuries are characterized by Bone Marrow Lesions (BML's) as detected by Magnetic Resonance Imaging (MRI).
- The occurrence and progression of BMLs have been shown to be associated with progression to osteoarthritis and joint pain (Osteoarthritis and Cartilage 2012, 20:1514-1518).
- Importantly, BMLs are also associated with structural changes in bone and cartilage and are a potent risk factor to joint pain and osteoarthritis (Rheumatology 2010, 49:2413-9).
- Patients who present with BML were nearly 9 times as likely to progress towards total knee replacement (Skeletal Radiol 2008, 37:609–617).

BME and Osteoarthritis

There is a growing link between BME and joint cartilage degeneration that leads to osteoarthritis (OA) and this is further evidenced by the above studies. It is believed that there are chronic health impacts associated with untreated BME, with patients having 10x greater likelihood of developing OA. It has been said by some industry participants that nearly 100% of people who have had an ACL injury will develop osteoarthritis at some point in their lives.

There is a growing link between BME and joint cartilage degeneration that leads to osteoarthritis (OA).

Assuming the direct link between BME and OA becomes proven, we see ZILOSUL® - PPS in BME – becoming a broader treatment for those suffering OA.

The Addressable Market for BME

The worldwide hip & knee surgical implant market is US$16.7bn, will be US$33bn by 2022[14]. There is a current focus is on acute knee injuries but we see potential to use PPS to treat other major joints (ankle, shoulder, elbow, hip, etc.) and chronic injuries (BME case study).

Addressable market based on acute traumatic injuries:

ACL injuries associated with BME per annum in USA[15]	160,000
Meniscal injuries associated with BME per annum in USA[16]	800,000
Ankle injuries associated with BME per annum in USA[17]	480,000
TOTAL - Knee & ankle Injuries Associated with BME in USA (Excludes shoulder, elbow and hip injuries as well as chronic injuries).	1,440,000

Source: Company Reports

Utilising the data above, the potential addressable market in the United States alone, based on a treatment cost of US$1,750 is **$2.52 billion**. It is important to note that this figure does not include shoulder, elbow, hip injuries and BME associated with invasive surgery.

The baseline BME market in the United States alone is US$2.52 billion.

14. Winter Green Research (2016), Hip and Knee Orthopaedic Surgical Implants Market Shares, Strategies, and Forecasts, Worldwide, 2016 to 2022
15. Based on 200k ACL injuries per annum, with 80% being associated with BME – Niall D, et al. (2004) and Friedberg R, et al. (2016)

Rationale to use ZILOSUL® (PPS) to treat Bone Marrow Lesions/Edema

The emergence of a BME is understood to be the initial signal demonstrating the pathophysiology of cartilage breakdown. The Synovial fluid of patients with an acute injury and consequent BME, presents substantial increases in inflammatory cytokines (principally TNFalpha and IL-1), cartilage degrading enzymes (MMP's and ADAMTS-5) and signs of hypercoagulability.

The emergence of a BME is understood to be the initial signal demonstrating the pathophysiology of cartilage breakdown.

To effectively address this pathophysiology a compound must have multiple pharmaceutical actions, namely, anti-inflammatory (importantly Anti TNFalpha and anti IL-1), block the matrix metalloproteinases (MMP's and ADAMTS) and improve microcirculation.

It has been published in a variety of peer-reviewed scientific studies that PPS has demonstrated the aforementioned pharmaceutical actions, supporting the rationale for its use to treat BME.

PPS has demonstrated:

- The inhibition of cartilage degrading enzymes that are released post-acute injury.[18]
- Anti-inflammatory effects, whilst blocking the effects of the pro-inflammatory cytokine TNF and pro-inflammatory interleukin IL-1.[19]
- Antithrombic and antilipadaemic effects, which enhance microvascular circulation in the subchondral bone. Improving the microvascular circulation is believed to be a critical factor in resolving BME.[20]
- To be safe and well tolerated in patients.[21]

Put simply, PPS is likely to reduce swelling (i.e. anti-inflammatory) improve blood flow which greatly assists the healing process.

Biomarkers (CTX I & CTX II)

Synovial fluid post an acute joint injury presents a rapid increase in levels of key inflammatory cytokines and cartilage breakdown biomarkers CTX I and CTX II, which are measurable in urine and serum. Increased levels of CTX I and CTX II indicates cartilage breakdown and subsequently the onset of osteoarthritis.

Increased levels of CTX I and CTX II results in cartilage breakdown and subsequently the onset of osteoarthritis.

Results from a placebo controlled pre-clinical study, demonstrated that PPS administered post-acute injury maintained the pre-injury levels of the key inflammatory cytokines and cartilage breakdown biomarkers CTX I and CTX II.[22] In comparison, the post-acute knee injury group administered with the placebo showed substantial increases in serum levels of cytokines (TNF alpha and IL-1beta) and the cartilage breakdown biomarkers of CTX I and CTX II. These increased levels occurred immediately and were maintained for up to 48 weeks, therefore it was concluded that PPS is protective to cartilage post acute injury.

The multiple pharmacological properties of PPS supports Paradigm's reasoning for further investigation into its application for the treatment of Bone Marrow Edema.

18. Troeberg L, Mulloy B, Ghosh P, Lee MH, Murphy G, Nagase H. Pentosan Polysulfate increases affi nity between ADAMTS-5 and TIMP-3 through formation of an electrostatically driven trimolecular complex: Biochem. J. 2012; 443, 307-315
19. Smith JG, Hannon RL, Brunnberg L, Gebski V, Cullis-Hill D. A multicentre clinical study of the efficacy of sodium pentosan polysulfate and carprofen (Pfizer) in canine osteoarthritis (osteoarthrosis), VETERINÄR-MÖTET 2002.
20. Ghosh P and Cheras P Vascular mechanisms in osteoarthritis: Best Practice & Research Clinical Rheumatology 2001; 15: 693-701.
21. Kumagai K, Shirabe S, Miyata N, et al .Sodium Pentosan Polysulfate Resulted in Cartilage Improvement in Knee Osteoarthritis - An Open Clinical Trial. BMC Clin Pharmacol. 2010; 10: 1-24.
22. Ibid.

Further clinical studies of PPS

It has been established that PPS has the ability to suppress osteoarthritis (OA) progression in dogs and substantially reduce pain and cartilage metabolism in humans with OA.[23]

Recent studies assessed the efficacy, safety and patient satisfaction in patients with a BME and associated mild radiographic knee OA. Twenty patients were administered 2mg/kg of PPS subcutaneously for a six week period. All patients demonstrated a significant improvement in clinical assessments, which included, knee flexion, pain while walking, pain after climbing up and down stairs, and more importantly these clinical improvements continued for approximately one year post-treatment[24].

Additionally, a randomised, double-blind, placebo controlled pilot study, administering 3mg/kg of PPS intramuscularly (IM) for a four week period, showed a significantly improved duration of joint stiffness and pain at rest in comparison to controls, for a duration of 20 weeks post-cessation of treatment. There was also significantly improved pain when walking and overall function for eight weeks post-cessation of treatment was observed in these patients with OA of the knee.[25]

Given its properties and the stage of clinical development of PPS for the treatment of joint pathologies, it was determined an ideal candidate for further investigation into its application for the treatment of BME and hence Paradigm moved in to clinical trials with it.

It has been established that PPS has the ability to suppress osteoarthritis (OA) progression in dogs and substantially reduce pain and cartilage metabolism in humans with OA.

PPS significantly improved duration of joint stiffness and pain.

