



# paradigm

BIOPHARMA

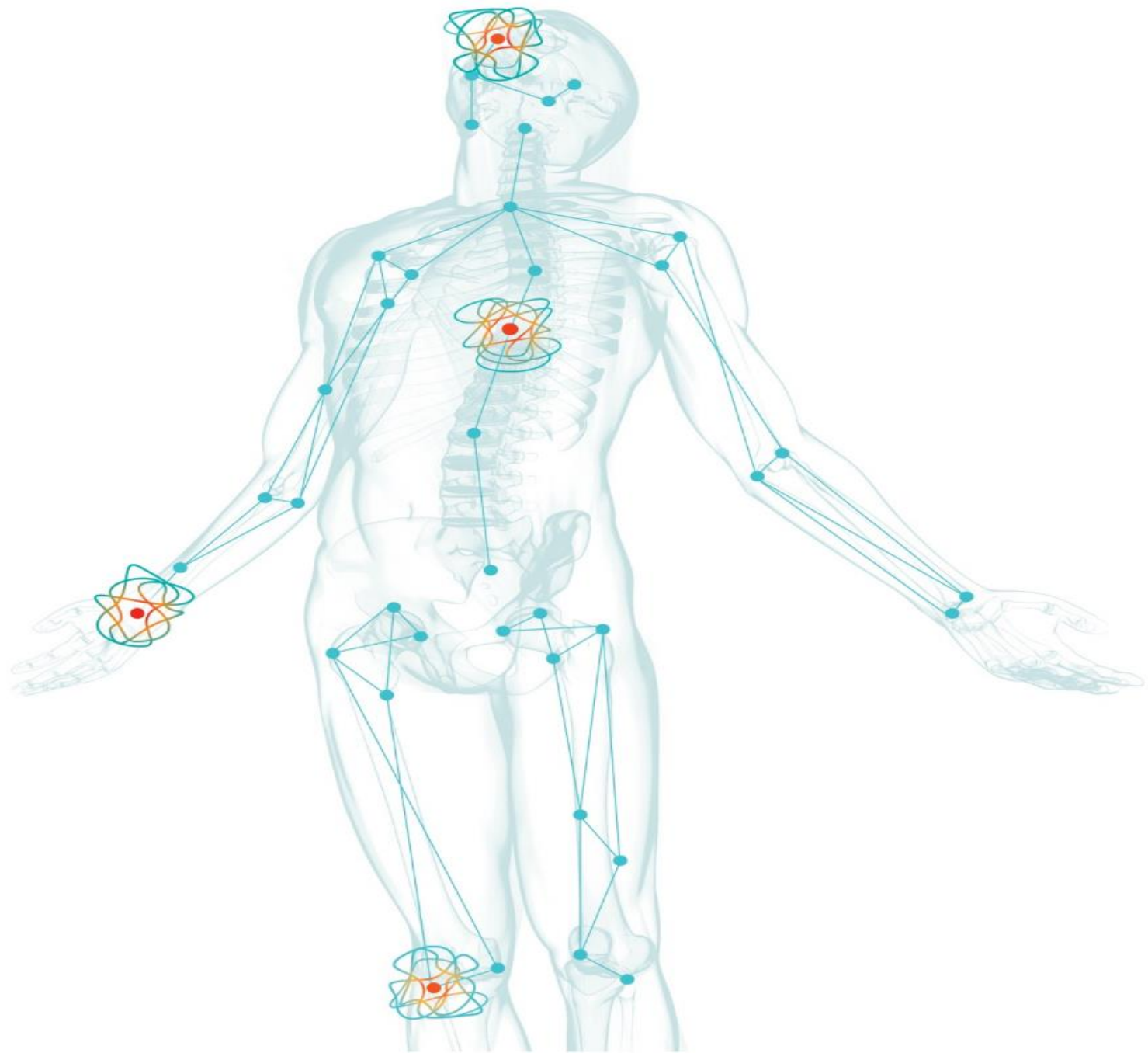
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(ASX: PAR)

Paul Rennie, CEO & MD

- Release of FDA minutes from OA Pre-IND Meeting
  - Release of TGA Special Access Scheme WOMAC Scores
  - A\$35m Placement
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6 March 2020



# Paradigm's Mission

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Paradigm Biopharmaceuticals LTD (PAR) is a late stage drug development company focusing on repurposing the drug Pentosan Polysulfate Sodium (PPS).

Paradigm Aim is to develop and commercialise an ethical, safe and effective Pharmaceutical Agent (PPS) for the treatment of musculoskeletal disorders in humans with degenerative disease driven by injury, viral infection, aging or genetic predisposition.

# Executive Summary

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- Repurposing Pentosan Polysulfate Sodium (“PPS,” “ZILOSUL®”): **FDA-approved, 60-yr track record** of treating inflammation
- Lead program: **Osteoarthritis (OA) – 31m sufferers in the US alone**
- **OA Phase 2b trial (n=112) met primary, secondary and exploratory endpoints (included pain, function, BML and biomarkers).**
- **Pre-IND meeting has confirmed key endpoints for Phase 3 as pain and function and required use of Bene Pharma produced PPS**
- **Planned FDA IND for Phase 3 trial in OA in 2020**, anticipate US trial readout Q3 CY 2022
- **Meeting with EMA in 2020 to ensure Phase 3 OA trial will also meet EU regulatory requirements. The second Phase 3 clinical trial could be run in Europe to assist with registration with the EMA.**
- **Zilosul granted FDA approval under Expanded Access Program (EAP) to treat 10 patients suffering with OA –Initiated-February 2020**
- Seeking Provisional Approval in Australia with TGA prior to completing Phase 3 trial
  - If successful, **Paradigm could be revenue-generating in Australia in Q1 CY2021 (subject to TGA Provisional Approval).**
  - **3m sufferers, revenue potential in Australia @ 20% market share = ~AUD\$1.5b p.a**
- **Revenue potential in US @ 10% market share = ~US\$9bn p.a**
- Strong portfolio of IP protection and patents on Zilosul – **patents in all key markets from 2030 to 2039**
- Secured scalable manufacturing supply from FDA approved facility – **exclusive agreement for 20 years**
- Paradigm is raising A\$35m via a Placement at A\$1.30 per share
  - **A\$108m cash on balance sheet post raising – fully funding company until end of 2022** (past readout of OA PH3 trial and MPS pivotal trial)
  - In combination the company is releasing a summary of the FDA Pre-IND minutes (p4) and the release of data of its first 34 patients treated under TGA SAS using WOMAC – 45% mean reduction from baseline (p5-10).

