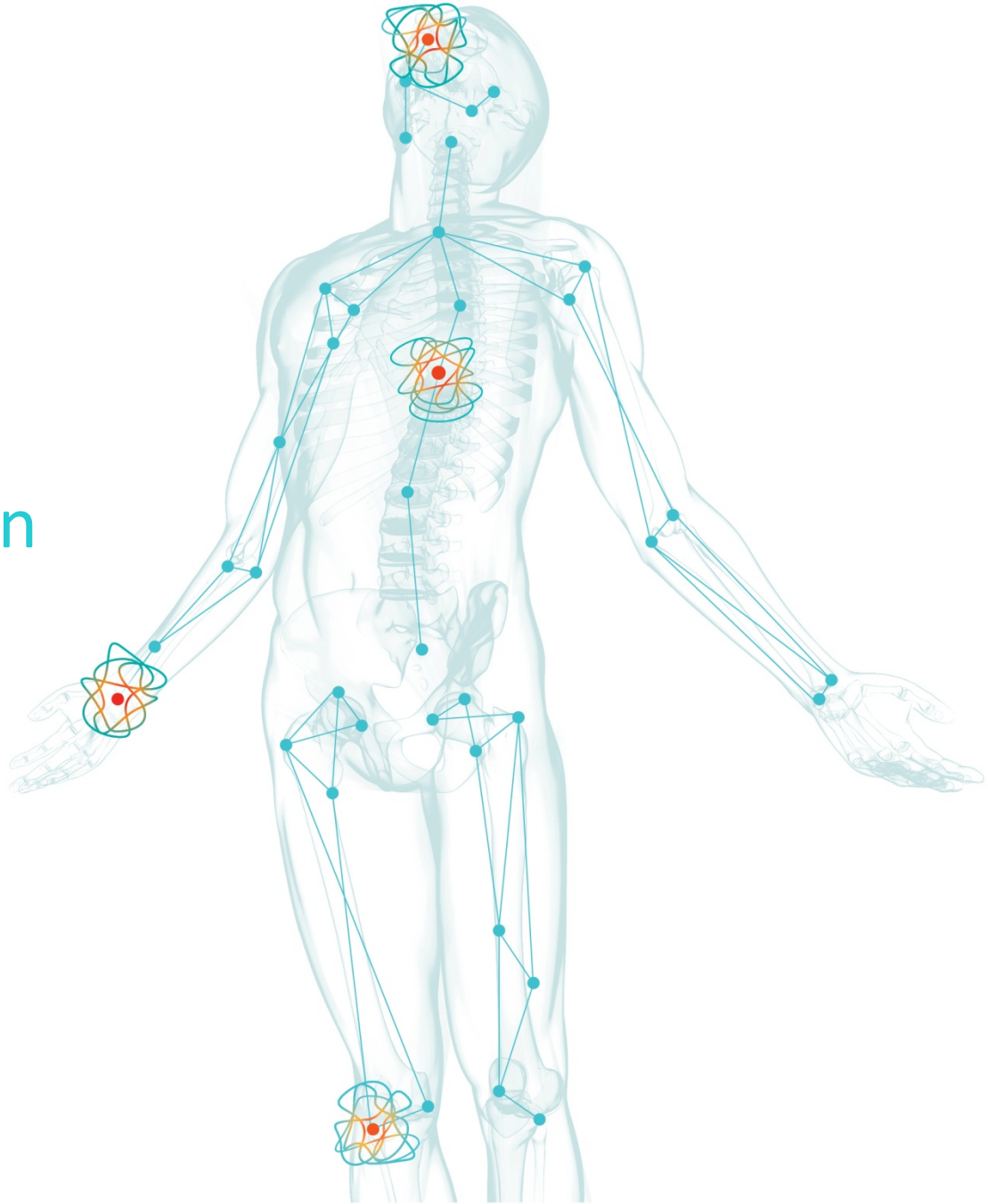
paradigm
BIOPHARMA

Investor Presentation



Paul Rennie, CEO & MD

25 October 2018

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Executive Summary

- **Paradigm Biopharmaceuticals Ltd (PAR)** is an ASX-listed biotechnology company focused on repurposing Pentosan Polysulfate Sodium (PPS), an **FDA-approved drug** that has a **long track record** of safely treating inflammation and dissolving blood clots over sixty years
- **Highly credentialed board and management team** with top tier experience at CSL Limited (CSL.ASX) and Mesoblast Limited (MSB.ASX)
- Initial focus on repurposing PPS (under the name ZILOSUL®) to treat **Osteoarthritis (OA) – a large $37bn+ p.a market.**
- Read out of **Phase2b 110 patient trial results in Mid December 2018**
- Already released data from 125 patients treated under TGA "special access scheme" – showing >50% reduction in pain. A further 375 patients data to be released over coming months
- PPS is expected to be a **more effective, safer, lower cost and longer term alternative to steroids and opioids** for the treatment of OA
- Subject to successful Ph2b results, the Company is aiming to achieve fast track designation and begin conducting a **Ph3 trial in the US in 2019, completing in 2020**. Successful Ph2b trials and fast track designation would be expected to generate significant big pharma interest.
- Company is conducting a **Two Tranche Placement of A$9m at $0.68 per share** predominantly to accelerate preparation for Ph3 OA trial in the US and fund a compassionate use program to be conducted in the US with the Pro Players' Elite Network (>11k retired NFL players and elite athletes)

Potential Share Price Catalysts / Newsflow

There is potential for significant news flow in the short term (<6 months) post capital raising