23. *Ghosh, P 2012 Treatment of bone marrow edema (oedema) with polysulfated polysaccharides. WIPO Patent Application WO/2012/103588.
24. Kumagai, K., et al., Sodium pentosan polysulfate resulted in cartilage improvement in knee osteoarthritis--an open clinical trial. BMC Clin Pharmacol, 2010. 10: p. 7.
25. Ghosh, P 2012 Treatment of bone marrow edema (oedema) with polysulfated polysaccharides. WIPO Patent Application WO/2012/103588.

ZILOSUL®/PPS - Multi-acting treatment that addresses the underlying pathology of BME

ZILOSUL®, a registered trademark of Paradigm is the injectable form of PPS produced by bene pharmaChem GmbH and is the formulation that is being utilised in the ongoing BME clinical trials. It is the only known compound that addresses multiple pathways to treat BME.

ZILOSUL®, a registered trademark of Paradigm is the injectable form of PPS.

In a proof of concept trial recently conducted by Paradigm, it was highlighted by the complete resolution of BME and associated pain in 5 patients that ZILOSUL® may be a complete solution to BME. ZILOSUL® has demonstrated it has the necessary characteristics (figure 3) to treat BME, which are not present in the limited competing treatments. Competing treatments have failed to capture market share due to limited efficacy and safety profiles, enabling ZILOSUL® to quickly establish itself as market leader if clinically successful.

ZILOSUL® Proof of concept trial demonstrated a complete resolution of BME and associated pain in 5 patients.

	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	✓		

Figure 3. Comparative Advantages of ZILOSUL®

Source: PAR Company Presentation

Blood Coagulation

There has been extensive investigation into the effect of PPS on the coagulation of blood in adult humans as it has been prescribed clinically as an antithrombotic agent for a number of decades throughout Europe.

Studies in human subjects, utilising intravenously, intramuscularly and subcutaneous forms of administration at doses up to 4 mg/kg/day revealed that PPS has little or no effect on primary haemostasis or bleeding time, or platelet numbers in peripheral blood. This is important as it shows that PPS is only a very mild anticoagulant and thus should not have any adverse side effects regarding bleeding.

Doses up to 4 mg/kg/day revealed that PPS has little or no effect on primary haemostasis or bleeding time.

PPS in Dogs and Horses

As a result of the established anti-inflammatory properties of PPS, it has become the leading treatment for arthritis/osteoarthritis related musculoskeletal disorders in dogs and horses. Sold under the name Cartrophen Vet by Biopharm Australia, it acts as a disease modifying osteoarthritis drug and importantly, it helps maintain joint health, including preserving joint cartilage that is damaged by the arthritic process.

PPS is the leading treatment for osteoarthritis in dogs and horses.

Similar to the Paradigm BME trial, the treatment requires an initial course of one injection a week for four weeks and has proven to be an effective treatment in over 80% of cases[26] by way of disease modification.

26. (Francis and Read, 1993; Cullis-Hill and Ghosh, 1994; Bouck et al, 1995; Read et al, 1996; Smith et al 2001)

BME: Clinical development program

In February 2016, Paradigm commenced an open-label Phase II(a) clinical trial in 40 patients to determine the safety and tolerability of ZILOSUL ® in patients with a BME lesion. Patients exhibiting a BME lesion identified by MRI in association with bone pain and reduced joint function following an Anterior Cruciate Ligament (ACL) injury are administered ZILOSUL® twice weekly for a period of three weeks. As it is an open-label trial, there are no placebo controls and no blinding, which promotes trial flexibility and enables interim result analysis.

Paradigm commenced their BME open-label Phase II(a) clinical in February 2016.

The clinical study is currently being undertaken across two Medical Centres in Australia, Southern Orthopaedics in Adelaide, South Australia and Box Hill in Melbourne, Victoria. Paradigm has indicated that it expects the duration of the study to be 12 months, subject to patient recruitment.

Clinical Trial Objectives:

Primary Objectives – Evaluate the:

- safety and tolerability of IM ZILOSUL® in subjects with bone marrow lesions following an ACL injury.

Primary Objective is to evaluate the safety and tolerability of ZILOSUL®.

Secondary Objectives – Evaluate the:

- effect of IM ZILOSUL® on bone marrow lesions following an ACL injury as assessed by magnetic resonance imaging (MRI)
- effect of IM ZILOSUL® on functional knee joint capacity following an ACL injury.

Exploratory Study Objectives – Evaluate the:

- effect of IM ZILOSUL® on pain following an ACL injury and to evaluate the effect of IM ZILOSUL® on biomarkers of inflammation, bone and tissue remodelling
- relationships between changes in bone marrow lesions with changes in functional knee joint capacity and changes in pain intensity.

Key inclusion criteria:

Subjects who have experienced an acute anterior cruciate ligament (ACL) injury a minimum of 2 weeks and maximum of 8 weeks prior to Day 0, and have been managed conservatively with physical therapy and medications.

OR

Subjects who have experienced an acute ACL injury and have been treated with surgical intervention a minimum of 2 weeks and maximum of 8 weeks prior to Day 0.

The Company is of the opinion that the commencement of Phase II(b) may be brought forward pending the strength of the results of interim analysis. We share this view because if the results are compelling enough then why waste time proving what is already known.

The Company is of the opinion that the commencement of Phase II(b) may be brought forward pending the strength of the results of interim analysis.

Paradigm may be able to rely on the FDA's findings of safety and/or efficacy for the previously approved reference drug. This has the potential to significantly reduce the size and number of additional clinical trials required. For example, while a standard 505(b)(1) New Drug Application (NDA) generally requires two phase III trials (an initial pivotal trial and a confirmatory one), products being assessed under the 505(b)(2) pathway may only need one phase III trial. By only having to conduct one Phase III trial Paradigm could save tens of millions of dollars and several years in the development and commercialisation of both ZILOSUL® and RHINOSUL®.

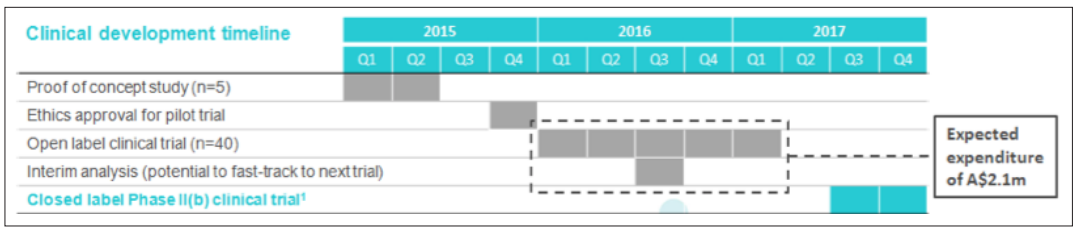


Figure 4. The Clinical Development Timeline for ZILOSUL® - PPS in BME

Source: PAR Company Presentation

Elite Athlete Case Study

The potential for ZILOSUL® to be a successful treatment for BME has been strengthened by the promising results from an 'elite athlete case study' conducted under the Therapeutic Goods Administration's (TGA's) Special Access Scheme (SAS).

The patient is an elite athlete within the Australian Football League (AFL) with an un-resolving bone marrow lesion as a result of an ACL injury, which has considerably restricted his training and ability to play over the past 2-3 years. The patient was able to gain access to the treatment under the SAS because treatments such as, prolonged rest, anti-inflammatories, corticosteroids, fluid draining and surgical intervention had failed to resolve the BME, leaving no other option.

Commencing in November 2015, the athlete had a total of six intramuscular injections of ZILOSUL® over six weeks. ZILOSUL® was well tolerated with no signs of adverse effects/events. The prescribing doctor has advised Paradigm that the initial clinical response to the ZILOSUL®, has been very positive/encouraging, particularly given the refractory nature of symptoms in this patient.