# Summary of FDA Pre-IND meeting for Phase 3 OA trial

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- PAR attended a Pre-IND meeting with FDA on 19 February re its Phase 3 OA trial
- The FDA has now provided the minutes of the meeting to PAR
- Key outcomes of the FDA meeting include:
  - Primary endpoint of mean change in pain using WOMAC questionnaire
  - 6-week dosing and observe duration of effect
  - Because PAR is proposing a new indication for PPS (Treatment of Pain in OA), bridging to literature will not serve as one of the two required efficacy studies, therefore the Agency requires two adequate and well controlled studies.
    - ~750 patients in 1<sup>st</sup> Phase 3 randomized controlled trial (22-month duration)
    - ~400 patients in 2<sup>nd</sup> Phase 3 randomized controlled trial (12-month duration but can be run concurrently, with centers' in Europe)
- **The positive outcomes from this meeting can be summarized as:**
  - ✓ Little chance of generic competition given the recognized uniqueness of bene pharmaChem's PPS.
  - ✓ Company now has certainty around size of Phase 3.
  - ✓ Company has clarity around the IND and NDA submissions.
  - ✓ Primary and secondary endpoints are the same as previous Ph2 trial (Pain and function, mean change from baseline).
  - ✓ Duration of effect of 12 months has been reported in most SAS patients
  - ✓ Modest increase in trial costs from expanded size will be funded post capital raising
  - ✓ We are anticipating a January 2021 start to Phase 3, readouts in Q3 CY 2022.

## **The Company plans to use:**

Saline as the placebo control

Sample size (n=750) and (n=400). Study size based on drug effect size of Phase 2 (pain change from baseline) and responder rates respectively.



## Release of first WOMAC scores from TGA special access scheme

*"We need real-world effectiveness data and the analytics to improve access to medicines from real-world data, not just from clinical trials<sup>1</sup>." CSL Chief Executive, Paul Perreault.*

- Paradigm previously reported greater than 50% reduction in knee OA pain across 205 patients under the TGA Special Access Scheme using the NRS acute pain scale.
- Pre-IND FDA meeting has confirmed Paradigms proposed Phase 3 trial in knee OA will use the industry standard WOMAC pain as the primary endpoint in the phase 3 trial.
- The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is widely used in the evaluation of Hip and Knee Osteoarthritis. It is a self-administered questionnaire consisting of 24 items divided into 3 subscales:[\[1\]](#)
  - Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing upright
  - Stiffness (2 items): after first waking and later in the day
  - Physical Function (17 items): using stairs, rising from sitting, standing, etc.
- In conjunction with the capital raising, **PAR is pleased to report the first cohort of 34 patients from the TGA SAS using WOMAC**
  - Mean reduction in WOMAC pain scores from baseline of 45%
  - Mean reduction in NRS (Acute) pain scores from baseline of 50.1% (consistent with previously reported ASX Announcement of 205 SAS patients with NRS (Acute) pain reduction of
  - Additional WOMAC Pain Scores on 100 patients from SAS, will be released in Q3 CY 2020
- To date Paradigm has treated over **450 patients** who have Knee OA with PPS (Zilosul®) via its Clinical Trials and SAS.

# Release of first WOMAC scores from TGA special access scheme



**Mean reduction in WOMAC pain from baseline to Day 81 was 45%**

WOMAC Pain Questionnaire	Mean Baseline value (95% Confidence Interval)	Mean Post-treatment value (95% Confidence Interval)	Mean Reduction in Pain (percentage) (N=34 patients)
1. Pain Walking on flat surface	5.94 (5.23, 6.65)	3.18 (2.46, 3.90)	44.8%
2. Pain Going up/down stairs	7.24 (6.56, 7.92)	4.3 (3.38, 5.22)	37.93%
3. Pain At night	4.97 (3.96, 5.97)	1.68 (0.96, 2.4)	75.11%
4. Pain Sitting/lying	4.15 (3.36, 4.94)	1.59 (0.87, 2.30)	61.39%
5. Pain Standing upright	5.29 (4.61, 5.97)	2.53 (1.78, 3.28)	48.54%
WOMAC Pain Subscale	27.38 (23.94, 30.81)	13.38 (9.97, 16.78)	44.93%

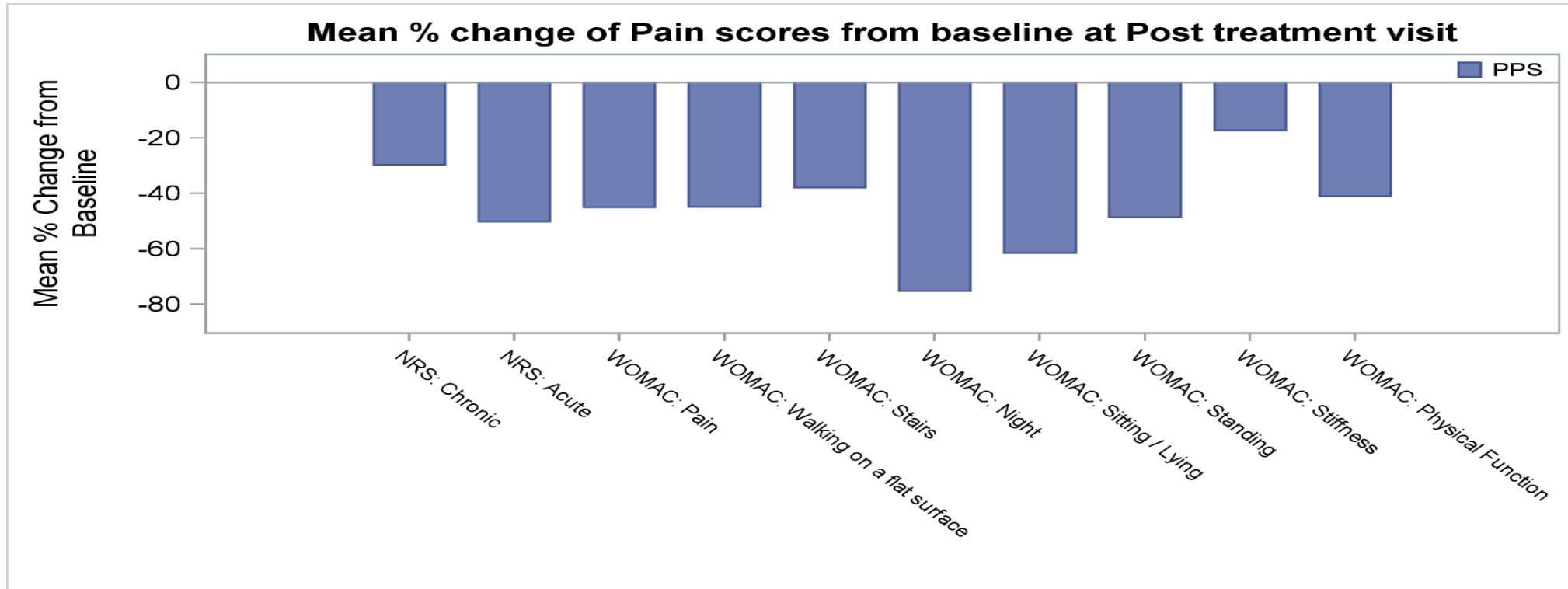
# Comparing WOMAC scores from TGA Special Access Scheme to Opiates