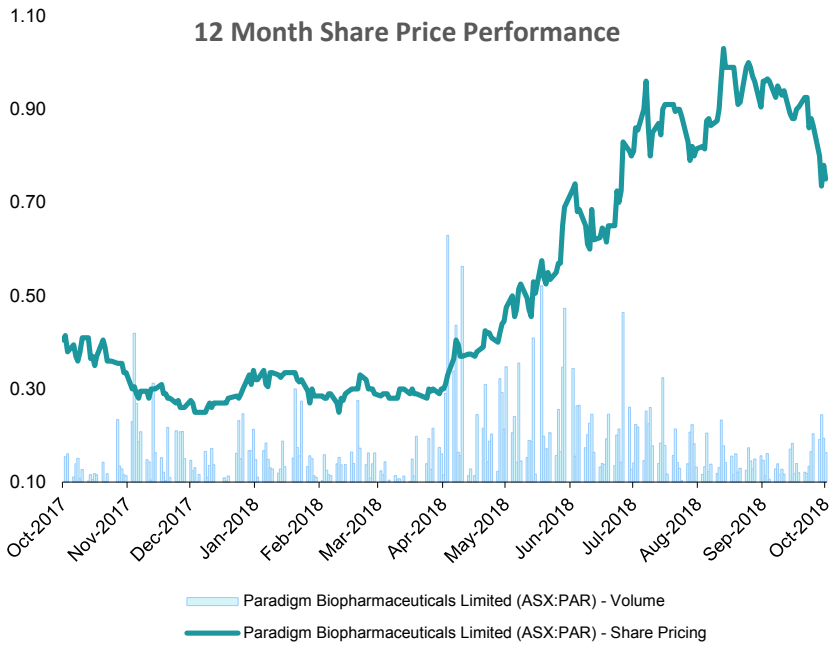
- ✓ OA Phase 2b trial results released – mid December 2018
- ✓ Further release of up to 75 patients OA data under the TGA special access scheme (by end of CY18).
- ✓ Ross River Phase 2a trial results release – mid/late December 2018
- ✓ Dose first compassionate use OA patient in the US at leading orthopaedic hospital (next 3-6 months)
- ✓ Up to 5 ex-NFL players likely to be dosed in conjunction with HOA with the Pro Players' Elite Network. Potential for significant media attention if treatment is successful.
- ✓ Finalise and announce recruitment of US based staff (Nov 2018)
- ✓ File IND and meet with FDA around PH3 trial in OA (Q1/2 2019). Possibility of being granted "fast track status" for Ph3
- ✓ Possibility of early revenue in 2019 via receiving provisional approval from TGA to sell Zilosul
- ✓ Upcoming release of peer review scientific paper/s

Corporate Snapshot

Financial information

Share price (22-October-2018)	A$0.73
Number of shares	126.2m
Market capitalisation	**A$92.1m**
Pro-forma Cash (Sept) inc R&D Rebate*	**~A$10.5m**
Pro-forma Enterprise value	**~A$81.6m**

*September cash including R&D Rebate and minimum Placement amount raised



Top shareholders[1,2]	Shares (m)	%
Paul Rennie (Managing Director)	21.6	17.2%
MJGD Nominees *(technology vendor)*	6.9	5.5%
Other Board and management	7.1	5.7%
Irwin Biotech *(technology vendor)*	6.3	5.1%

Board and Management

High quality Board and management, with top-tier pharmaceutical experience

- Board and management are renowned leaders in the biopharmaceutical industry, having held senior management positions with top ASX-listed companies, CSL (CSL.ASX) and Mesoblast (MSB.ASX)
- Extensive experience bringing biopharmaceutical products from clinical development to commercialisation
- Small and highly specialised team focused on product development utilising outsourcing effectively

Board and management

Graeme Kaufman – Non-executive Chairman
- Broad experience in development and commercialisation of pharmaceutical drugs, previously CFO at CSL, executive VP of Mesoblast (MSB) and Chairman of Bionomics (BNO)

Paul Rennie – Managing Director
- Extensive experience in drug development and commercialisation, previously COO & Executive VP, New Product Development of Mesoblast

John Gaffney – Non-executive Director
- 30+ years experience as a lawyer, previously Director of Patrys (PAB.ASX)

Christopher Fullerton – Non-executive Director
- Chartered Accounting and investment banking expertise, previously Non-executive Chairman of Bionomics (BNO) and Cordlife (now Life Corporation (LFC.ASX))

Dr Ravi Krishnan – Chief Scientific Officer
- Significant experience in experimental pathology and investigating novel compounds with immune modulatory effects and anti-inflammatory properties

Kevin Hollingsworth – CFO & Company Secretary
- Previously CFO and Co-Sec of Mesoblast and Patrys (PAB.ASX)

Drug Repurposing Strategy

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

- **Lower cost:** average development cost of ~US$30-50m compared to US$1.3bn for “de novo” development[1]
- **Faster:** FDA 505(b)(2) pathway leveraging previous clinical efforts**,** which accelerates the development timeline
- **Lower risk:** safety already established so less chance of failure (safety issues account for 30% of clinical failures[1])
- **Higher success rates:** 25% chance of successful commercialisation compared to 10% for “de-novo” drugs[1]
- **Repurposed drugs have the same potential** to reach ‘blockbuster drug status’ as de novo drugs

Standard clinical development[1,2]

10-17 year process

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

Paradigm’s drug repurposing timeline

3-5 year process to approval

Often only 1 pivotal Phase II trial Can use RWE open label case studies	1 pivotal Phase III trial for each indication	Regulatory approval
1 year	1 – 2 years	1 – 2 years

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

Pentosan Polysulfate Sodium (PPS)

PPS has a long safety history and is currently being sold in the US and Europe

Pentosan Polysulfate Sodium

- Pentosan polysulfate sodium (PPS) is a semi-synthetic drug manufactured from beech-wood hemicellulose
- PPS has been used in humans for more than 60 years
- The oral formulation is FDA approved and sold under the name Elmiron, by Janssen Pharmaceuticals (Johnson & Johnson), for the treatment of interstitial cystitis (painful bladder syndrome). Also used to treat deep vein thrombosis
- Paradigm has been granted patents to use PPS for new indications

Ideal biological characteristics

- ✓ Anti-inflammatory
- ✓ Prevents cartilage degeneration
- ✓ Anti-histamine
- ✓ Dissolving blood clots
- ✓ Prevents necrosis (premature cell death)
- ✓ Non performance enhancing (WADA & ASADA Cleared)
- ✓ Non-addictive

Excellent Safety Profile

- PPS has a well established safety profile with no reported serious adverse events
- Approved by FDA over 30 years ago for oral use, over 100 million injectable doses of PPS have been administered
- PPS is a semi-synthetic, complex carbohydrate, which makes it well tolerated by the human body
- PPS is a weak anti-coagulant compared to Heparin. PPS has $1/15^{th}$ – $1/20^{th}$ the anti-coagulant activity of Heparin. Data on file with US FDA
- The clearance of PPS from the body, as measured by activated partial thromboplastin time (aPTT), is 300 minutes (5 hours).

Opioid Epidemic – Demand for New Treatments

What is the Opioid Epidemic?