The potential for ZILOSUL® to be a successful treatment for BME has been strengthened by the promising results from an 'elite athlete case study'.

Results – Elite Athlete Case Study

Pre-Treatment Wellbeing

- ✗ Un-resolving bone marrow lesion (2-3 year issue)
- ✗ No success with multiple therapeutic and surgical interventions
- ✗ Fluid had to be drained from the knee at least once a week

Post-Treatment

- ✓ Patient completed whole pre-season training at full capacity, first time in 2 years
- ✓ Patient has not had to drain fluid from knee since the treatment in November 2015
- ✓ Encouraging result that significantly improved patient's well-being

Patient completed whole pre-season training at full capacity, first time in 2 years.

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

Allergic Rhinitis (Hay Fever) – what is Hay Fever?

Paradigm is developing RHINOSUL®, the first intra-nasally applied PPS product to be used in humans for the treatment of allergic rhinitis/hay fever, a common disease that affects between 10-30% of the world's population depending on region. Due to hay fever's prevalence, it attracts a growing market in excess of US$11 billion.

Hay fever is the result of an excessive immune system reaction to widespread allergens in the air, such as pollen, dust and pet hair. The current treatments for sufferers are somewhat lacking, as the two prevalent treatments for hay fever, antihistamines and intranasal corticosteroids do not provide a complete resolution to the issue and have perceived negative side effects.

Two Phases of Hay Fever

Upon exposure to a particular allergen, an early, acute phase response is educed within 30 minutes. Subsequently a chronic phase response occurs after 6-8 hours, which continues throughout the allergen exposure (Figure 5).

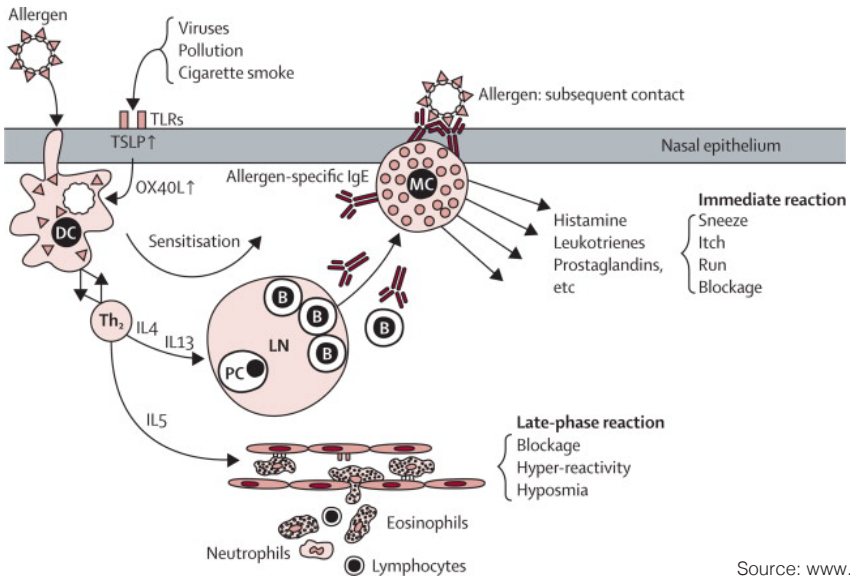
Acute Phase Response

- The acute phase of hay fever is identified by nasal itching, sneezing and rhinorrhea, resulting in the activation of mast cells, by cross-linking of IgE-allergen complexes on the cell surface[27]. Once activated, mast cells release histamine, which, in conjunction with additional mediators including prostaglandins, leukotrienes and cytokines, mediates the acute inflammatory effects and local symptoms.[28] The prevalence of histamine in the acute phase is highlighted the initial effectiveness of anti-histamines.

Chronic Phase Response

- The chronic phase response of hay fever is characterised by the permeation of inflammatory cells into the nasal mucosa, and capsular changes that result in nasal congestion. Eosinphilic infiltration usually predominates, and a range of leucocytes (TH-2 lymphocytes, neutrophils), cytokines (IL-4, IL-5, IL-13), chemokines (eotaxin, RANTES) and adhesion molecules (VCAM-1, ICAM, E-selectin) are involved.[29] Anti-histamines are not effective during the late stage response, leaving corticosteroids as the next available treatment option.

Figure 5: Allergic Rhinitis (Hay fever) Cycle – showing the dual state of the reaction[30]



Source: www.nature.com

The understanding in the market about the two phases of hay fever leads to miss treatment and subsequent consumer dissatisfaction. Paradigm's compound RHINOSUL® has been shown, in preclinical models, to have both anti-histamine and anti-inflammatory effects, making it a potential fist in class non-steroid based treatment for hay fever.

Paradigm is developing Rhinosul®, the first intra-nasally applied PPS product to be used in humans for the treatment of allergic rhinitis/hay fever.

Hay fever is a common disease that affects between 10-30% of the worlds population.

Two Phases of Hay Fever:
1. Acute Phase Response
2. Chronic Phase Response

27. Min 2010
28. Ibid
29. (Howarth 2000)
30. Alexander N Greiner, et al, Lancet 2011; 378: 2112–22

Allergic Rhinitis (Hay Fever) – what is Hay Fever? Continued

Increased Prevalence of Hay fever

The global incidence of allergic rhinitis has been on the rise for the past century. According to the American College of Allergy, Asthma and Immunology (ACAAI), allergic rhinitis has increased 100 percent in each of the last three decades.[31]

Allergic rhinitis has increased 100 percent in each of the last three decades.

Experts continue to debate on the reasoning for this trend, whether it is due to mounting air pollution, indoor environmental factors, improved hygiene practices, genetics, geographic location or all of the above, but there is little doubt that the disorder has been increasing at an alarming rate.

"There is clear evidence that much of that increase has occurred in developing countries," said Matthew Ryan, MD, assistant professor of otolaryngology at the University of Texas Southwestern Medical Center in Dallas. Although it is difficult to get a handle on the epidemiology of allergic rhinitis, studies have shown that the occurrence of allergic rhinitis is increasing in areas that used to have a low prevalence, such as developing countries, Dr. Ryan said.[32] The leading theoretical reasoning for the dramatic increase in hay fever is related to the fact that developing countries are adopting more western lifestyles. People are moving from rural, agricultural settings, which traditionally have had lower rates of allergies, to more urban settings, which have higher levels of air pollution.[33]

Addressable market for Hay Fever

There are in excess of 600 million people worldwide[34] that suffer from hay fever. The market for therapeutic hay fever treatments is over US$11 billion.[35] As noted above the prevalence of hay fever is increasing, leading to these market size figures to be understated.

There are in excess of 600 million people worldwide that suffer from hay fever.

The market for therapeutic hay fever treatments is over US$11 billion and growing.

Notwithstanding the direct therapeutic expense of hay fever there is a growing, substantial economic burden, such as missed days at work/school. A Swedish study (2016) indicated the size of the AR market may be significantly underestimated in current literature. The total cost of hay fever in Sweden (population 9.5 million) is estimated to be US$1.4 billion annually.[36]

An additional report by the Australian Institute of Health and Welfare on the cost of care for allergic rhinitis alone in 2011 estimating that 3.1 million (or 15% of the population) were affected (mainly those aged 25-44 years) with medication costs doubling from an estimated $107.8 million/year in 2001 to $226.8 million in 2010

Current Hay Fever Treatment Options

Treatment of hay fever is typically treated with 'over the counter' oral and nasal formulations at a pharmacy level. The leading treatments are:

Treatment of hay fever is typically treated with 'over the counter' oral and nasal formulations at a pharmacy level.

