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RESEARCH NOTE

28 February 2017

RECOMMENDATION

Buy

PRICE
\$0.41

TARGET PRICE
\$1.16

RISK
High (Speculative)

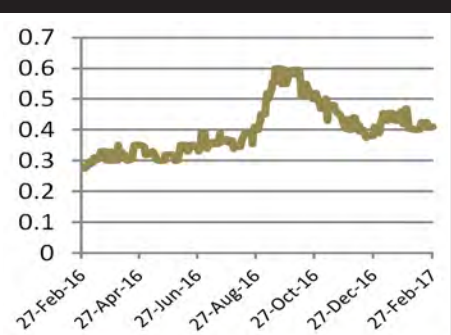
BRIEF COMPANY DESCRIPTION

Paradigm Biopharmaceuticals listed on the ASX in August 2015, is focused on repurposing pentosan polysulphate sodium (PPS) for new orthopedic, respiratory and viral 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), the allergic inflammatory response in allergic rhinitis (AR), which is commonly known as 'hay fever' and alpha-viruses for which there are currently no cures (Ross River and CHIKV). The combined markets for these indications are well in excess of US\$14.5B.

COMPANY DATA (28.02.2017)

ASX Code	PAR.ASX
Market Capitalisation (fully diluted)	~\$44.3m
Enterprise Value	~\$38m
Shares on Issue	~101.5m
12 Month High/Low	\$0.62/0.27
Ave Monthly Turnover	~1.06m
Cash – Dec 2016 (inc R&D)	~\$6.3m

12 MONTH SHARE PRICE



Paradigm Biopharmaceuticals Ltd

Hay fever Phase II Trial Nears Completion – Results Readout Q2/Q3 CY2017

The Australian Biotechnology company, Paradigm Biopharmaceuticals Ltd ('Paradigm' or 'PAR') are repurposing the existing drug Pentosan Polysulphate Sodium (PPS) for conditions that start with and are sustained by inflammation. Pentosan Polysulphate Sodium has well known anti-inflammatory and anti-thrombotic properties and Paradigm has three major programs exploring its use in treating:

- ❖ Hay fever (Allergic Rhinitis), Phase II clinical trial,
- ❖ Bone Bruising (Bone Marrow Edema), Phase IIa open label clinical trial and
- ❖ Alphavirus (Ross River and Chikungunya virus - viral arthritis), plans to enter Phase II clinical trial shortly.

There is also great potential for other disease states involving inflammation such as chronic obstructive pulmonary disease (COPD), asthma, osteoarthritis and rheumatoid arthritis with bone marrow edema lesions to be treated with PPS, thus opening up new markets and increasing the potential value of the compound.

Paradigm is significantly undervalued versus biotech peers (see peer comparison section) and the upcoming completion and readout of results from its Phase II hay fever clinical trial should see the company attract dramatically increased investor interest. Paradigm has a novel approach to targeting multi-billion dollar markets (combined US\$14.5B) and 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 upon conclusion of the upcoming Phase II hay fever and/or BME trials – with the pivotal Phase II hay fever trial expected to have results readout Q2/Q3 CY2017. For those interested the detailed analysis of Paradigm and its programs please [CLICK HERE](#) to view our October 2016 Research Report.

We maintain coverage of Paradigm with a BUY recommendation and have increased our valuation to \$1.16 per share due to Phase II hay fever trial nearing completion. Our valuation is derived from using a combination of probability weighted DCF methodology (\$1.18) and peer group valuation (\$1.14 implied PAR share price). Our target price of \$1.16 per share sits in the midpoint of our valuation range.

Highlights

Positive hay fever results will be a major re-rate catalyst

Generally speaking, all biotech companies receive a positive re-rating when they enter and complete Phase II clinical trials, and most certainly when they report positive Phase II results. We believe this is about to happen to Paradigm as investors wake up to the fact this company is only months away from releasing pivotal Phase II data that has the potential to bring a new hay fever treatment into the market that could displace incumbent corticosteroid treatments.

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). 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 time-lines and a reduced risk of clinical failure. It is this primary factor, which distinguishes Paradigm from the majority of biotechnology companies on the ASX.