- The opioid epidemic is a crisis throughout North America that involves the widespread use of prescription painkillers and subsequent popularity of illegal opioids, resulting in unprecedented addiction and consequential overdoses, many of which are fatal

Opioids:

- **A class of narcotic substances**, both legal and illicit, derived from the opium poppy plant (synthetic or naturally occurring)
- **Not disease modifying** (only mask pain)
- **Highly addictive** with crippling withdrawals
- **Highly dangerous** – significant risk of overdose/death
- **Are incorrectly used** in chronic pain settings (i.e. Osteoarthritis)

Demand for new effective treatments

- **FDA Commissioner Scott Gottlieb -** "Our goal is to support more rational prescribing practices, as well as **identify and encourage development of new treatment options that don't have the addictive features of opioids."**[1]

115

opioid overdose deaths per day in the United States[2]

US$78.5 billion

total economic burden of prescription opioid misuse in the United States p.a.[3]

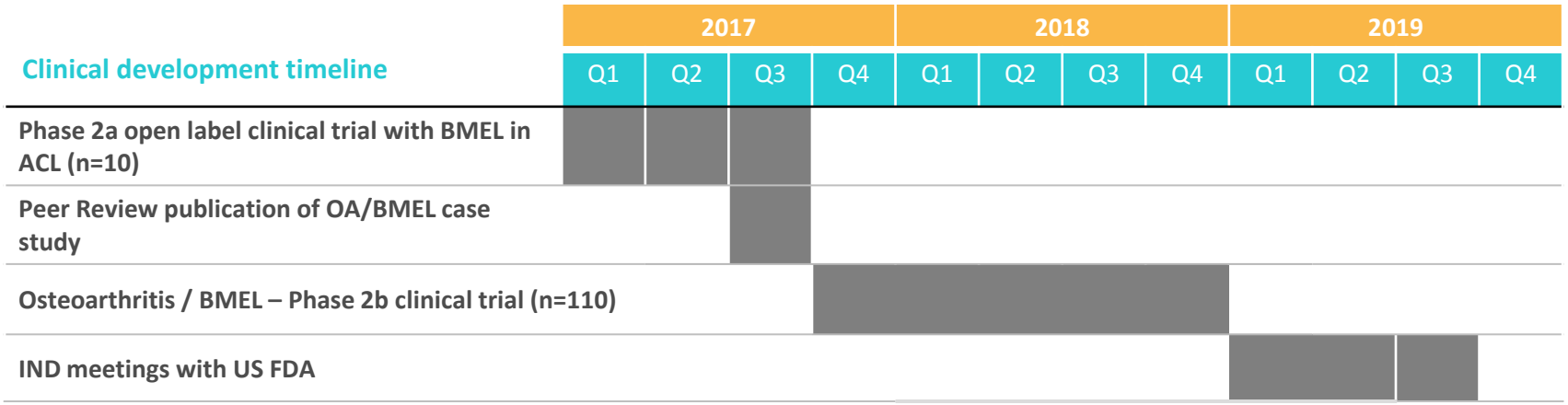
Given PPS is non-addictive and possibly disease modifying, it has the potential to receive FDA Fast-Track/Break-through Designation to address the Opioid Epidemic

1. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612779.htm 2. CDC/NCHS, National Vital Statistics System, Mortality. CDC Wonder, Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wonder.cdc.gov.
3. Florence CS, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. *Med Care*. 2016;54(10):901-906. doi:10.1097/MLR.0000000000000625.

OA with BML: Clinical Timeline

Comprehensive clinical pathway to commercialisation

- **OA/BMEL case study published in peer reviewed scientific journal**
- **Successful completion of the Phase 2a open label clinical trial**
  - Trial demonstrated the safety, tolerability and efficacy of ZILOSUL® in patients with a bone marrow edema lesions from a recent ACL (acute knee) injury
- **370+ additional patients treated under the TGA SAS scheme. Very positive clinical signals from BML patients with osteoarthritis (OA)**
- **100% recruited for Phase 2b placebo controlled (110 patient) clinical trial for BML with OA – Results due late Q4 CY2018**
- **Plan to undertake pilot studies in BML patients with other joint issues and rheumatoid arthritis (RA)**



Osteoarthritis with BMEL: The Market for ZILOSUL®

ZILOSUL® (the renamed PPS) has the potential to fill the current gap in osteoarthritis treatment options

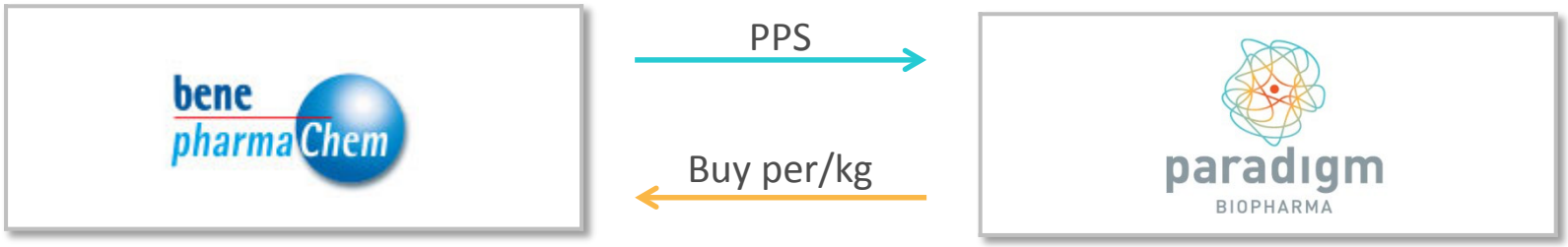
- There is currently **no effective treatment for osteoarthritis and BMELs** that treats the underlying pathology of the disease.
- **Current therapies treat the symptoms** of osteoarthritis and bone marrow edema lesions but **prolonged use results in undesirable side-effects.** It is widely accepted that NSAIDs and corticosteroids are contraindicated having a detrimental effect on the metabolism of bone and cartilage.
- **Opioid's are widely misused globally as patients form serious addictions whilst mitigating pain.**[1]
- **ZILOSUL® treats the underlying pathology of osteoarthritis** by reducing inflammation, resolving the bone marrow edema lesions and down regulating cartilage degrading enzymes (MMP's and ADAMTS-5).

	paradigm (ZILOSUL®)	NSAID (ibuprofen etc)	Opioid (oxycodone etc)	Corticosteroid / Cortisone	Joint Replacement
Treats the symptoms of OA (pain & function)	✓	✓	✓	✓	✓
Treats underlying pathology	✓				✓
No undesirable side-effects	✓				
Non-addictive	✓	✓		✓	✓
Anti-inflammatory	✓	✓		✓	
Non-Surgical	✓	✓	✓	✓	