Antihistamines

- Administered orally or intra-nasally
- Typically a first line approach for mild forms of hay fever.
- Block the histamine response in the early acute phase of hay
- Ineffective treatment for the chronic phase of hay fever, which result in chronic symptoms
- Additional downsides include drowsiness or cardiac arrhythmias in some patients

Intranasal Corticosteroid ("INCS")

- Leading treatment for more severe and chronic hay fever symptoms
- Anti-inflammatory targeting both acute and chronic phase inflammatory responses
- Prolonged, long-term use causes concern for suffers because of side effects, such as, the thinning of the nasal lining, potential systemic effects including growth retardation in children and hormonal complications.[37]

Combination – Dual Acting Treatment (Antihistamine + INCS)

- Meda (MEDA.STO, A$8.7bn market cap) have commercialised 'Dymista®' a new class of dual acting treatment.
- Has a number of undesirable side effects

31. http://www.enttoday.org/article/upward-trend-whats-to-account-for-the-increased-prevalence-of-allergic-rhinitis/
32. (Allergy. 2008;63 Suppl 86:8-160)
33. http://www.enttoday.org/article/upward-trend-whats-to-account-for-the-increased-prevalence-of-allergic-rhinitis/
34. PAR Company Presentation
35. PAR Company Presentation
36. PAR Company Presentation
37. (Licari et al 2014)

Allergic Rhinitis (Hay Fever) – what is Hay Fever? Continued

Immune Response

- Newer therapies are aimed at modulating specific aspects of the allergic immune response, however so far none have been as effective as the INCS at relieving symptoms.

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

Figure 6.
Current Hay Fever Treatments

Source: PAR Company Presentation

Consumer Dissatisfaction

A survey conducted in 2005 by the Asthma and Allergy Foundation of America, identified that more than half of patients were dissatisfied with the available medications, with 60% indicating they would be very interest in new treatments. Based on the high level of dissatisfaction for current treatment options, through RHINOSUL®, Paradigm is aiming to disrupt the forever growing US$11 billion hay fever market.

More than 50% of hay fever suffers are dissatisfied with the available medications.

Rationale for the use of RHINOSUL® (PPS) to treat Hay Fever

Utilising a range of pre-clinical data it is anticipated that in comparison to other hay fever treatments, Rhinosul® may have the following advantages:

- Inhibiting histamine release from mast cells within the nasal passage. It has been indentified that RHINOSUL® restricts histamine released from the mast cells in a greater degree than clinically available mast cell stabilizer, disodium cromoglycate (Cromolyn, IVAX Pharmaceuticals).[38]
- Demonstrating significant efficacy in reducing infiltrating leukocytes in the nasal passage post an allergen challenge. The reduction of eosinophils is essential in both the acute and chronic phases of hay fever.[39]
- Blocking key pro-inflammatory cytokines (IL-4, IL-5 and IL-13) that target cell populations (TH2 cells, B cells, mast cells, eosinophils) involved in Hay Fever.[40]
- Imposing an aggressive action against eotaxin-1 (CCL11) and eotaxin-2 (CCL24) involved in the penetration of eosinophils into the nasal passage.[41]
- Demonstrating in pre-clinical studies to have a notable action against chemokines IL-8, MIP-1 alpha, MCP-1, consequently restricting the infiltration of leukocytes (eosinophils; neutrophils) to sites of allergen induced inflammation in the nasal passage.[42]

Peer Reviewed Scientific Publication:

Paradigm is finalising a publication of pre-clinical animal research, which investigated the performance of RHINOSUL® in comparison to the leading intranasal corticosteroid, AtraZeneca's Rhinocort® / Budesonide). The study utilised a local pre-treatment with PPS in acute challenge, OVA sensitised Guinea Pig models of Hay Fever, producing statistically significant, dose dependant reductions in the allergic inflammatory response (measured by eosinophil count, total leucocyte count and protein content of nasal fluid).

The peer reviewed scientific publication will qualify the statistically significant results and could potentially attract interest from key industry participants.

38. Cromolyn, IVAX Pharmaceuticals
39. MacDowell and Peters 2007
40. Howarth 2000
41. Ibid.
42. Ibid.

AR - Clinical Development Program

Phase I Clinical Trial

Paradigm plans to initiate a phase I, randomised, double blind, placebo-controlled clinical trial in June 2016. The trial has been designed to evaluate the safety and tolerability of single and multiple doses of RHINOSUL® (intranasal pentosan polysulfate sodium) in healthy individuals. The trial includes 18 randomised individuals, with 9 individuals per dose level cohort and 2 dose level cohorts.

Phase I Hay fever trial expected to start in June 2016.

Timeframe

The trial is expected to be initiated in June and run for approximately 6 weeks, with the results collated and read out thereafter. The fact the trial is in healthy individuals enables an instantaneous recruitment time, dramatically reducing the length of the trial.

Phase II(a) Clinical Trial

The phase II(a) clinical trial is a challenge study, which will be randomised, double blinded, cross over with placebo control. Paradigm is utilising the leading facility in Sweden and clinical trial model, which was implemented by AstraZeneca to screen for its hay fever compounds (Budesonide), including the top selling Rhinocort®.

Following AstraZeneca's trial design is a significant advantage for Paradigm, as the trial process and therefore data collected will be in a format that is accepted by big pharma and the regulatory bodies. Positive results are expected to attract significant partnering interest.

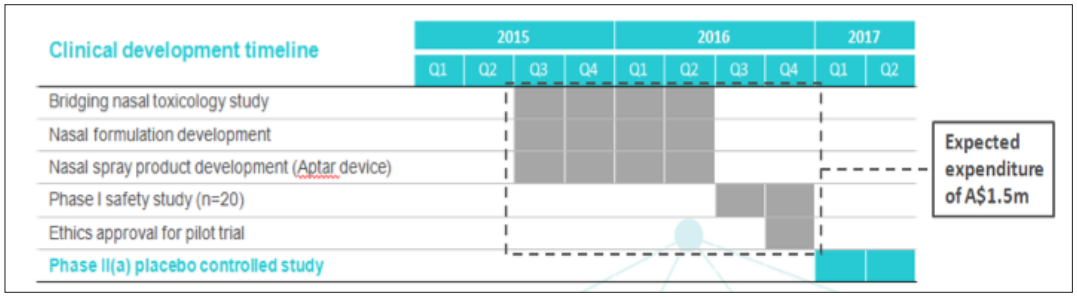
Timeframe

It is estimated that first enrolment for the Phase II(a) placebo controlled allergen challenge study will commence in December 2016. The trial will be completed with a subsequent results read out within 6 months of first enrolment.

Phase II(a) placebo controlled allergen challenge study will commence in December 2016.

Paul Rennie, Managing Director and CEO, commented: "We are very pleased with the rapid progress we have made on the hay fever clinical trial program. The next 6 months represents an exciting time for the Company and we look forward to being able to report further clinical outcomes. Hay fever represents a very large addressable market for the Company and we look forward to progressing our hay fever clinical program to potentially provide a superior and safer treatment."

Figure 7: Hay fever Clinical Trial Timeline*



Source: PAR Company Presentation

* Phase II(a) placebo controlled study has been brought forward and will now commence in December 2016

Manufacturing

The Company has entered into a long term supply agreement (20 years) with the German pharmaceutical company, bene pharmaChem, for the supply of FDA-approved cGMP-grade PPS.

Long term supply agreement (20 years) with the German pharmaceutical company, bene pharmaChem, for the supply of FDA-approved cGMP-grade PPS.