Highlights - Continued

Significantly undervalued versus peers

ASX listed biotech company Innate Immunotherapeutics Ltd's (ASX:IIL) share price ran from circa \$0.20 to a recent high of \$1.83 (mkt cap was circa \$440m at peak vs PAR's current mkt cap of ~\$40m). There are many similarities between the two companies, however we consider PAR to be the superior of the two (see peer comparison section). We also note that Viralytics Ltd (ASX:VLA) has several Phase I and II trials for oncology virotherapy and after delivering positive Phase II and more recently positive phase I results its market capitalisation increased to a recent high of ~\$330m.

- PAR, VLA and IIL are in Phase II clinical trials, however PAR has two Phase II clinical trials, hay fever and BME (open label) and is on the verge of entering its 3rd Phase II trial for Alphavirus (Ross River etc). VLA has completed one Phase II trial and a number of Phase I trials. IIL is in one Phase II trial.
- Both IIL and PAR have patients treated under TGS Special Access Scheme or NZ's equivalent, the Compassionate Use Programme, and results (whilst not placebo controlled) have been encouraging for both companies.
- All companies are targeting blockbuster (\$1Bn sales p.a.) treatments.
- Success in hay fever will most likely lead to the development of PPS as a treatment for Asthma and COPD thus significantly increasing its potential target market. Further reinforcing the view that PPS has the same anti-inflammatory properties of steroids without the side effects and could potentially be useful in other indications where there is an inflammatory response.

Multiple share price catalysts expected over the coming 12 months

Over the next 12 months Paradigm will have numerous major clinical milestones, namely: Phase II completion and results, BME Phase II ongoing and interim results, peer review publication for hay fever, peer review publication for osteoarthritis patients with BME and initiation of RRV/viral arthritis Phase II. This newsflow will be complemented by the Company's reporting on operations, IP and other programs.

Paradigm is not a 'one trick pony'

Paradigm is currently in Phase II trials for two different indications and is about to enter its Phase II trials for its third indication. Approximately 40 patients have been treated with PPS under the TGA Special Access Scheme for both BME and RRV-arthralgia (joint pain) demonstrating safety, tolerance and potential clinical effects. This SAS data is incredibly valuable for Paradigm in determining the trial design protocols and optimal dosing in addition to proving useful evidence.

Recent Transactions highlight big pharma interest in respiratory and BME spaces

The Merck & Co acquisition of the respiratory drug developer Afferent Pharmaceuticals (lead asset is Phase IIb for chronic cough) for US\$1.25Bn (inc milestones) in June 2016. Last year 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.

Paradigm is fully funded through 2017

Paradigm had ~\$6.3m in cash as of the December 2016 Quarter (~inc \$1.3m R&D tax incentive). The company is fully funded for the completion of the hay fever clinical trial and its other programs in 2017. Paradigm has arguably one of the best R&D to overheads spend in the ASX biotech sector.

Global Pharmaceutical Company Janssen Pharmaceuticals (J&J Co.) is already selling oral PPS

We would like to remind the market that the oral formulation of PPS is FDA approved and sold under the name Elmiron, by Janssen Pharmaceuticals (a division of the global pharma Johnson & Johnson) for the treatment of interstitial cystitis (painful bladder syndrome – inflammation of the bladder lining). Bene pharma, the Company that Paradigm has the exclusive supply agreement with also supplies the oral PPS to Janssen. This is a very good example of one the world's largest pharma buying and distributing PPS. J&J is naturally an obvious group for Paradigm to open dialogue with and we would expect J&J would have interest in Paradigm's hay fever/Respiratory program as this could satisfy a broad target market.

Upcoming Newsflow that will drive Paradigm's share price

We have detailed the upcoming newsflow that we believe will increase investor interest and drive PAR's share price.