1. https://www.drugabuse.gov/news-events/news-releases/2017/07/pain-relief-most-reported-reason-misuse-opioid-pain-relievers

Pentosan Polysulfate Sodium – Supply & License

Exclusive Supply



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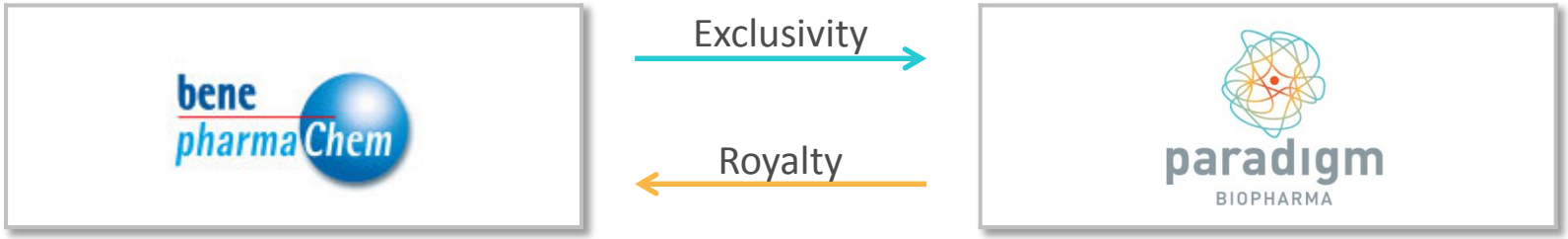


- Paradigm has executed a 20 year exclusive supply agreement with bene pharmaChem Gmbh & Co. KG
- Bene pharmaChem are the original developer of PPS and the only FDA-approved manufacturer
- Agreement grants exclusive supply of only FDA approved PPS for all orthopaedic (inc. alphavirus), respiratory and cardiovascular indications
- Paradigm to pay bene pharmaChem small single digit royalty on commercial sales

Long Term IP Protection

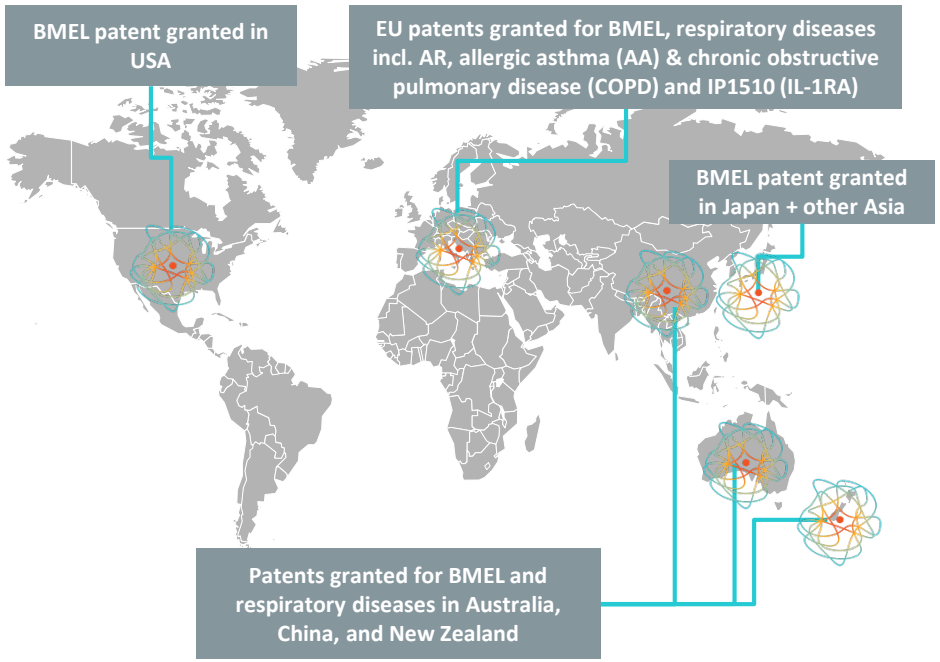
Multi-faceted IP protection increases barriers to entry for potential competitors

Valuable patent portfolio

- Paradigm has patent protection because it is using PPS for new indications
- Minimum life on patents is 2030 and beyond for more recent patents - i.e. 2035
- Patents granted for specific indications
- Established regulatory exclusivity and trademarks
- Patent applications for Ross River virus and Chikungunya virus
- Patent applications for osteoarthritis and concurrent BMEL
- Global patent for Heart Failure indication
- Assessing additional patent applications

Secure manufacturing and supply

- Exclusive 20 year supply agreement with bene PharmaChem[1]
- bene pharmaChem makes the only FDA-approved form of PPS
- **Manufacturing methods are highly complex and a well kept trade secret**
- Reduces risks associated with manufacturing and supply



1. bene pharmaChem is a private company located in Germany and manufactures the only officially approved and clinically tested medicinal PPS in the USA, Europe and Australia

Osteoarthritis with Bone Marrow Edema Lesions

TGA Special Access Scheme – Real World Evidence – 125 patients treated

All patients (median age of 57.8 years - range 31 to 84 years) had pain and failed current standard of care - analgesics, NSAIDs or corticosteroids.

At six weeks after the initiation of PPS treatment:

Pain

- 85 out of 100 patients (85.0%) showed a reduction in pain with the average pain reduction being clinically meaningful at 52.9% compared to pre-treatment

Function

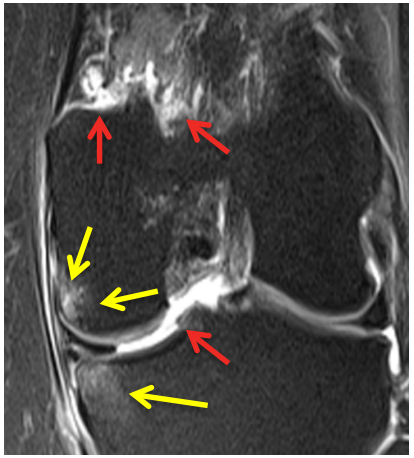
- 92 out of 100 patients (92%) showed an improvement in knee function with the average improvement in knee function being clinically meaningful at 67.0% compared to pre-treatment function