In first 34 patients under TGA SAS, PPS has shown a mean reduction in WOMAC pain scores of 45% following the initial 6-week treatment course.,

	Mean reduction in WOMAC pain score at week 12.	Additional Comments
Pentosan Polysulfate Sodium (iPPS) Paradigm results iPPS under SAS.	<b>45%</b>	The WOMAC pain score reduction of PPS treatment from baseline to 12 weeks is 45%. PPS response is present 6 weeks after the last PPS injection.
Tramadol (Opiate) 300 mg	<b>46%</b>	Opiate <u>once a day for 12 weeks</u>
Tramadol (Opiate) 200 mg	<b>43%</b>	Opiate <u>once a day for 12 weeks</u>
Source:	Fishman RL et al Efficacy and safety of 12 weeks of osteoarthritic pain therapy with once-daily tramadol (Tramadol Contramid OAD).2007. <a href="#">J Opioid Manag.</a> 2007 Sep-Oct;3(5):273-80.	

# Release of first WOMAC scores from TGA special access scheme



- Note: All subjects with NRS and WOMAC scores at baseline and post-baseline are summarised.  
% Change from Baseline = ((Result at post-baseline visit - Result at baseline)/Result at baseline)\*100  
WOMAC scores are grouped into three categories (Pain, Stiffness and Physical Function) based on the general guidelines. Also, the individual questions inside Pain category are listed.  
Abbreviations: PPS = Pentosan Polysulfate Sodium; SD = Standard Deviation; Min = minimum; Max = maximum; NRS = Numerical Rating Scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index



**Release of PGIC Scores from WOMAC cohort  
TGA special access scheme (Patient Global Impression of Change).**



PGIC Score (Subjects with WOMAC scores)	
Visit PGIC Scores	WOMAC Subjects (N = 34)
Post-Baseline	
No Change (or condition has got worse)	0
Almost the same, hardly any change at all	2 ( 5.7%)
A little better, but no noticeable change	2 ( 5.7%)
Somewhat better, but the change has not made any real difference	0
Moderately better, and a slight but noticeable change	8 (22.9%)
Better and a definite improvement that has made a real and worthwhile difference	13 (37.1%)
A great deal better and a considerable improvement that has made all the difference	9 (25.7%)
Missing	1 ( 2.9%)
Note: PGIC scores are summarised for subjects with WOMAC scores. Abbreviations: PGIC = Patient Global Impression of Change ; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index Program Name: t-14-2-3-pgic; Source data: PGIC, WOMAC	

**85.7% (30 out of 34) of SAS patients had reported Patient global impression of Change (PGIC) of moderately to definite and considerable improvement in their OA condition with iPPS (Zilosul®) treatment.**

# Upcoming Milestones/News Flow



## 2020

- **Compassionate Use program with NFL 'Pro Players Elite Network'**
  - ✓ Early 2020: US Trial initiation (n=10) – First Patient Dosed Feb, All patients dosed March (See ASX ANN 21<sup>st</sup> Feb, 24<sup>th</sup> Mar)
  - Q3 CY2020: Results released
- **Pivotal Phase 3 OA US Clinical Trial**
  - ✓ Pre-IND meeting with FDA (19<sup>th</sup> Feb 2020)
  - Q4 2020: Submit IND with FDA
  - Early 2021: Commence multi-centre Phase 3 trial in US & EU (n=750+400)
- **Pivotal Phase 2/3 Mucopolysaccharidosis (MPS) trial**
  - Mid 2020: Joint Parallel Scientific Advice Submission to FDA and EMA
  - Late-2020: Commence multi-centre Phase 2/3 US & EU under 505(b)(2)
  - Q3 CY 2020 Paradigm to commence Phase 2 clinical trial in MPS-1.
- **TGA (i.e. Compassionate Use) Provisional Approval for iPPS to treat OA in Australia**
  - Q4 2020/Q1 2021: Potential for approval to begin selling in Australia, initial launch/revenue update
  - Ongoing: Additional release of over 100 TGA SAS patient WOMAC results
- **Additional News flow**
  - Potential for ASX300 index inclusion in next rebalance – expected in June
  - Peer reviewed publication of Phase 2b OA/BMEL Results & peer reviewed publication of Phase 2a Viral Arthritis clinical trial

## 2021

- **Phase 2/3 MPS trial:** potential pivotal trial readout
- MPS partnering discussions to commence
- Trials launches in additional pre-clinical indications (e.g. viral arthritis)

## 2022

- OA Phase 3 trial completion and readout Q3 2022



# CAPITAL RAISING DETAILS

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# Capital Raising Structure



- A\$35m Placement to Sophisticated and Professional investors at A\$1.30 per share
- A\$1.30 per share represents:
  - 23% discount to last closing price of \$1.69
  - 39% discount to 30 day VWAP of \$2.13
  - 71% discount to the all time high on 5 Feb 2020 of \$4.50
- Bell Potter Securities Ltd is Sole Lead Manager to the Offer

CAPITAL STRUCTURE	
Current Shares on issue	197.8m
Placement Shares Issued	26.9m
Shares on issue post Placement	224.7m
Market capitalisation at A\$1.30	A\$292m
Pro-forma cash position 31-March-20 (incl proceeds of offer minus costs)	A\$108m
Pro-forma Enterprise Value	A\$184m

## Use Of Funds & Cash Outflows



- A\$35m will be applied to the additional cost of the 2nd Phase 3 OA trial and put PAR in a fully funded position until the end of 2022 with pivotal trial readouts in OA and MPS.
- Updated cost of PH3 OA trials is estimated at A\$80m comprising:
  - 1<sup>st</sup> Phase 3 trial (n=750) estimated at A\$45m (fully funded via 2019 capital raising)
  - 2<sup>nd</sup> Phase 3 trial (n=400) estimate at A\$35m (funded via this capital raising)

Reconciliation of Pro-Forma cash and trial costs	
March 2020 cash at bank	A\$74.5m
+ Proceeds from capital raising	A\$33.5m
= Pro-Forma cash at bank March 2020 post raising	A\$108.0m
- Estimated Cost of Phase 3 OA trial	A\$80.0m
- Estimated Cost of Pivotal MPS trial	A\$9.0m
= Cash remaining for operational costs of the business, further R&D and working capital for at least 2 years	A\$19.0m

# Indicative Timetable

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Trading Halt	6 April 2020
Company resumes trading	8 April 2020
Settlement of New Shares issued under the Placement	T+3 trading days



# OVERVIEW OF PPS / ZILOSUL

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# Background - Pentosan Polysulfate Sodium (PPS) / Zilosul