Hay fever Program

- Paradigm recently completed recruitment for all forty subjects in their Phase II hay fever clinical trial
 - All clinical trial subjects (n=40) have been recruited into the Phase IIa clinical trial;
 - Treatment has commenced in 30 subjects;
 - Last patient out of the study by 31 March, 2017.
 - Readout of results anticipated in late Q2 or early Q3 CY2017.
- The Phase IIa clinical trial is an allergen challenge study in subjects with allergic rhinitis (hay fever). It is a double blind, placebo controlled, cross over clinical trial design being conducted in 40 subjects.
- Being a cross over study means that all 40 patients switch to the other arm of the trial once they have received drug or placebo. This effectively means there is data for 80 patients in the trial and the data is much stronger as it shows both the drug and placebo effect on the one patient.
- The trial is being conducted in Lund, Sweden, under the leadership of Dr Lennart Greiff at Skane University Hospital who has previously conducted similar clinical trials, using the established allergen challenge clinical model for allergic rhinitis. This allergen challenge clinical model is the same model that Big Pharma use and what Astra Zeneca used in the development of Budesonide (Rhinocort®).
- The Company stated it is pleased with the progress of the Phase IIa clinical trial and importantly confirmed the clinical trial is on schedule and on budget.
- RHINOSUL® has unique properties consisting of both histamine stabilising and non-steroidal anti-inflammatory properties without the known side-effects of anti-histamines and steroids. The company believes its product can meet market needs that are not effectively managed by current nasal sprays.
- Upcoming release of peer reviewed publication of the comparative study between PPS and Budesonide. This publication has been submitted to the renowned scientific journal 'Allergy' by internationally recognised respiratory researcher, Professor Jonas Erjefält. The publication is titled; "Th2, Neutralisation and In Vivo Anti-inflammatory Action of Pentosan Polysulphate Sodium (PPS) in an Allergic Rhinitis Model".
- Professor Jonas Erjefalt has shown that 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 first in class non-steroid based treatment for hay fever. Furthermore PPS was shown to be as good as/better than the leading intranasal corticosteroid, AstraZeneca's Rhinocort® / Budesonide.
- To get a paper published in a renowned scientific journal is difficult and the journal will only publish the paper if they believe the paper is reporting some scientific findings that are novel and of relevance. Furthermore, the publication is reviewed and critiqued by the researchers peers (i.e. other world leading researchers) and will not be published if there are questions raised about the findings. That is why peer review publications in renowned scientific journals often spark big pharma interest.

Upcoming Newsflow that will drive Paradigm's share price - Continued

Bone Marrow Edema (BME – ‘Bone Bruising’)

The Open Label Phase IIa BME trial

- Currently conducting an open label clinical trial investigating the safety, tolerability and efficacy of ZILOSUL® in patients with bone marrow edema from a recent anterior cruciate ligament (ACL) injury;
- Ten participants already treated under the Phase II open label clinical trial;
- Interim results from patients with ACL injuries due over coming months;
- Close-out study expected 2017;
- Ten additional patients treated under the TGA SAS scheme with very positive clinical signals from BME patients with osteoarthritis (OA) and rheumatoid arthritis (RA);
- Peer Review Publication for osteoarthritis patients with BME; and
- Plan to undertake two pilot studies in BME patients with OA and RA.