This is anticipated to overcome potential manufacturing and scale-up issues for Paradigm and is aimed at ensuring the clinical trials are conducted using PPS with the same pharmaceutical activities as would be available in commercial quantities.

Paradigm are the first to formulate PPS into a nasal spray. Paradigm has established this manufacturing capability through a partnership with MoNo chem-pharm GmbH. This partnership enables global distribution scalability at a low and sustainable cost base. It is important to note that the formulation can be manufactured with or without preservatives, which enables Paradigm to satisfy regional preference.

The spray device technology has been sourced from Aptar Group Inc, the worldwide leader in nasal spray pumps for Allergic Rhinitis, Nasal Decongestant and Nasal Saline.

Investment View

The key factor in making Paradigm a desirable biotech investment revolves around the repurposing of an existing, safe drug that is known to work in similar indications. Thus we believe Paradigm is well positioned to provide a new treatment for both Hay fever and BME and potentially a number of inflammatory/coagulant related diseases through their novel but logical approach of using PPS's known anti-inflammatory properties. The established medical evidence and extensive publications confirm PPS's use in other areas of inflammation and importantly confirm and reconfirm its safety profile – something that the FDA considers to be more and more important.

When looking at BME there are now well established links that bone bruising leads to the early onset on OA and while it may be years before ZILOSUL® could be called a treatment for OA caused by BME we believe its acceptance as treatment for BME (and other associated bone bruising i.e. surgical implants etc) will lead to market launch and subsequent reputation as the standard of care. It is well established that PPS reduces the biomarkers for cartilage breakdown CTX-1 and CTX-2 and that the cytokines and proteins for inflammation (TNF-Alpha and IL-1b) which are released from the stress of a bone bruise. These cytokines and proteins degrade and destroy cartilage – the hallmarks of Osteoarthritis. By PPS targeting these inflammation channels and blocking the production of these harmful proteins, logic would dictate that PPS will have a positive effect on recovery and therefore the long term health of one's cartilage. The plethora of animal data and anecdotal evidence showing dogs/horses recovering from debilitating OA adds further weight to our view on this matter.

We believe that should Paradigm be successful in proving ZILOSUL® is an effective treatment for bone bruising in humans as a result of sports injuries, it will be viewed as an additional valuable treatment solution for other surgeries in humans where the bone is bruised – i.e. pins and plates being hammered/screwed into bones as a result of break and factures. We are of the view that complexity of the disease state for both BME and Hay fever is somewhat lesser than that of oncology but in no way does this mean the target market and ultimately the end prize is any less. But it does possibly indicate that it may be easier for Paradigm to bring (via a partner) a drug successfully to market.

Furthermore, should RHINOSUL® be successful in its Phase I and pivotal Phase II trials for Hay fever i.e. the data shows that RHINOSUL® is as good or better than Rhinocort® at treating Hay fever than the unmet clinical need, sheer market size and potential economic opportunity represents a significant opportunity to big Pharma. This opportunity is further enhanced by repurposing likely requiring only one Phase III trial to enable FDA approval for either treatment. Despite the potential reward for junior drug discoverers and large Pharma, development in this area has been somewhat lacking, another reason which indicates that a superior safe treatment will become class leading and likely hold a market leading position for some time. We believe Paradigm ticks all the necessary boxes to be positioned to enter partnering discussions on both indications of Hay fever and BME, assuming Phase II clinical success:

- Excellent safety profile and very well known drug tolerability,
- Hypothesis backed by very good pre-clinical and clinical data,
- Long history of being a safe effective treatment for OA in animals,
- Small but very effective treatment in SAS & a scoping study in humans with BME,
- Known and well understood mechanism of action,
- Multi-faceted IP protection comprised of Disease specific patents and manufacturing IP surrounding the production of PPS,
- Trials have been designed following the same protocols as Astra Zeneca established for Rhinocort® and will adhere to the strict expectations surrounding analysis of clinical data required by big pharma,
- Potential for PPS to treat other joints (hips, ankles, shoulders and elbows) and further potential indications in other respiratory diseases which will increase the overall attractiveness of PPS,
- Due to existing long term contracts struck with Bene Pharma, PPS is not an expensive drug to make or deliver intranasally thus increasing its marketability,
- RHINOSUL® could be an Over the Counter (OTC) treatment, meaning it would not be required to be prescribed thus dramatically opening up potential markets, and
- Corporate transactions in this space demonstrate the interest by big pharma and large sums they are willing to pay to acquire such companies.

Novel but logical approach of using PPS's known anti-inflammatory properties.

PPS reduces the biomarkers for cartilage breakdown CTX-1 and CTX-2 and that the cytokines and proteins for inflammation (TNF-Alpha and IL-1b) which are released from the stress of a bone bruise.

ZILOSUL® could be an additional valuable treatment solution for other surgeries in humans where the bone is bruised – i.e. pins and plates being hammered/screwed into bones as a result of break and factures.

Repurposing often requires only one Phase III trial to enable FDA approval for either treatment.

Investment View Continued

Experienced management are crucial

When talking biotechs, equally important as the actual compound under investigation is the board and management who will be driving the company forward and ultimately negotiating any licensing transactions. Not many junior ASX listed biotech companies can boast a Board/Executive that has top tier experience at CSL and Mesoblast. Paul Rennie was the inaugural COO at Mesoblast and was solely responsible for the in-licensing of the dental pulp stem cells from the US National Institute of Health. The dental pulp stem cells were key to the CNS component of the Cephalon licensing transaction with Mesoblast in 2010 worth up to US$1.7B and accompanied by a US$220m equity investment in MSB. Paul's other previous experience includes senior positions at Boehringer Mannheim (now Roche Diagnostics), Merck KGGA and Soltec (FH Faulding Ltd). Chairman Graeme Kaufman is renowned in the Australian biotechnology industry where he has held various top level executive roles at Mesoblast until 2013 (and was likewise heavily involved in the Cephalon transaction). He was instrumental in the privatisation and ASX listing of CSL, including the negotiation of key contracts with stakeholders prior to listing and served as its Chief Financial Officer. Ravi Krishnan, also ex-Mesoblast, is the Chief Scientific Officer at Paradigm and was instrumental in the formative stages which led to Paradigm acquiring the rights to PPS for the given indications.

Few junior ASX listed biotech companies can boast a Board/ Executive that has top tier experience at CSL and Mesoblast.

Strong Newsflow will stoke and maintain investor interest

From an investor viewpoint the key attractiveness for investing in Paradigm now as opposed to six months time is a strong amount of newsflow from this point until mid CY2017. This newsflow can be summarised as the following major events:

Strong amount of newsflow from this point until mid CY2017.

- BME Phase II Open Label results on a selected basis
- News around the commencement, completion and results of the Phase I Hay fever Trial
- Publication of the Peer Review Journal comparing PPS (RHINOSUL) vs Budesonide (Rhinocort)
- News of the commencement of the pivotal Phase II Challenge Study for Hay fever
- Results from the Phase II Challenge Study in Hay fever

This newsflow will stoke investor interest, both domestically and internationally and will display to the market (and potential partners) the company's ability to achieve important milestones. The results from the Open Label Phase II BME trial which should have multiple patient data read outs over the coming months will no doubt be associated with high profile media given the relevance to sport. The Phase I Hay fever trial is expected to complete July/August with results due out there after (i.e. in 2-3 months onwards). The Hay fever Phase I results are expected to continue to reinforce the safety and tolerability profile of PPS, as well as provide the necessary data to support the pivotal Phase II Challenge study in patients with Hay fever, planned to commence late 2016. During this period the Company is expecting the release of a Peer Review Publication which compares PPS to Budesonide through various pre-clinical/animal models using the same protocols and trail design that Astra Zeneca used for Budesonide. Assuming the outcomes detailed in the Peer Review Publication show PPS is as good as/better then Budesonide than this will highlight to various big Pharma that Paradigm are on to something very exciting. The importance of a successful peer review publication should never be underestimated due to its power in confirming that other respected scientists support the said hypothesis and findings and this has enormous weight in the industry.