Patient A MRI – Pre PPS Treatment

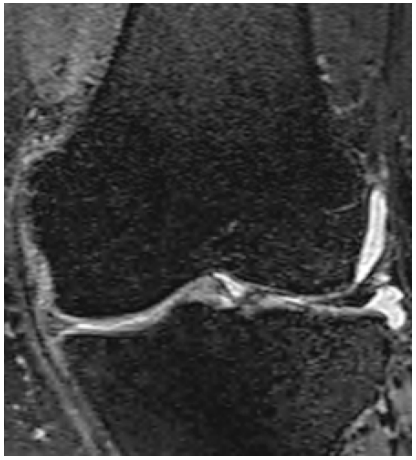
Pre treatment Scores

- High NRS Pain Score = **8**
- Lysholm Score: **37 (Poor knee function)**

BME Lesions
Joint Space Effusions



Patient A MRI – Post PPS Treatment



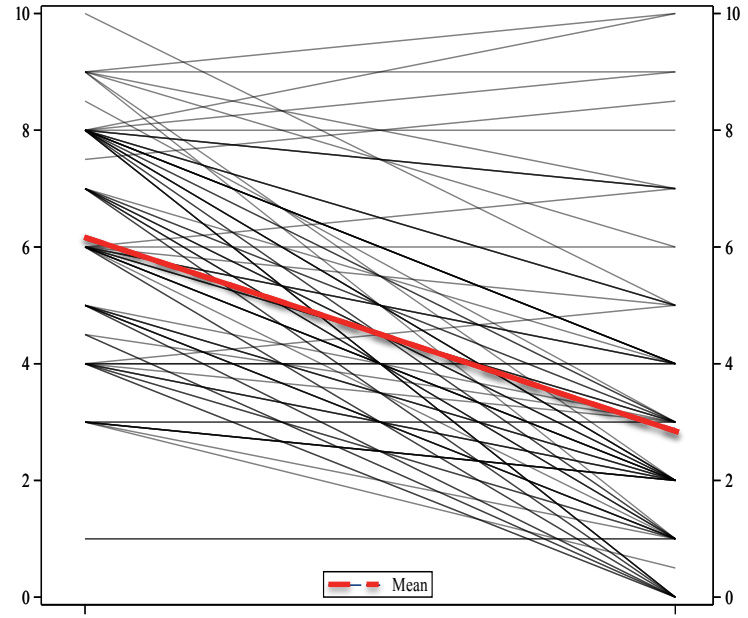
Post Treatment Results

- **Complete resolution** of BME lesions and effusions
- Pain NRS = **0 (pain resolved)**
- Lysholm Score: **65 (Fair knee function)**

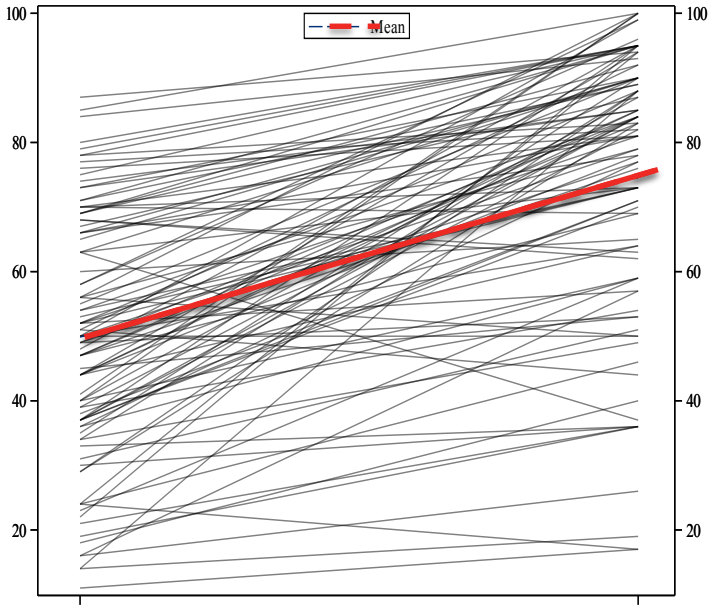
OA/BML – First 125 Patients treated via TGA SAS

A Paired t-test was used to compare the before and after scores for knee pain (NRS) and knee function (LKS).

Pain (NRS) Before – After = 3.2 p<0.0001 51.5 % reduction in knee pain	Function (LKS) Before – After = 25.1 p<0.0001 69.1% improvement in knee function



Before 6.2 After* 3.0



Before 49.0 After* 74.1

***After = Results taken from patients six weeks post final treatment, i.e. twelve weeks from first dose, therefore it is anticipated that any placebo response will be somewhat reduced. Injections are Subcutaneous, NOT intra-articular.**

Peer Comparison

Attractive investment given low risk development and large market opportunity

Peer	Ticker and exchange	Market cap (A$m)	Rationale	Clinical stage of key product	Addressable market size
flexion Transformative Medicine... Where It Matters	FLXN.NASDAQ	~$1.1Bn	Marketing a slow release corticosteroid that is injected into the knee joint to treat OA pain. Granted Fast Track Status by the FDA and drug registration in Nov 2017.	Commercialisation	US$4.6bn+ (~7.8m ppl receiving IA corticosteroid injections in USA)
Medical Developments International	MVP.ASX	260	Developing new markets and applications for Penthrox for treatment of acute pain, recent focus on respiratory diseases, significant manufacturing IP	Phase III & commercialisation	US$3bn+
CENTREXION THERAPEUTICS	Unlisted	N/A	Development of CNTX-4975, a selective, highly potent, ultra-pure, synthetic form of trans-capsaicin. It inactivates local pain fibres transmitting pain signals to the brain	Phase III	US$5bn+
AXSOME THERAPEUTICS	AXSM.NASDAQ	89	Developing novel therapies for the management of central nervous system disorders, focusing on treatment of BMEL	Phase III	US$2.5bn+[2]
verona pharma	VRP.LN	215	Focused on commercialising an old compound for respiratory diseases, with dual inhibition of key enzymes	Phase I/II(a)	US$12bn+[3]
paradigm BIOPHARMA	PAR.ASX	125	Focused on the clinical development of PPS as a multi-target treatment for complex conditions, such as BMEL/OA, AV, Cardiovascular & AR	Multiple Phase II	US$37bn+[4]

Source: Bloomberg, company filings

1. Market data as at 14 August 2018, exchange rates of AUDGBP 0.57 and AUDUSD 0.727 **2.** Based on BMEL addressable market size, excludes CRPS addressable market due to lack of available information and thus likely understates true market size **3.** Only includes the market size for COPD which is US$12b+, excludes market sizes for other respiratory disease indications **4.** Includes AR market US$11bn+ and OA/BMEL market US$8bn+ & $0.5bn for viral arthritis ,excludes COPD addressable market size of US$12bn+ and Asthma addressable market size of US$15bn+ and Heart failure Figures between 2014 & 2016 - Statins $13.2bn (Research and Markets - Global Statin Market 2015-2016), Clopidogrel bisulphate $1.8bn, Beta-blockers $1.55bn, Ace inhibitors 0.47bn, Aspirin $0.54bn, Vitamin K antagonist $0.5bn (www.pharmacompass.com)