Viral Arthritis – Alphavirus - Ross River Virus & Chikungunya Virus

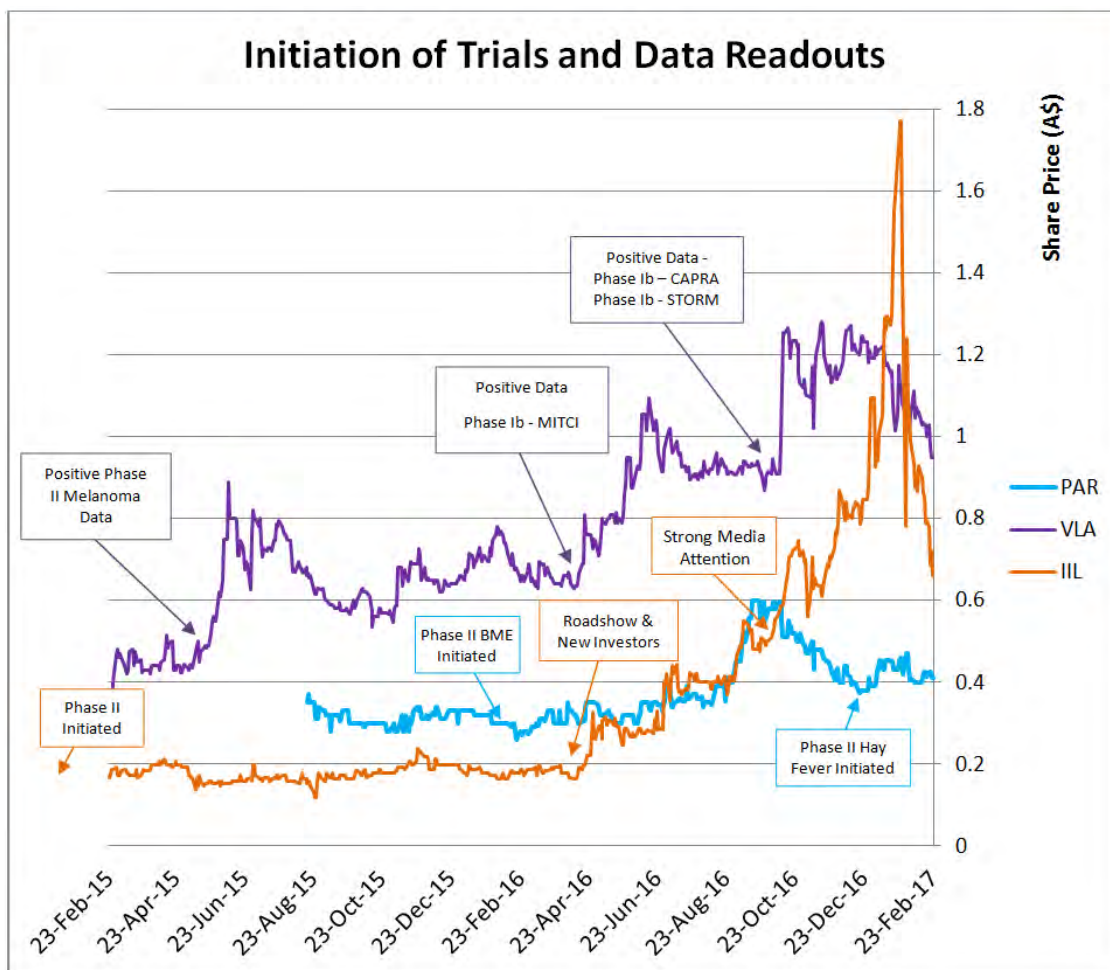
Upcoming Phase II – PPS to treat RRV and CHIKV

- Paradigm plans to embark on two Phase II clinical trials to develop PPS for the treatment of RRV-and CHIKV-induced arthritis and arthralgia;
- Given there is currently no effective disease modifying treatment for RRV or CHIKV we believe these programs represent great potential for Fast-Track /Breakthrough/Accelerated Approval;
- Preclinical studies have been conducted by the Institute of Glycomics at Griffith University. The results suggested that:
 - PPS significantly alleviated the severity of disease and reduced both the inflammatory response and the loss of articular cartilage;
 - PPS has the potential to treat both acute and chronic symptoms associated with mosquito transmitted alphavirus infections (RRV and CHIKV);
- 30 patients with RRV-arthralgia (joint pain) already treated with PPS under the TGA Special Access Scheme demonstrating tolerability and potential clinical effects.

Initiation of clinical trials and effect on prevailing share price as companies near results readout

This chart highlights the investor interest that starts to occur in biotechs once they enter Phase II clinical trials. As history shows, this interest increased dramatically the closer a biotech is to 'readout' of their Phase II (or significant Phase I) trial results. We feel confident Paradigm is on the verge of 'playing catch up' in terms of filling the valuation gap compared to IIL and VLA.











It is important to note that Paradigm does not need to do formal Phase I clinical trials to determine safety as PPS is already considered a very safe drug. This means the company can go straight to Phase II clinical trials which determine efficacy. Through SAS scheme Paradigm can treat patients with PPS and review this open label data which helps the company determine optimum dosing. Ultimately this saves Paradigm significant of money and time.



Recent significant Respiratory Deals

The below table highlights the size of recent respiratory deals. Of particular relevance are:

- **The Afferent acquisition by Merck & Co for US\$1.25Bn (\$US\$500m+US\$750m).** Afferent's lead investigational candidate, AF-219, is a selective, non-narcotic, orally-administered P2X3 antagonist currently being evaluated in a Phase IIb clinical trial for the treatment of refractory, chronic cough as well as in a Phase II clinical trial in idiopathic pulmonary fibrosis (IPF) with cough.
- **Meda's acquisition by Mylan for US\$7.2Bn.** One of Meda's main proprietary products was Dymista – a combination of anti-histamine and corticosteroid as an intra-nasal treatment for hay fever. Dymista is relatively expensive and has several negative side effects such as leaving a bad taste in the mouth/throat and including a corticosteroid.