## Pentosan Polysulfate Sodium

- Semi-synthetic drug manufactured from beech-wood hemicellulose
- Has been used in humans for more than 60 years
- 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

## Potential biological characteristics

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

## Excellent Safety Profile

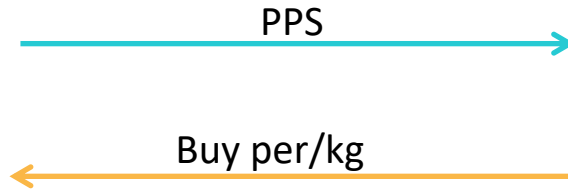
- Well established safety profile with no reported serious adverse events
- FDA Approved 30+ years ago for oral use, 100 m+ injectable doses administered
- Semi-synthetic, complex carbohydrate makes it well tolerated by the human body
- Weak anti-coagulant: 1/15<sup>th</sup> – 1/20<sup>th</sup> the anti-coagulant activity of Heparin. Data on file with US FDA
- Clearance from the body, as measured by activated partial thromboplastin time (aPTT), is 300 minutes (5 hours).
- Suggested sports physician treatment protocol:
  - Administration at least 48 – 72 hours before any contact sport is played
  - Blood test prior to contact sport to test coagulation parameters are within the normal range
- Weak anti-coagulant properties should not present any notable issues



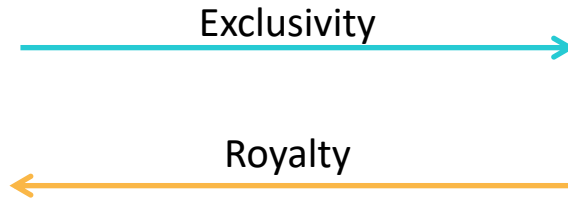
# Exclusive Supply & Manufacturing



## Exclusive Supply



## License



- **Long term exclusive supply agreement** with bene pharmaChem GmbH.
- Bene pharmaChem: original developer of PPS and **only FDA-approved manufacturer**.
- Johnson & Johnson have been sourcing PPS from bene for a different application (bladder pain).
- Agreement grants exclusive supply of only FDA approved PPS for Paradigm's orthopaedic and respiratory programs.
- Paradigm to pay bene pharmaChem small single digit (2% on net sales) royalty on commercial sales.

# Strong Patents & IP Position



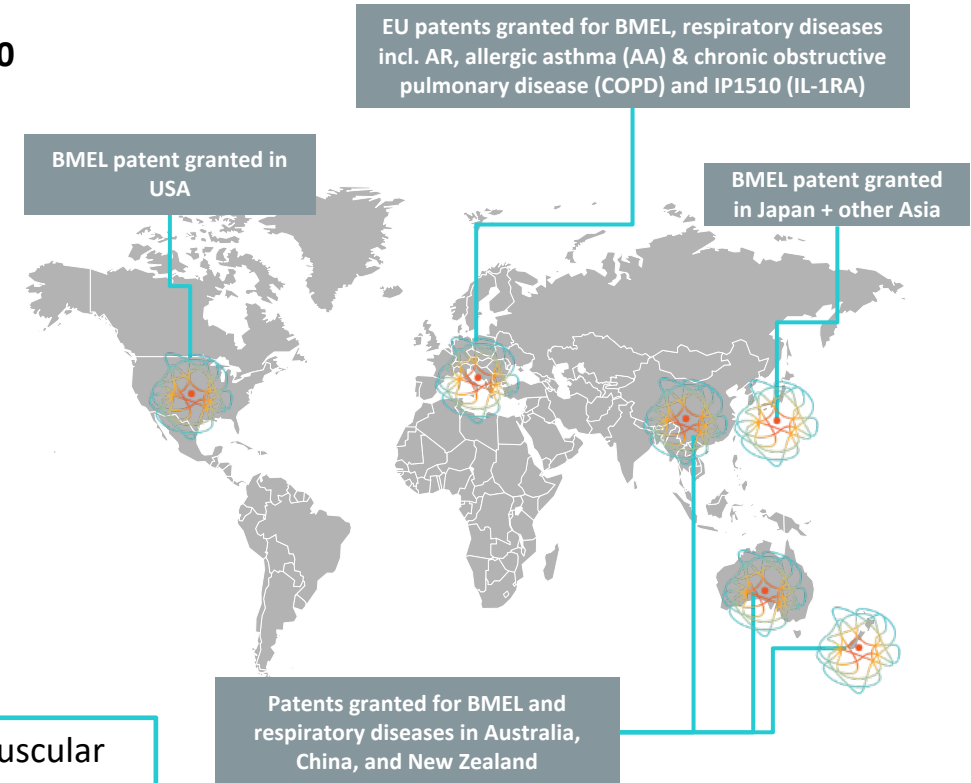
## Multi-faceted IP protection increases barriers to entry for potential competitors

- Patent protection using PPS for new indications
- Minimum life on patents is 2030 and beyond for more recent patents - i.e. 2035 - 2040**
- Established regulatory exclusivity and trademarks
- Patents for MPS (ex Japan) + Orphan Status
- Patent applications for Ross River virus and Chikungunya virus
- Patent applications for osteoarthritis and concurrent BMEL
- Patent for Heart Failure indication
- Prosecuting new patent applications

## Secure manufacturing and supply

- Exclusive long term supply agreement with bene PharmaChem<sup>1</sup>
- bene pharmaChem makes the only FDA-approved form of PPS
- Manufacturing methods are highly complex and a well kept trade secret
- Bene pharmaChem has been supplying J&J for over 20 years for oral use**

Patent's claim where treatment is administered by an injection that includes the intra-muscular (IM) or subcutaneous (SC) routes, intra-venously (IV), intra-articularly (IA), peri-articular injections but also includes topical or **oral administration**. Oral use of PPS, for the indications which Paradigm has patented, is covered under Paradigm's patents and any oral use thereof would be an infringement of Paradigm's patent.