Phase II Challenge study in patients with Hay fever, planned to commence late 2016.

Peer Review Publication which compares PPS to Budesonide due to be released 2HCY2016

The Phase II Trial results due early CY2017 and the BME interim results will ultimately determine the near term value for PAR stock as they will dictate the ability of the two programs to be partnered and for how much, however we anticipate there will be a growing investor interest in PAR stock from commencement of the Phase I trials. We note that investor interest in biotechs always starts to increase with upcoming clinical trial outcomes and given the process is effectively 'sped up' with Paradigm we don't expect it to be any different, suffice to say more pronounced.

Growing investor interest in PAR stock from commencement of the Phase I trials

We are interested in Paradigm's novel approach to treating inflammation and have often asked how something as simple and logical has been overlooked by the industry? But it is often the case in drug development and medicine that serendipity results from simple logical thinking and we certainly see compelling logic to Paradigm's different approach.

Investment View Continued

Investment View Summary

For the reasons outlined above we think ZILOSUL® and RHINOSUL® will provide investors with the opportunity for a significant licensing event upon the release of successful Phase II trial results from either clinical trial. We feel the best way to play this type of investment is investing early, whilst the company represents good value compared to other drug discovery companies. Management/ board have extensive experience in designing and managing clinical trials and drug discovery and importantly have designed the trials in the fashion that is expected (demanded) by big Pharma, thus significantly reducing the risk that a prospective partner will ask for additional clinical data. The company has funds to be able to complete the trials and the management/board have the proven ability to execute a licensing transaction given their roles at MSB and CSL. So the only variable is the actual trial results and given the plethora of animal data but even more importantly the first people treated under the special access program we feel this risk is somewhat reduced, at least for the BME trial, which in itself would be a company maker. But, this clinical risk is the case with every biotech investment and hence why investors can achieve extraordinary returns (i.e. many multiples on their initial investment).

Significant licensing opportunity upon the release of successful Phase II trial results from either clinical trial.

Given the inherent difficulty in arriving at a current value for Paradigm we have used the probability weighted DCF methodology of what ZILOSUL® and RHINOSUL® (and hence Paradigm) would potentially be worth under licensing transaction. This gives us a DCF valuation of $1.06 per share. We have then combined this with an implied price of $0.87 per PAR share derived from an average enterprise valuation of listed peers .We therefore arrive at a current day combined average valuation of $0.96 per share assuming successful Phase II trial results and a partnering (or takeover) transaction of US$750m for Hay fever and US$500m for BME. We note that Meda was acquired for A$8.7bn and manufacture the only commercialised new class of dual acting treatment – Dymista® and Rhinocort®, the current 'gold standard' for Hay fever, is a multi-billion dollar OTC Hay fever treatment and this just further reinforces the fact that Paradigm is hunting in elephant country and in the event their trial results point to a new treatment, it will likely result in a circa billion dollar licensing transaction with potential $50-100m upfront payment.

We therefore arrive at a combined average valuation of $0.96 assuming successful Phase II trial results and a partnering (or takeover) transaction of US$750m for Hay fever and US$500m for BME.

IP Portfolio & Market Exclusivity

Paradigm has multi-faceted IP protection that increases barriers to entry for potential competitors in a number of ways:

- Disease specific patents for BME treatment with PPS have been secured in the US, Japan, Australia, and New Zealand with other geographic regions to follow.
- The company is likely to attain reformulation patents for alternative PPS delivery methods in humans (once a form of injectable PPS is approved for human use).
- Established and standard regulatory exclusivity and trademarks around products.

Furthermore, bene pharmaChem's manufacturing process add further layers of protection

- The only FDA-approved form of PPS from bene pharmaChem.
- PPS is an incredibly complex drug to manufacture and bene pharmaChem's manufacturing methods (decades of established safe manufacturing) are a well kept trade secret making it a key component of Paradigm's IP. Although other companies make PPS, the activity and chemical signatures appear to vary widely. Paradigm has exclusively licensed the Australian, New Zealand and ASEAN (Association of South-East Asian Nations) rights for the supply of PPS for BME.
- The FDA grants a product an automatic three to five year period of exclusivity as long as the drug approval is for a new indication, and there is no other marketed product protected by IP that would prohibit the product's marketing.

Patent protection is, thus, likely to extend out beyond 2030.

Paradigm has multi-faceted IP protection that increases barriers to entry for potential competitors in a number of ways.

Patent protection is, thus, likely to extend out beyond 2030.

Recent Transactions

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

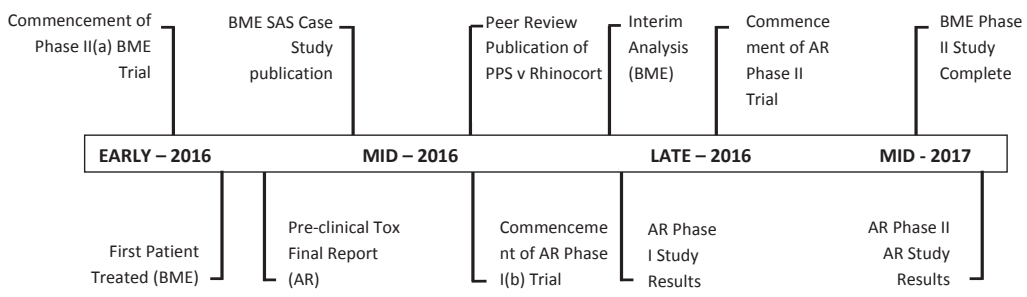
Figure 8: Recent Transactions in the respiratory and BME spaces

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

Recent transactions highlight big pharma interest in respiratory and BME spaces.

Source: PAR Company Presentation

Timeline



Valuation Methodology & Assumptions

Given the inherent difficulty in valuing junior biotech companies we have had to make a series of assumptions and use the probability weighted valuation methodology which we feel is most appropriate for a company like Paradigm.

- We have assumed a Weighted Average Cost of Capital (WACC) of 16% in line with industry standard for early stage drug discovery companies.
- Market size and sales are predicted in US$ but revenues to PAR are converted to AU$ using a AUD:USD exchange rate of 0.75
- Two years post marketing approval, we have assumed RHINOSUL® will be Over the Counter (OTC) and thus equally available as market leading Hay fever treatments Rhinocort and Dymista – both multi-billion dollar treatments.
- We have used the global market size of all Hay fever treatments and assumed RHINOSUL® will account for 20% (due to its superior action) of the market in its 10th year – date of patent expiry thus making peak sales of $2.2B before dropping off by 95% as generics come in.
- ZILOSUL total market penetration - assume 40% of the current US$2.5B Market in 2029 - 10 years from launch as it will be first in class and will make $940m pa at peak sales.
- We have assumed a CAGR of ~3% in line with growth estimates for similar markets.
- Based on the launches for other blockbuster drugs we assume to following growth rates.