Date ↓	Target	Acquirer	Deal value (US\$)	Relevance
Jun-16			\$1.25Bn (inc \$750m milestones)	<ul style="list-style-type: none"> Afferent developed novel drugs (phase II/III) for the treatment of a range of neurogenic conditions - chronic respiratory and urologic sensory pathologies. E.g. idiopathic pulmonary fibrosis (IPF)
Feb-16			\$7.2Bn	<ul style="list-style-type: none"> Major product was Dymista®, which is a dual acting AR product Meda's focus was respiratory and inflammation
Dec-15			\$575m	<ul style="list-style-type: none"> Acquired Takeda's respiratory business only Acquisition includes expanded rights to roflumilast, used to treat COPD
Jul-14			\$2.1Bn	<ul style="list-style-type: none"> Acquired Almirall's respiratory products only Products focused on asthma and COPD
May-13			Undisclosed	<ul style="list-style-type: none"> Zimmer Biomet acquired Knee Creations for its Subchondroplasty procedure, designed to treat BME

Source: Bloomberg, company filings

Peer Comparison

Paradigm's closest exchange listed peers are detailed below. What is plainly evident is that Paradigm is significantly undervalued vs its peers, especially taking into account its repurposing strategy and greater diversification. Going forward we are confident Paradigm will close the gap on its valuation compared to its peers.

Company Name	ASX Code	Share Price	Market Cap (fully Diluted)	Enterprise Value (EV)	Indication	Stage	Market Size
Paradigm Biopharmaceuticals Ltd.	PAR.ASX	A\$0.41	A\$44m	A\$38m	Hay Fever, BME, Alphaviruses	Phase II, II(a), I/II	US\$15bn+
Medical Developments Int. Ltd.	MVP.ASX	A\$4.85	A\$286m	A\$281	Respiratory Disease	Commercialisation	US\$1.5bn+
Starpharma Holdings Limited	SPL.ASX	A\$0.630	A\$237m	A\$200m	Oncology	Phase III & Com	US\$3bn+
AXSOME Therapeutics	AXSM.NASDAQ	US\$4.30	A\$107m	A\$63m	BME/CNS Disorders	Phase III	US\$2.5bn+
Verona Pharma PLC	VRP.LN	£0.034	A\$105m	A\$103m	Respiratory Disease	Phase I, II(a)	US\$12bn+
Suda Limited	SUD.ASX	A\$0.023	A\$27m	A\$27m	Oro-mucosal	Phase II, III	US\$11bn+
Invision Limited	IVX.ASX	A\$0.003	A\$4m	A\$4.6m	COPD & Inflammation	Phase II	US\$10bn+
Innate Immunotherapeutics Limited	IIL.ASX	A\$0.660	A\$133m	A\$127m	SPMS	Phase II	US\$7bn+
Viralytics Limited	VLA.ASX	A\$0.925	A\$235m	A\$196m	Oncology	Phase Ib, Ib & II	US\$42bn+
			Average Mkt Cap	A\$131m			
			Ave. Enterprise Valuation	A\$125m			

Source : IRESS & Bloomberg (24 Feb 2017)

Investment View

We maintain the view that should RHINOSUL[®] be successful in its pivotal Phase II trials for hay fever (Phase I successfully completed) and 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.

We combined our probability weighted DCF valuation of PAR's programs (\$1.14 per share) with the implied price of \$1.18 per PAR share derived from an average enterprise valuation of listed peers (A\$125m ave). Thus we increase our present day combined average valuation to \$1.16 per share assuming successful Phase II trial results and a partnering (or takeover) transaction of US \$750m for hay fever/respiratory program, US\$500m for BME and \$40m for RRV alone (not including CHIKV).



Board and Management

Paul Rennie, Managing Director

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Mr Christopher Fullerton, Non-Executive Director

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Mr John Gaffney, Non-Executive Director

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Graeme Kaufman, Non-Executive Chairman

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Chief Scientific Officer - Dr Ravi Krishnan

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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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