Global Big Pharma Interest

Recent transactions highlight big pharma interest in BMEL/OA and Heart failure

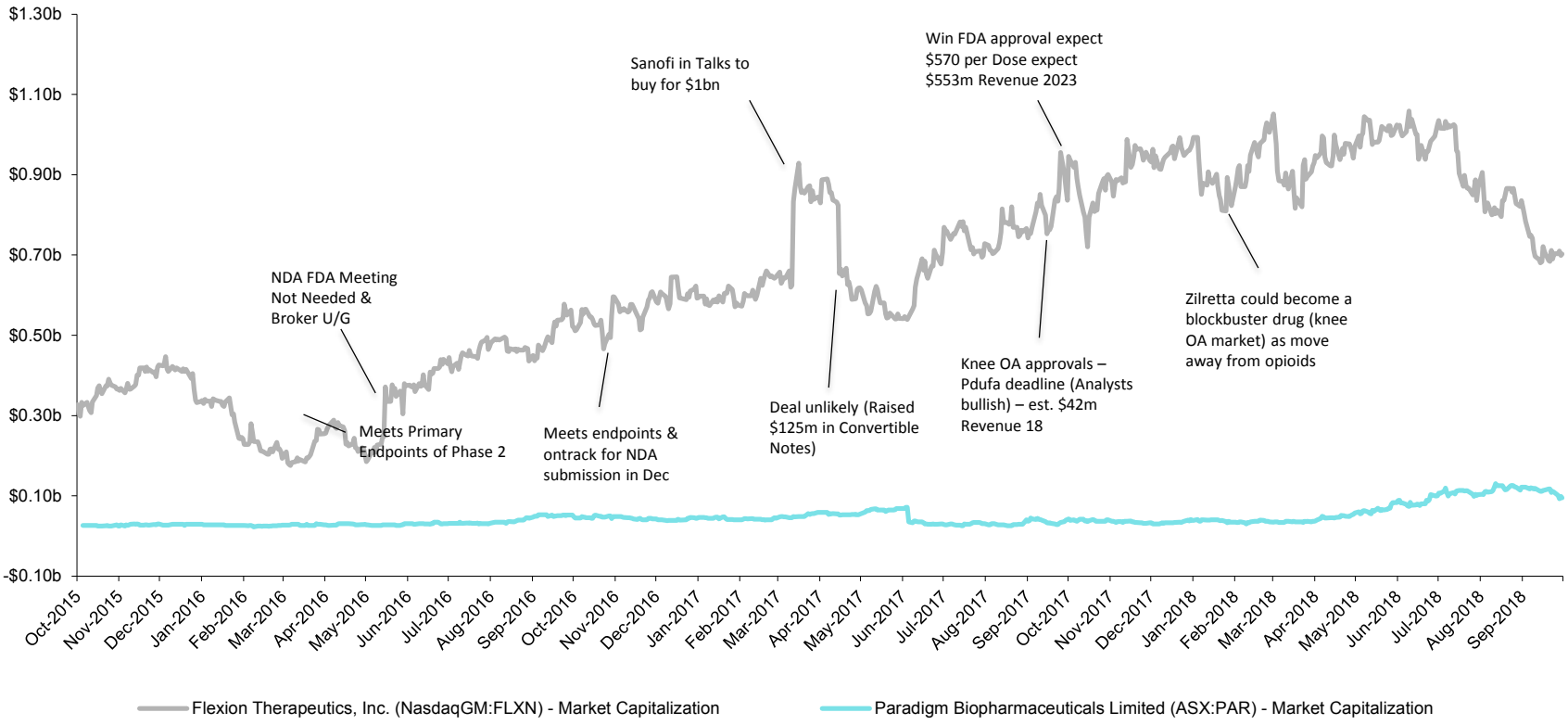
Date ↓	Target	Acquirer	Deal value (US$)	Relevance
Jul - 17	Galápagos	SERVIER	**$346m** EU Rights Only	▪ Galapagos licensed GLPG1972, a potential disease-modifying oral therapy for osteoarthritis to Servier ▪ GLPG1972 is a potent and highly selective inhibitor of ADAMTS-5.
Mar-17	flexion Transformative Medicine... Where It Matters	SANOFI	**Rumoured $1 Billion+** *(did not occur)*	▪ In March 2017 Sanofi was rumoured to be in talks to buy Flexion Therapeutics for >US$1 billion in cash[1]. ▪ Flexion's knee injection for osteoarthritis, Zilretta, said to fit in with Sanofi's biosurgery division. ▪ Both co's did not comment on why transaction did not occur.
Nov-16	TissueGene, Inc. Cell Technologies		**$434m**	• TissueGene, Inc. Licensed the rights for its degenerative osteoarthritis drug Invossa to Japan's Mitsubishi Tanabe Pharma
Jan-14	Pfizer	Lilly	**$1.8bn**	▪ Pfizer struck a deal with Eli Lilly of Indianapolis, to jointly develop its anti-nerve growth factor (anti-NGF)drug, tanezumab.
May-13		ZIMMER BIOMET	**Undisclosed**	▪ Zimmer Biomet acquired Knee Creations for its Subchondroplasty procedure, designed to treat BMEL

1. https://www.fiercepharma.com/pharma/sanofi-verge-1b-plus-deal-for-arthritis-focused-biotech-flexion

Source: Bloomberg, company filings

Flexion Case Study (FLXN.NASDAQ)

- Flexion is marketing a slow-release corticosteroid for the treatment of OA in the knee.
- 6x increase in valuation to A$1.4bn post meeting Ph2 endpoints in April 2016. Also received big pharma interest.