Year Sales	1	2	3	4	5	6	7	8	9	10
Percentage of RHINOSUL® Peak Sales	20.0%	35%	44%	53%	62%	71%	80%	88%	94%	100%

Source: BYS Estimates

- RHINOSUL® will be considered a superior product to Rhinocort and therefore will be able to be priced at a slight premium.
- We apply a probability weighting of 25% on net gross sales for ZILOSUL® and 12.5% probability to RHINOSUL® in line with the industry standard commercialisation success rate for repurposed drugs.
- We estimate that R&D and Overheads to be minimal and a company tax rate of 30%.
- We assume Paradigm will have pivotal Phase II results in Q1 2017 Calendar year. Based on the successful result Management would seek to partner RHINOSUL®. Paradigm and their partner would then commence a Phase III Trial which we estimate would take 1 year to complete i.e. CY2018. We envisage registration will occur FY2018/19 thus we estimate sales will commence in FY2018/19.
- We assume a License Agreement with a large Pharmaceutical company will be US$750m for Hay fever and US$500m for BME total deal size + 12.5% royalties on sales (low double digit royalties in line with industry standards). For our model will have applied the 25% and 12.5% probability respectively to all milestones.
- We assume manufacturing costs to Bene are 2% of the gross sale price.
- We assume royalties to Bene are 2% on gross sales and view this as being conservative.
- In the event of partnering we assume this cumulative 4% to Bene will continue to be paid and will need to come out of what Paradigm receive from the transaction.
- We assume upfront payments will be 10% of total deal size and milestones will be:
  - Phase III Completion 20% of total deal size
  - FDA Approval and Registration 25% of total deal size
  - First US$1B cumulative sales 45% of total deal size
- As a market measure that gives us comfort in our probability weighted valuation of PAR we note that:
  - On the low end:
    - Bionomics was able to licence their pre-clinical CNS Ion Channel Modulator compound BNC375 to Merck in 2014 for $526m total deal size
    - AstraZeneca acquired Takeda respiratory business for US$575 in December 2015
  - On the high end:
    - Mylan acquired Meda for US$7.2B of which the Dymista Hay fever drug was a significant revenue generator
    - AstraZeneca acquired Almirall's respiratory business only for US$2.1B in May 2013
- Our DCF Valuation arrives at a $1.06 per share valuation on a fully diluted basis or $97.4m market capitalisation which we feel is not too onerous assuming positive results from the upcoming trials and in fact this could be well conservative.
- We cross check our DCF valuation by comparing this to peer companies as per the table below which give us an average enterprise value of A$112m, however we remove MVP.ASX due to it being a more mature company with revenues and arrive at an peer average enterprise valuation of $75.8m or an implied peer valuation of $0.87 per share for PAR.
- **We use a 50:50 combination approach of peer group valuation and DCF to arrive at a weighted valuation and target price of $0.96 per share.**

Peer Comparison Chart

Company Name	ASX Code	Share Price	Market Cap (fully Diluted)	Enterprise Value (EV)	Indication	Stage	Market Size
Paradigm BioPharama	PAR.ASX	$0.30	A$28m	A$24m	Hay Fever and BME	Phase I(b) & II(a)	US$15bn+
Medical Developments International	MVP.ASX	$5.97	A$346m	A$336m	Respiratory Disease	Commercialisation	US$1.5bn+
Starpharma	SPL.ASX	$0.71	$260.1m	A$209m	Oncology	Phase III & Commercialisation	US$3bn+
Verona Pharma	VRP.LN	£3.40	A$68.76m	A$62.5m	Respiratory Disease	Phase I/ii(a)	US$12bn+
AXSOME Therapeutics	ASXM. NASDAQ	US$7.50	A$196m	A$134m	BME/CNS Disorders	Phase III	US2.5bn+
Suda Limited	SUD.ASX	$0.02	A$24.35m	A$20.9m	Oro-mucosal	Phase II/III	US$11bn+
Invion	IVX.ASX	$0.005	A$6.3m	$A4.1m	COPD & Inflammation	Phase II	US$10bn+
		Average Mkt Cap	**A$153.82m**				
		Average Mkt Cap ex MVP	**A$75.8m**				

Top 10 Shareholders

No	Investor	No. of Shares	%
1	PAUL JOHN RENNIE	10,313,468	11.78%
2	KZEE PTY LTD <KZEE SUPERANNUATION FUND A/C>	10,301,075	11.76%
3	MJGD NOMINEES PTY LTD <BSMI A/C>	7,055,094	8.06%
4	IRWIN BIOTECH NOMINEES PTY LTD <BIOA A/C>	6,735,313	7.69%
5	BRETT LANGAN	4,386,429	5.01%
6	NANCY EDITH WILSON-GHOSH <GHOSH FAMILY A/C>	3,910,935	4.47%
7	V REDFORD PTY LTD <REDFORD SUPER FUND A/C>	2,505,419	2.86%
8	BILL PASPALIARIS	2,436,905	2.78%
9	JGM INVESTMENT GROUP PTY LTD <MUCHNICKI FAMILY A/C>	2,285,715	2.61%
10	GRAEME ROY KAUFMAN	1,900,000	2.17%

Financial Summary

PARADIGM BIOPHARMA LTD (PAR.ASX)

Date:	6-Jun-16	
Share Price ($A):	$0.30	
Year End:	30-Jun	
Probability Weighting	BME	25%
(applied to sales and milestones)	Hay fever	12.5%

Shares on Issue	87,580,220 Un-Diluted		Mkt Cap $26.3 million	
Share + Options	92,318,317 Fully Diluted		Mkt Cap $27.7 million	
Share Price	$0.30	Cash (Mar Qtr)		
Rating:	Buy			
Price Target	$0.96 per Share			
Valuation: High Case/Base Case	$1.06/0.87	DCF	WACC	16.0%
Valuation Method	Probability Weighted DCF combined with implied PAR peer share price			
Upside/(Downside) to Base Case:	220%			
Risk	High (Speculative)			

PROFIT & LOSS (A$mn) - year ended 30th June	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
Revenue	0.00	0.00	12.50	34.30	56.80
Other Income	0.01	1.25	2.00	3.70	5.50
Total Revenue	**0.01**	**1.25**	**14.50**	**38.00**	**62.30**
Total Operating Expenses	1.56	4.50	7.40	12.40	15.10
EBITDA	**-1.55**	**-4.50**	**5.10**	**25.60**	**47.20**
Depreciation & Amortisation	0.00	0.00	0.00	0.00	0.00
Share based payments	0.00	0.00	0.40	0.41	0.42
EBIT	**-1.55**	**-4.50**	**4.70**	**25.19**	**46.78**
Interest Revenue	0.00	0.10	0.10	0.35	1.30
Net Interest Expense	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Net Profit Before Tax	**-1.55**	**-4.40**	**4.80**	**25.54**	**48.08**
Income Tax Expense	0.00	0.00		7.66	14.42
Net Profit After Tax	**-1.55**	**-4.40**	**4.80**	**17.88**	**33.66**

BALANCE SHEET (A$mn)	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
Current Assets					
Cash	0.12	3.72	9.52	21.40	50.06
Receivables	0.15	0.37	0.40	0.56	0.83
Inventories	-	-	-	-	-
Other	0.70	0.02	0.03	0.05	0.10
Total Current Assets	**0.97**	**4.11**	**9.95**	**22.01**	**50.98**
Non Current Assets					
Property, Plant and Equipment	0.00	0.03	0.06	0.15	0.50
Intangibles	0.36	7.70	8.00	9.00	9.00
Other	0.00				
Total Non Current Assets	**0.36**	**7.73**	**8.06**	**9.15**	**9.50**
Total Assets	**1.33**	**11.85**	**18.01**	**31.16**	**60.48**
Current Liabilities					
Trade and other Payables	0.59	0.57	-0.77	-3.84	-7.08
Other - Deferred Income	0.00	0.09	0.00	0.00	0.00
Total Current Liabilities	**0.59**	**0.65**	**-0.77**	**-3.84**	**-7.08**
Non-Current Liabilities					
Borrowings	0.00				
Total Non Current Liabilities	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Total Liabilities	**0.59**	**0.65**	**-0.77**	**-3.84**	**-7.08**
NET ASSETS	**0.74**	**11.19**	**17.25**	**27.32**	**53.40**
Contributed Capital	1.57	12.00	22.00	22.00	22.00
Other component of equity	0.75	0.00			
Accumulated Losses	-1.72	-9.00	-4.20	13.68	47.33
Total Equity	**0.60**	**3.00**	**17.80**	**35.68**	**69.33**