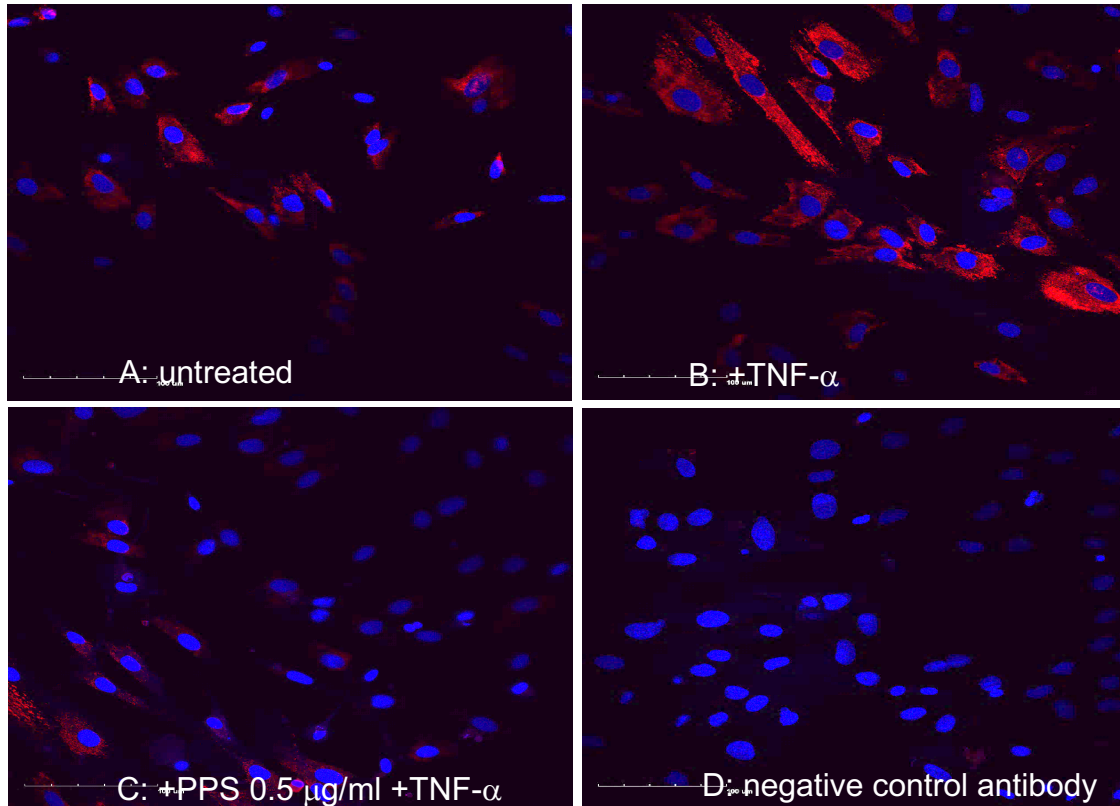


<sup>1</sup>.bene pharmaChem is a private company located in Germany and manufactures the only officially approved and clinically tested medicinal PPS in the USA, Europe and Australia

# Mechanism Of Action (MOA)

## Reduction of NGF as mediator of PAIN.

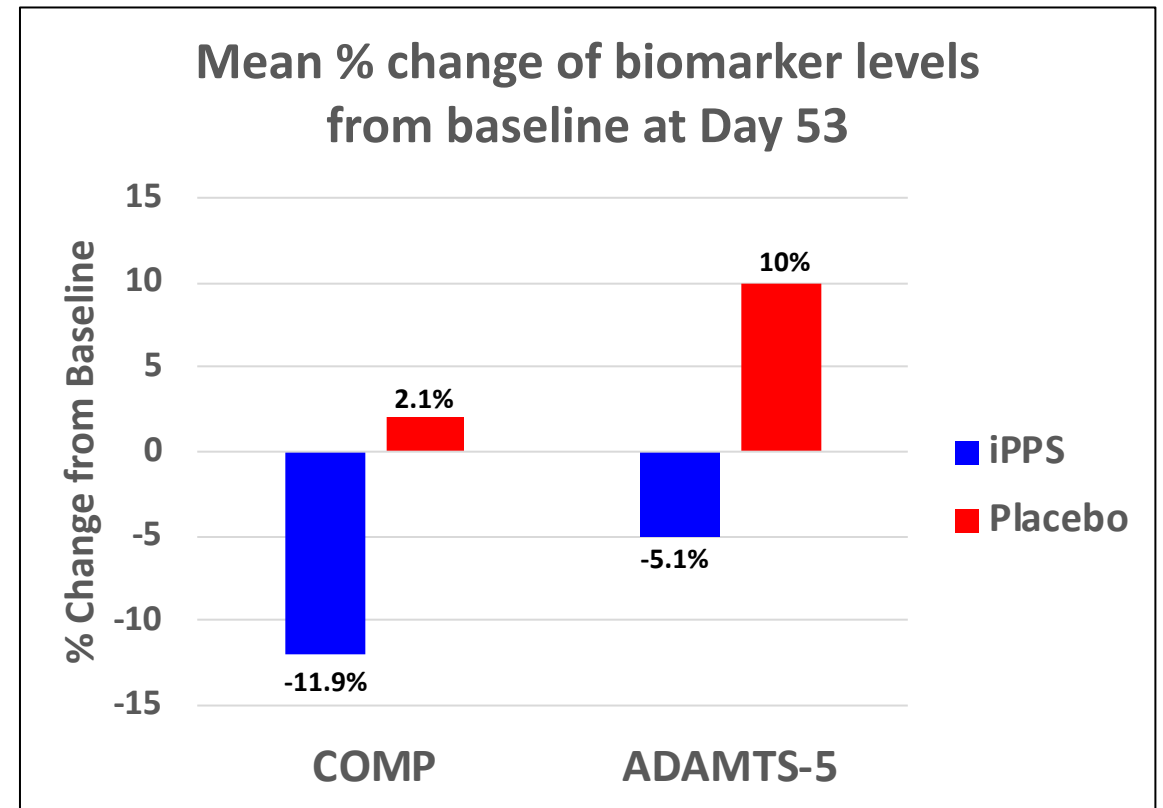
- PPS downregulates NGF expression in osteocytes knee OA patients



Confocal microscopy images showing NGF protein expression (red) by freshly harvested human osteocytes. Nuclei (blue) (*Stapeldon et al PLOS One 2019*)

## Inhibition of the cartilage degrading enzymes that are known to play a key role in the progression of OA.

- Reduction in serum **COMP** & **ADAMTS-5** in P2 study of knee OA.



**Among subjects with symptomatic knee OA, a single measurement of increased COMP predicted subsequent cartilage loss on MRI.** Hunter et al.