Viral Arthritis: Clinical Timeline

Potential to gain Orphan status, resulting in fast-tracked clinical development

- **Pre-clinical studies have been conducted by the Institute of Glycomics at Griffith University. The results suggested that:**
  - PPS significantly alleviated the severity of disease and reduced both the inflammatory response and the loss of articular cartilage;
  - PPS has the potential to treat both acute and chronic symptoms associated with mosquito transmitted alphavirus infections (Ross River virus (RRV) and chikungunya virus (CHIKV);
  - There currently is no effective disease modifying treatment for RRV or CHIKV.
- **Patients with RRV-arthralgia (joint pain) already treated with PPS under the TGA Special Access Scheme** demonstrating tolerability and potential clinical effects
- **Phase 2 Clinical Trial – PPS to treat RRV and CHIKV– Potential for Fast-Track /Breakthrough/Accelerated Approval**
  - Queensland Government have provided a A$300,000 grant for Ross River research
  - Phase 2a, randomised, double-blinded placebo-controlled clinical trial treating RRV induced arthritis and arthralgia **– 80% recruited – Read-out due late Q4 CY2018**
  - Phase 2 clinical trial in CHIKV-induced arthritis and arthralgia to be initiated post RRV read-out

Clinical development timeline	2017				2018				2019			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Proof of concept study under SAS (n=30)	Completed CY2016											
Design and Ethics approval for Phase II Trial												
Phase 2 Clinical Trial Ross River (n=24)												
Plan for a Phase 2 Clinical Trial - Chikungunya												

Viral Arthritis – Alphavirus

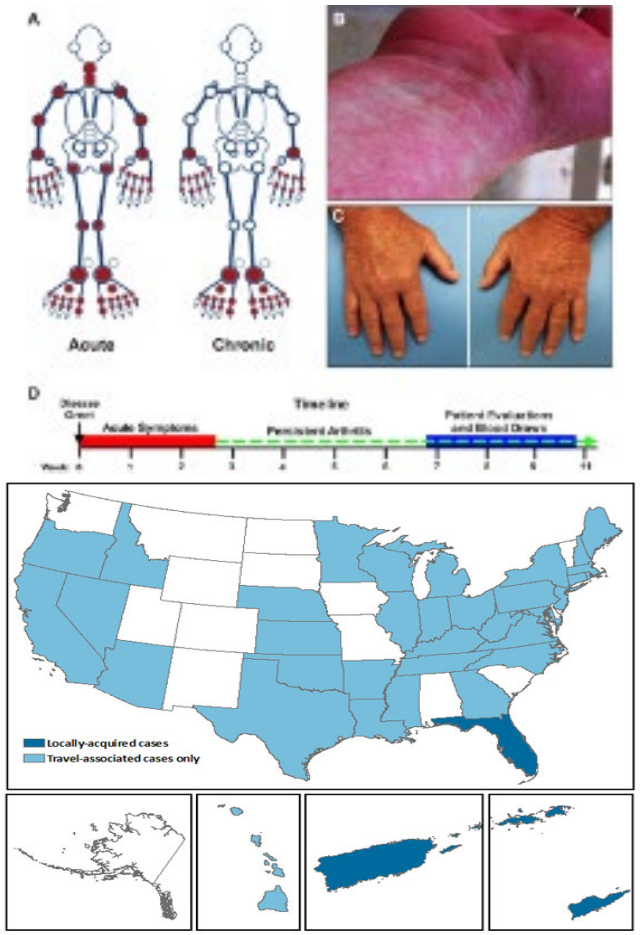
No approved treatment for severely debilitating viral infection

Viral Arthritis

- Alphavirus infections result in the clinical symptoms of joint and muscle pain, fever and joint inflammation.
- Ross River Virus (RRV) and Chikungunya (CHIKV) are mosquito-transmitted arthritogenic alpha viruses that cause epidemics of severe musculoskeletal disease in many countries.
- No effective treatment, with sufferers left incapacitated
- Symptoms can persist for a number of years

Ross River Virus & Chikungunya Virus

- Paradigm acquired the patent from the Institute for Glycomics research at Griffith University.
- The patent claims the use of PPS to treat alphaviruses, including Ross River Virus (RRV) and Chikungunya Virus (CHIKV).
- Potential interest from the **US Department of Defense** to co-develop for treating CHIKV
- Paradigm is reviewing the potential for the **FDA's Tropical Disease Priority Review Voucher Program (PRV)**
  - Being granted **Voucher Status can have significant value**



Chikungunya cases ,USA

CAPITAL RAISING DETAILS

Capital Raising Use Of Funds

Two Tranche Placement to Professional and Sophisticated investors of A$9.0m at $0.68 per share which represents a 19.2% discount to the 30 day VWAP.

	Amount	Comments
Osteoarthritis – regulatory submissions to FDA / TGA	A$1.5m	• Engage consultants early for IND submission to FDA for Ph3 / fast track. Accelerate the timeline to get into Ph3 clinical studies by 3-6 months • Draft submissions to TGA for XYZ to apply for
Manufacturing PPS for Phase 3 clinical studies	A$1.0m	• Advance manufacturing of Zilosul/® PPS in two forms to be ready for pivotal Phase 3 clinical trial and compassionate use • New packaging glass vial with rubber stopper
Fund Compassionate Use Scheme in USA & HOA with past players elite network (comprising 13,000 past NFL players)	A$1.0m	• Seek compassionate use status in the USA • Treatment to be provided in collaboration with one of the leading orthopaedic hospitals in USA • Signed HOA with past players elite network – will begin treating “marquee” ex-players
Employ US based staff x 2	A$2.0m	• Establish US presence to prepare for US focus in 2019 and compassionate use program • Fund clinical trials, wages, infrastructure, insurance etc
Working capital and future IP acquisitions	A$3.5m	• Ongoing working capital and costs of the offer • Future acquisitions of Intellectual Property outside of PPS to further broaden portfolio

Offer Timetable

Trading halt	**Tuesday, 23 October 2018**
Placement bids due	**5pm Tuesday, 23 October 2018**
Offer announced and Company resumes trading	**Thursday, 25 October 2018**
Settlement of New Shares issued under Placement Tranche 1	**Wednesday, 31 October 2018**
Allotment of New Shares issued under Placement Tranche 1	**Thursday, 1 November 2018**
Shareholder meeting to approve Placement Tranche 2	**On or around 26 November 2018**
Settlement of New Shares issued under Placement Tranche 2	**On or around 29 November 2018**
Allotment of New Shares issued under Placement Tranche 2	**On or around 30 November 2018**

APPENDIX

Orthopaedic – Bone Marrow Edema Lesions

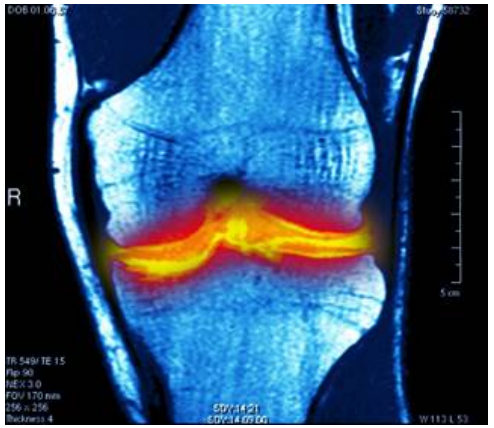
PPS – The first effective treatment for bone marrow edema lesions

What are bone marrow edema lesions (BMELs)?