CASH FLOW (A$mn)	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
Cash at Start	0.01	0.12	3.72	9.52	21.40
Cash Flow from Ops	1.55	-4.40	4.80	17.88	33.66
Cash Flow From Investing	1.56		-7.00	-6.00	-5.00
Cash Flow From Financing/Options		8.00	8.00		
Net Cash Flow	0.12	3.60	5.80	11.88	28.66
Cash At End	0.124	3.72	9.52	21.40	50.06

EARNINGS	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
EPS - Basic	-0.006	-0.031	0.003	0.045	0.067
EPS - Diluted	-0.006	-0.031	0.003	0.045	0.067
EPS Growth (%)	n/a	n/a	110.71%	1271.43%	48.31%
DPS	0	0	0	0	0
Franking (%)	0%	0%	0%	0%	0%
Payout Ratio (%)	0%	0%	0%	0%	0%

VALUATION	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
P/E (x)	-22.26	-4.54	42.40	3.09	2.08
EV/EBIT (x)	-24.03	-4.84	45.76	3.43	1.94
EV/EBITDA (x)	-27.46	-4.93	38.44	3.37	1.92
Dividend Yield (%)	0%	0%	0%	0%	0%
Price/Book (x)	10.96	4.77	3.21	1.52	0.67
Price/NTA (x)	10.88	4.02	2.76	1.39	0.64
Price/Cash/Flow per Share (x)	-11.87	6.85	35.61	3.12	1.78

GROWTH	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
Total Rev. Growth (% pcp)	n/a	65%	51%	73%	36%
Op. Exp. Growth (% pcp)	n/a	137%	-20%	6%	7%
EBITDA Growth (% pcp)	n/a	457%	113%	1040%	75%
EBIT Growth (% pcp)	n/a	396%	111%	1236%	76%
NPBT Growth (% pcp)	n/a	390%	111%	1271%	74%
NPAT Growth (% pcp)	n/a	390%	111%	1271%	48%

MARGINS & RETURNS	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
EBITDA Margin (%)	-23%	-76%	6%	43%	55%
EBIT Margin (%)	-26%	-78%	5%	42%	55%
NPBT Margin (%)	-26%	-77%	5%	43%	56%
ROIC (%)	-156%	-101%	10%	57%	46%
ROE (%)	-156%	-101%	10%	57%	46%
ROA (%)	-45%	-25%	2%	22%	20%
Effective Tax Rate (%)					

GEARING	FY14/15A	FY15/16E	FY16/17E	FY17/18E	FY18/19E
Net Debt (A$mn)	0.15				
Net Debt/Equity (%)	0.8%				

Board and Management

Paul Rennie, Managing Director

Paul Rennie BSc, MBM, Grad Dip Commercial Law, MSTC, has sales, marketing, business development, operational and IP commercialisation experience in the biopharmaceutical sector. Paul's experience includes working for Boehringer Mannheim (now Roche Diagnostics), Merck KGGA as national sales and marketing manager and Soltec (FH Faulding Ltd) as their director of business development. Paul also led the commercialisation of Recaldent® a novel biopharmaceutical arising from research at the dental school, University of Melbourne. Paul took an R&D project from the laboratory bench to a commercial product now marketed globally as an additive to oral care products. More recently Paul worked in a number of positions with Mesoblast Ltd. Paul was the inaugural COO and moved into Executive Vice President New Product Development for the adult stem cell company. For the past 2 years Paul has worked full time at Paradigm BioPharmaceuticals Ltd.

Graeme Kaufman, Non-Executive Chairman

Graeme Kaufman BSc, MBA, has wide ranging experience across the biotechnology sector, spanning scientific, commercial and financial areas. His experience with CSL Limited, Australia's largest biopharmaceutical company included responsibility for all of their manufacturing facilities, and the operation of an independent business division operating in the high technology medical device market. As CSL's General Manager Finance, Mr Kaufman had global responsibility for finance, strategy development, human resources and information technology. Mr Kaufman has also served as an executive director of ASX-listed Circadian Technologies and a non-executive director of Amrad Corporation, and held the role of Executive Vice President Corporate Finance with Mesoblast Limited until 2013. He is currently Chairman of Bionomics Limited and IDT Australia Limited, and non-executive director of Cellmid Limited.

Mr Christopher Fullerton, Non-Executive Director

Christopher Fullerton, BEc, has extensive experience in investment, management and investment banking and is a qualified chartered accountant. He is an investor in listed equities and private equity and his current unlisted company directorships cover companies in the property investment and agriculture sectors. Mr Fullerton's exposure to and experience in the fields of biotechnology and health care technology was gained through his non-executive chairmanships of Bionomics Limited, Cordlife Limited and Health Communication Network Limited and his non-executive directorship of Global Health Limited.

Mr John Gaffney, Non-Executive Director

John Gaffney LL.M is a lawyer with over 30 years experience and has undertaken the AICD Company Directors qualification. He brings to the board a compliance and corporate governance background and is experienced in financial services compliance. John also has corporate and commercial experience having worked with a major national law firm as a senior lawyer and also practised as a Barrister at the Victorian Bar. Previously John has been a non executive director of a US based biotechnology company.

Chief Scientific Officer - Dr Ravi Krishnan

Dr Ravi Krishnan is a basic scientist with a long-standing interest and experience in experimental pathology, transplantation immunology, gene and stem cell therapy. He has also had significant experience in investigating novel compounds with immune modulatory effects, anti-inflammatory and anti-angiogenic properties. Dr Ravi has both biotech and large pharma experience having previously worked at Mesoblast.

Key Risks

Dependence on a partnership to drive value: Paradigm must engage strategic partnering deals for its lead drug formulations RHINOSUL® and ZILOSUL® in order to execute its business model and receive notable cash flows. Failure to enter a favourable partnership will have detrimental consequences.

Clinical Trial Risk: Despite there being ample evidence that PPS could be an effective treatment for the indications that Paradigm is investigating there is no guarantee that trials will be successful and that the Company's drugs will make it to market.

Poor Design of Clinical Studies: It is imperative that the correct personnel are in place to optimally design the Phase II clinical trial. As many biotech companies have experienced, an incorrectly designed study will inevitably lead to detrimental results, which will adversely affect our valuation and forecasts.

Paradigm derives its value from PPS™, which is currently undergoing a Phase II(a) study for the treatment of Bone Marrow Edema and is set to initiate a Phase I study for the treatment of Allergic Rhinitis. Unsuccessful results and a subsequent failure to attract a partnering deal will significantly adversely impact the valuation and forecasts we have formulated for Paradigm.

Timing Risks: The Company will be looking to partner at the completion of their phase II trials. Delay in timelines may inhibit optimal potential partnerships. Furthermore, once partnered, timeline delays will affect milestone payments as well as long-term revenues.

Funding Risks: A delay in achieving a partnership and subsequent upfront/milestone payments may have an impact on Paradigm's funding capabilities.

Competition Risks: The emergence of new competitors in the market or advancements in the treatment of either BME or AR may render ZILOSUL® or RHINOSUL® redundant. This may affect the commercial value of the compound.

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