# BONE MARROW LESIONS (BML):

## CLINICAL IMPLICATIONS FOR KNEE OA AND DISEASE REGRESSION WITH iPPS THERAPY



BML appear as increased signal intensity within the bone marrow



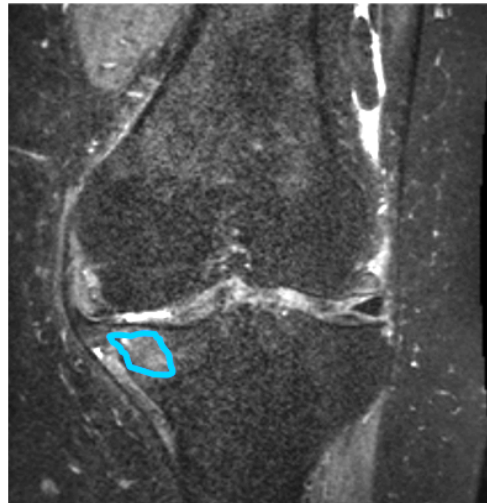
Grade 3 medial tibial BML at baseline

INCREASING PAIN

INCREASED CARTILAGE LOSS

HIGH RISK OF JOINT DESTRUCTION

HIGH RISK OF TOTAL KNEE REPLACEMENT



Grade 2 medial tibial BML at follow-up

REDUCED PAIN

REDUCED CARTILAGE LOSS

REDUCED RISK OF JOINT DESTRUCTION

REDUCED RISK OF TOTAL KNEE REPLACEMENT

# OA PHASE 2B TRIAL RESULTS

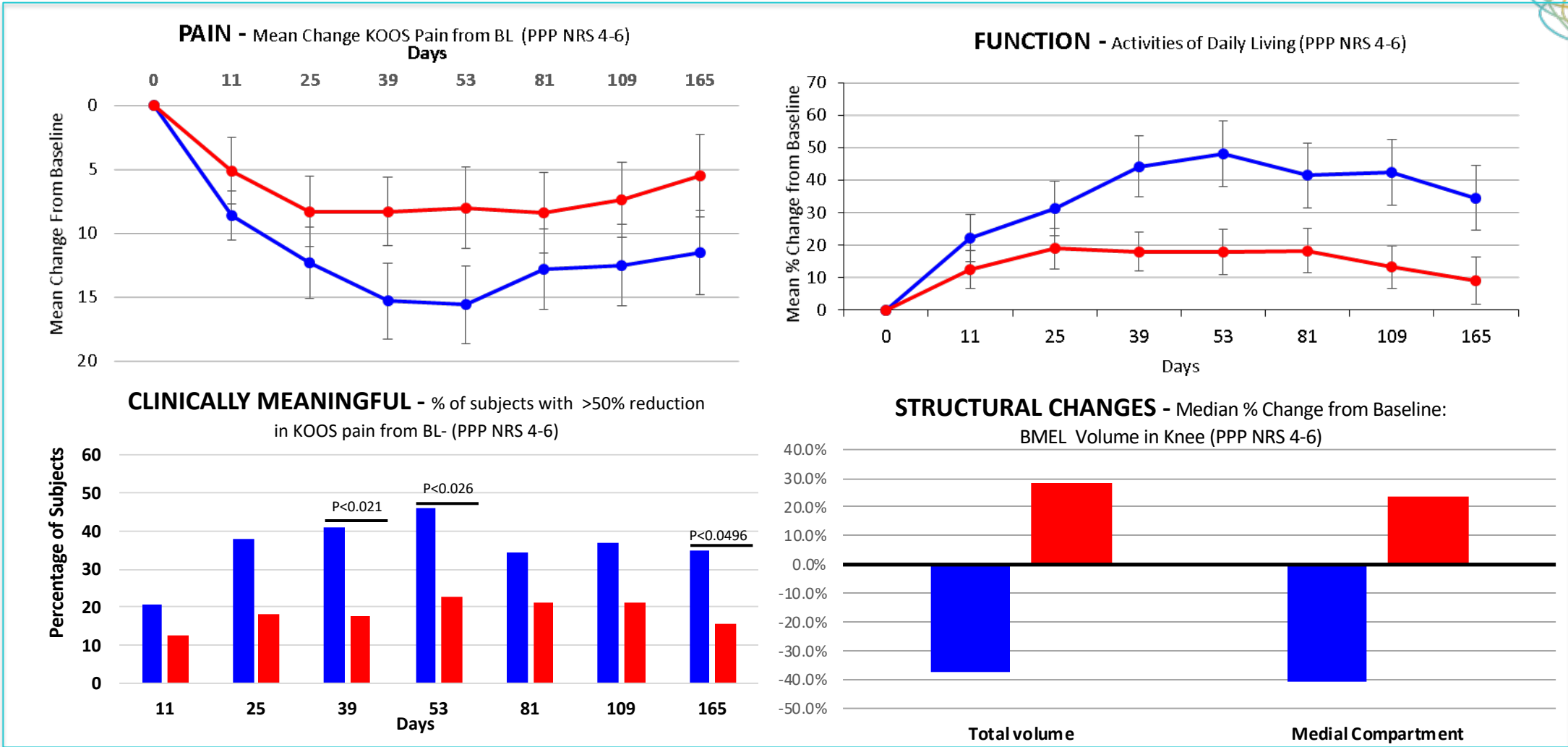


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**PRIMARY, SECONDARY &  
EXPLORATORY ENDPOINTS  
MET**



# SUMMARY PHASE 2 DATA – PPP (NRS 4-6)



- Paradigm also achieved statistically significant and clinically meaningful result in Patient Global Impression of Change (PGIC) (p=0.0062)

■ iPPS ■ Placebo

# Phase 2b OA/BML Clinical Trial – Primary And Secondary Endpoints

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**iPPS was well tolerated, effective and clinically meaningful in a Phase 2b randomised, double-blind, placebo-controlled, multi-centre clinical trial**

- **Primary endpoint met** - change in KOOS pain score from baseline at Day 53 for total trial population ( $p < 0.0001$ )
  - Number of subjects with >50% Reduction from Baseline in KOOS Pain Score at Day 53 – Clinically meaningful and stat sig results ( $p < 0.026$ )
  - Patient Global Impression of Change (PGIC): total iPPS population vs placebo was stat sig (PGIC,  $p = 0.0062$ )
  - BML data suggests iPPS has potential to reduce progression of OA
  - Decreasing serum levels of COMP and ADAMTS-5 consistent with **iPPS preservation of cartilage**
- 
- ✓ **Reduction in BML grade, volume and area indicates iPPS potential for reducing rate of progression of OA**
  - ✓ **Decreased serum levels of COMP and ADAMTS-5 indicate iPPS potential for reducing cartilage loss**

*All data will be the subject of a peer-review publication*

# Recent OA Transactions - Highlights Pharma Interest In OA



COMPANIES		COMPOUND	REGION	UPFRONT	TOTAL VALUE	STATUS
		Anti-NGF	Global	US\$200m	US\$1.8bn	Phase 3 (Failed)
		Anti-NGF	Global	US\$250m	US\$1.25bn	Phase 3
		Corticosteroid	Global	Take-over*	US\$1.0bn*	Commercialised
		Anti-NGF	Global (ex Japan)	US\$50m	US\$435m	Discontinued
<b>GLOBAL AVERAGE</b>				<b>US\$166m</b>	<b>US\$1.12bn</b>	
		ADAMTS-5 Inhibitor	EU	Unknown	US\$346m	Phase 1
	Mitsubishi Tanabe Pharma	Gene therapy	Japan	US\$24m**	US\$434m**	Handed Back
		Gene therapy	Japan	US\$27m	US\$591m	Phase 3
	Mitsubishi Tanabe Pharma	Anti-NGF	Asia	US\$55m	US\$325m	Phase 3
<b>REGIONAL AVERAGE</b>				<b>US\$35m</b>	<b>US\$424m</b>	