- Bone marrow edema lesions are the accumulation of interstitial fluid or inflammation within the bone marrow
- Typically occur as a consequence of a direct impact to bone:
  - Post an acute injury such as a ruptured ACL
  - Degenerative osteoarthritis

Consequences of bone marrow edema lesions

- Bone marrow edema lesions promote inflammation and degeneration of cartilage, prohibiting recovery and joint health
- Currently no effective treatment for bone marrow edema lesions



Source - https://www.rheumatologyadvisor.com/osteoarthritis/the-predictive-value-of-bone-marrow-lesions-in-degenerative-joint-disease/article/466050/

Clinical Programs

Osteoarthritis

- Double blinded placebo controlled phase 2b clinical trial
  - **100% recruited – Results due Q4 CY2018**
- **Signs of strong efficacy established**
- **Blockbuster market -** 30 million people in the US alone diagnosed with osteoarthritis
- **No effective treatment –** ineffective NSAIDs and dangerous opioids are typical treatments

Acute Injury

- **Successful phase 2a open label**, established:
  - Primary Endpoint - Safety met
  - Secondary Endpoint - Efficacy met
- Demonstrated ability to **enhance recovery post injury/surgery**
- Currently being **utilised by a number of professional sports clubs (AFL, NRL, A-league)** under the TGA Special Access Scheme, with success.

Acute Injuries – Bone Marrow Edema Lesions

Bone marrow edema lesions as a result of an acute injury

- BMELs occur as a consequence acute injuries where the bone sustains strong impact, such as a ruptured ACL
- Resolution of the BMEL, reduces inflammation and inhibits cartilage degeneration, enabling the joint and ligaments to effectively repair

Successful Phase 2 Clinical Trial in BMELs as a result of ACL injury

- The primary endpoint of safety & tolerability was met
- Paradigm was also successful in meeting its secondary endpoint, demonstrating a statistically significant reduction in bone marrow edema lesion (BMEL) volume as measured by MRI
- Trial success confirms the Company's hypothesis that Pentosan Polysulfate Sodium (PPS) could be a new treatment for acute joint injuries

Addressable market based on acute traumatic injuries:

1.4 million

knee & ankle injuries associated with bone bruising[1,2,3]

US$2,000-$3,000

potential price per ZILOSUL® treatment

US$2.8-4.2+ billion

ZILOSUL® market in USA

Andrew Walker - Carlton Football Club

200+ game player with severe knee pathologies resolved with PPS

Source:

1. Based on 200k ACL injuries per annum, with 80% being associated with BMEL – Niall D, et al. (2004) and Friedberg R, et al. (2016)
2. Based on 1m meniscal injuries per annum, with 80% assumed as being associated with BMEL – Jones C, et al. (2012)
3. Based on 600k ankle injuries per annum, with 80% assumed as being associated with BMEL – Waterman B, et al. (2010)

Osteoarthritis with Bone Marrow Edema Lesions

Osteoarthritis - A blockbuster indication with no effective treatments

Osteoarthritis and bone marrow edema lesions

- **BMEL are commonly associated with OA** and have been **linked to early onset of OA** and joint cartilage degeneration.[1]
- BMEL sustains inflammation and the release of MMP's and ADAMTS-5 enzymes, causing cartilage degeneration
- Resolution of the BMEL, **reduces inflammation and promotes joint health**
- Patients treated with PPS have reported **statistically significant improvement in pain and function**
- **Osteoarthritis** is the most common form of arthritis, affecting over **30 million people** in the United States, with over 36 million outpatient visits and 750,000 hospitalisations per year[2]

OA Market Facts:

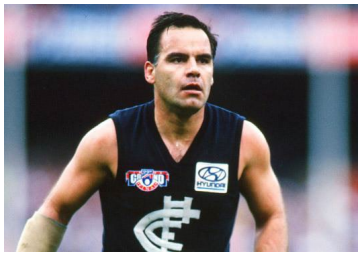
Market of therapeutics to treat OA

~US$5 billion pa Globally[3]

Cost to US Economy

US$128+ billion pa[4]

AFL Legend Greg 'Diesel' Williams diagnosed with OA, experienced significantly improved pain and function scores post PPS treatment



Source:

1. 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) and (Rheumatology 2010, 49:2413-9).
2. http://ard.bmj.com/content/annrheumdis/early/2017/07/12/annrheumdis-2017-211396.full.pdf
3. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.
4. *Ibid.*

Clinical Pipeline

Paradigm hosts a deep clinical pipeline

	Indication(s)	Clinical Status	Market Size
IL-1RA Peptide	▪ Inflammatory bowel disease ("**IBD**") ▪ Cancer-related cachexia ▪ Ulcerative colitis ▪ Crohn's disease	Safety and efficacy confirmed in Phase 1/2 clinical trial (n:26)	Inflammatory Bowel Disease Medicines predicted to reach **US$9.3 Billion**[1]
Cardiovascular	▪ Heat Failure	Demonstrated beneficial effects in an established preclinical heart failure model	**US$18+ Billion**[2]
Respiratory	▪ Hay Fever ▪ COPD ▪ Allergic Asthma	▪ Pre-clinical safety and efficacy in guinea pig model ▪ Safety confirmed in Phase 1b clinical trial (n:18) ▪ Paradigm to reassess Phase 2b clinical trial (n:40)	**US$11+ Billion**[3]

1. https://www.visiongain.com/Press_Release/932/The-World-Market-For-Inflammatory-Bowel-Disease-Medicines-will-reach-9-3-billion-in-2019
2. Forbes – The best selling drugs since 1996 (2012) 2. *Heart failure: preventing disease and death worldwide,* P.Ponikowski et al (2014) 3. Sales of six leading compounds – Figures between 2014 & 2016 - Statins $13.2bn (Research and Markets - Global Statin Market 2015-2016), Clopidogrel bisulphate $1.8bn, Beta-blockers $1.55bn, Ace inhibitors 0.47bn, Aspirin $0.54bn, Vitamin K antagonist $0.5bn (www.pharmacompass.com)
3. Visiongain: Allergic Rhinitis Drugs Market Forecast 2015-2025

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