Safety Issues

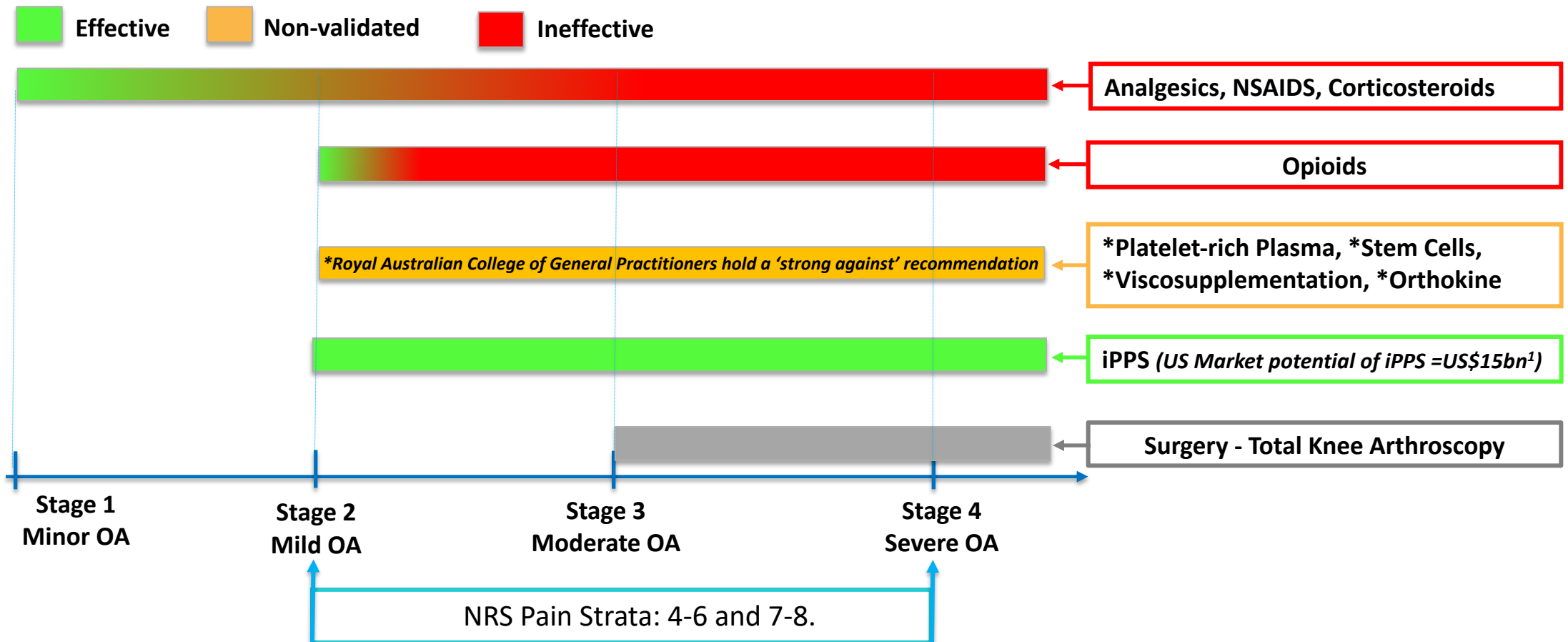
Sources: Bloomberg, company filings; \*Sanofi-Flexion take-over rumoured – Fierce Biotech; \*\*Mitsubishi handed back rights to TissueGene who executed deal with MundiPharma



# Market Demand – OA Stages And Treatments



There are no effective treatments for Moderate to Severe OA



1. 14m American have symptomatic knee OA – 7m are eligible for knee replacement (late stage 3/stage 4) – PAR Estimate - 5m x US\$3,000 per iPPS treatment = US\$15bn p.a. - <https://www.arthritis.org/Documents/Sections/About-Arthritis/arthritis-facts-stats-figures.pdf>

# Successful Re-Purposed Drugs



BRAND NAME	ORIGINAL INDICATION	NEW INDICATION	PHARMA COMPANY	PEAK ANNUAL SALES
<b>SPRAVATO</b>	Anaesthetic (Ketamine)	Treatment Resistant Depression	<b>Janssen/J&amp;J</b>	<b>Approved March 2019</b>
<b>REVLIMID</b>	Structural Analogue of THALOMID (below)	Multiple Myeloma	<b>Celgene</b>	<b>\$9.7B (2018)</b>
<b>TECFIDERA</b>	Psoriasis	Multiple Sclerosis	<b>Biogen/IDEC</b>	<b>\$4.0B (2017)</b>
<b>VIAGRA</b>	Angina	Erectile Dysfunction	<b>Pfizer</b>	<b>\$2.05B (2008)</b>
<b>GEMZAR</b>	Anti-viral	Various Cancers	<b>Lilly</b>	<b>\$1.72B (2008)</b>
<b>RITUXAN</b>	Various Cancers	Rheumatoid Arthritis	<b>Biogen &amp; Roche</b>	<b>\$7.1B (2015)</b>
<b>EVISTA</b>	Osteoporosis	Invasive Breast Cancer	<b>Lilly</b>	<b>\$1.07B (2011)</b>
<b>PROSCAR</b>	Hypertension	BPH	<b>Merck</b>	<b>\$741.4M (2005)</b>
<b>THALOMID</b>	Anti-Nausea	Leprosy Multiple Myeloma	<b>Celgene</b> <b>Celgene</b>	<b>\$535.2M (2008)</b>
<b>REVATIO</b>	Angina/ED	PA Hypertension	<b>Pfizer</b>	<b>\$525.0M (2008)</b>
<b>PROPECIA</b>	Hypertension	Male Pattern Baldness	<b>Merck</b>	<b>\$429.1M (2008)</b>
<b>ELMIRON (PPS)</b>	DVT	Interstitial cystitis	<b>Janssen/J&amp;J</b>	<b>US\$280m (2015)</b>

Source: Therapeutic Drug Repurposing, Repositioning and Rescue, Drug Discovery World Spring 2015; \* Elmiron Use Patents ended in 2012, despite this no generic has been approved in US

# REVENUE POTENTIAL IN OA



## Key Assumptions:

- 31m OA sufferers in the US
- 3m OA sufferers in Aus
- Annual dosing/treatment – assumed 12 month duration of effect as observed in TGA special access scheme
- Pricing is indicative only

		US MARKET – aiming for approval 2022		
		10% Market Penetration	20% Market Penetration	30% Market Penetration
INDICATIVE POTENTIAL PRICING	US\$1.5k p.a	US\$6.2B p.a	US\$12.0B p.a	US\$18.6B p.a
	US\$2.0k p.a	US\$7.7B p.a	US\$15.5B p.a	US\$23.2B p.a
	US\$2.5k p.a	US\$9.3B p.a	US\$18.6B p.a	US\$27.9B p.a

		AUS MARKET – aiming for provisional approval 2020		
		10% Market Penetration	20% Market Penetration	30% Market Penetration
INDICATIVE POTENTIAL PRICING	A\$1.0k p.a	A\$450M p.a	A\$900M p.a	AUD\$1,300M p.a
	A\$2.0k p.a	A\$ 600M p.a	A\$1,200M p.a	AUD\$1,800M p.a
	A\$2.5k p.a	A\$ 750M p.a	A\$1,500M p.a	AUD\$2,250M p.a

# Mucopolysaccharidoses (MPS)

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# Mucopolysaccharidoses (MPS)



## MPS – An Orphan Indication in need of new treatments

In November 2018, Paradigm in-licensed the MPS indication from the Icahn School of Medicine at Mount Sinai, New York. **The License includes successful Phase 2a safety and efficacy data**

### What is MPS?

The mucopolysaccharidoses (MPS) are a family of Orphan Diseases. The cumulative rate for all types of MPS is around 3.5 in 100 000 live births and generally the patients present in one of three ways:

1. As a **dysmorphic syndrome** (MPS IH, MPS II, MPS VI) often with early onset middle ear disease, deafness, or upper airways obstruction
2. With **learning difficulties**, behavioural disturbance and dementia and mild somatic abnormalities (MPS III)
3. As a **severe bone dysplasia** (MPS IV)<sup>1</sup>

**The current standards of care are not adequate in treating pain** associated with joint inflammation and musculoskeletal issues and these drugs currently equate to a market size of around **US\$1.4b per annum**, BioMarin's ERT treatments cost US\$300k – US\$600k p.a. **Paradigm believes iPPS may be an effective adjunct/combination therapy with current ERT treatments.**

**Compelling Phase 2a data suggests iPPS may be an effective adjunct therapy for various types of MPS**

**MPS Market Facts:**  
**13,000+ patients in US**

**Potential iPPS treatment cost:**  
**US\$50k - \$100k p.a.**

**Potential iPPS Market Share:**  
**US\$650m – US\$1.3bn**

Three MPS-VI patients



1. <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/mucopolysaccharidosis>

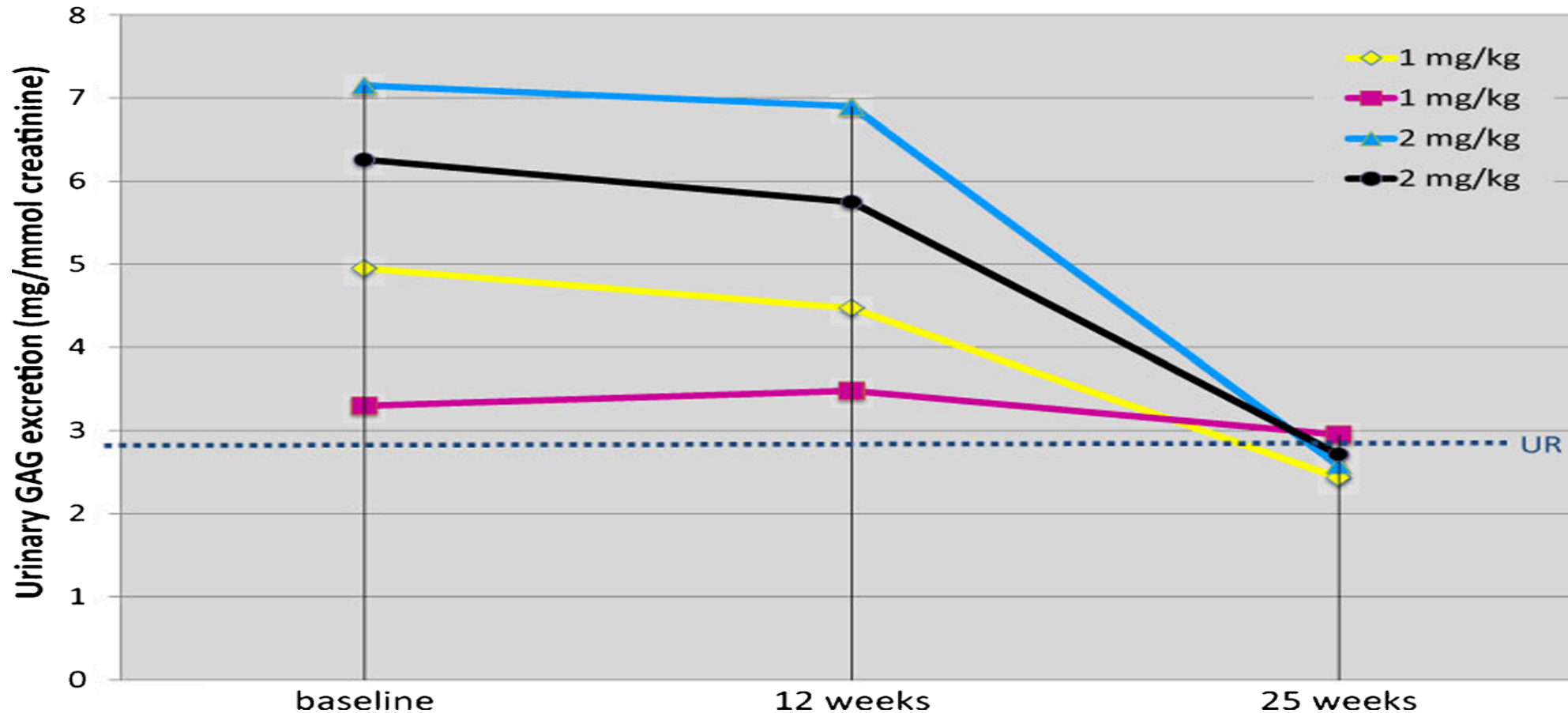
# Mucopolysaccharidoses (MPS) – Patient Centric Program

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- Paradigm presented its MPS VI poster at the MPS World Symposium in Orlando, Florida on the 11<sup>th</sup> Feb.
- Poster presented outcomes of patient focus group which aimed to identify and validate clinical development program endpoints and measurements.
- The **FDA and EMA** have agreed to a **joint Parallel Scientific Advice Submission**, the procedure commences in March.
- MPS 1 – Clinical trial to begin Q3 CY2020 in Adelaide.
- Joint submission to both FDA and EMA expected Q3 2020.
- Commence multi-centred Phase 2/3 US & EU under 505(b)(2) expected late 2020.

# Mucopolysaccharidosis (MPS) Objective Clinical Data – Phase 2 PPS In Subjects With MPS Type 1. PPS Administered Concomitantly With Aldurazyme (ERT).



Hennermann J et al “Treatment with pentosan polysulphate in patients with MPS I: results from an open label, randomized, monocentric phase II study” J Inherit Metab Dis (2016) 39:831–837

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