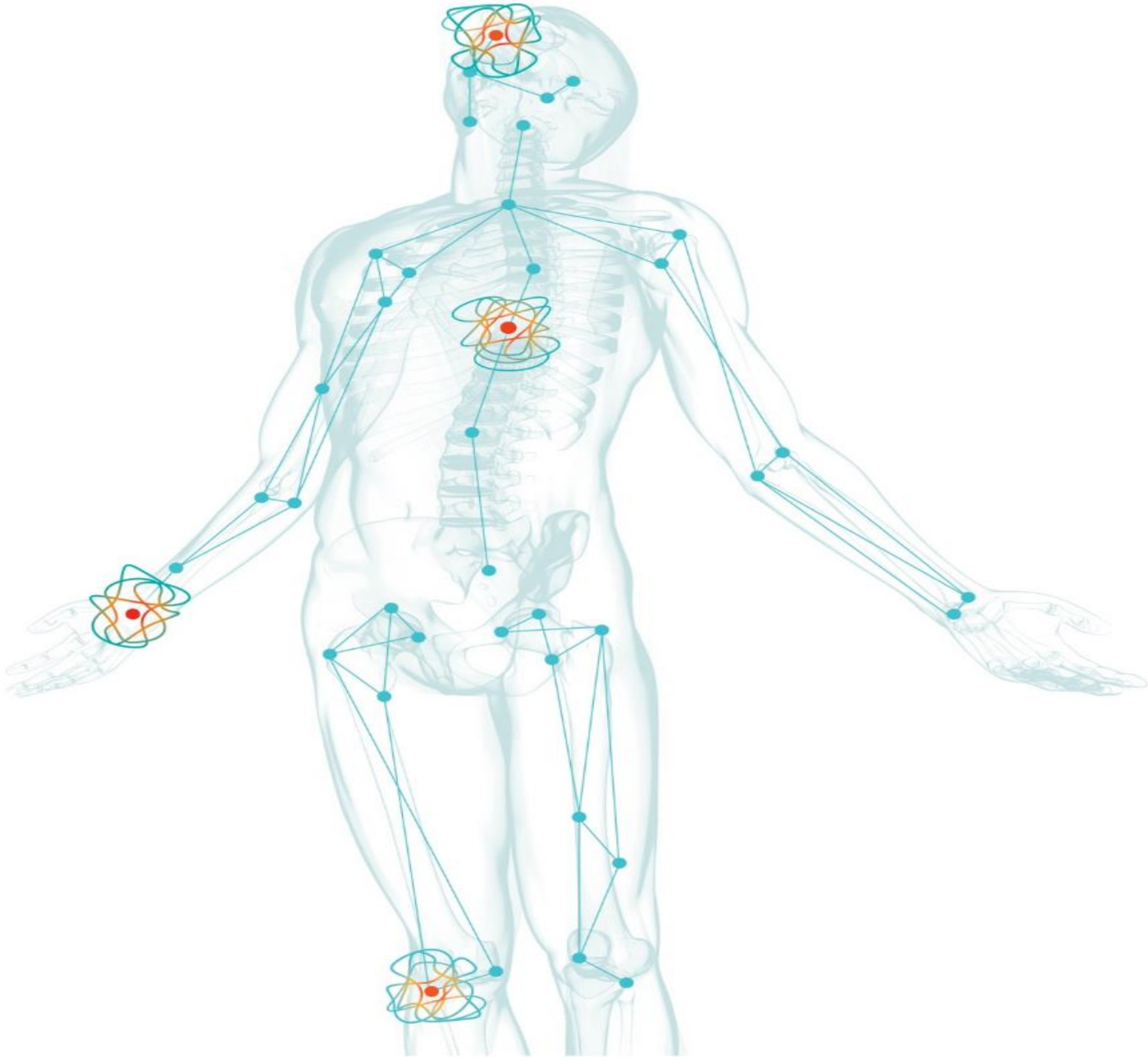
paradigm
BIOPHARMA

INVESTOR PRESENTATION



Paul Rennie, CEO & MD

March 2019

DISCLAIMER

This document, together with any information communicated by Paradigm Biopharmaceuticals Ltd (known as “Paradigm”, “Paradigm Biopharma” or “the Company”), in any presentation or discussion relating to this document (collectively, “Information”) is confidential, and has been prepared by the Company on the condition that it is for the exclusive information and use of the recipient. The Information is proprietary to Paradigm and may not be disclosed to any third party or used for any other purpose without the prior written consent of the Company.

The Information is based upon management forecasts and reflects prevailing conditions, which are accordingly subject to change. In preparing the Information, the Company has relied upon and assumed, without independent verification, the accuracy and completeness of all information available from public sources, or which was otherwise reviewed by it. In addition, the analyses are not and do not purport to be appraisals of the assets, stock or business of the Company. Even when the Information contains a kind of appraisal, it should be considered preliminary, suitable only for the purpose described herein and should not be disclosed or otherwise used without the prior written consent of Paradigm. The Information is provided on the understanding that unanticipated events and circumstances may occur which may have significant valuation and other effects.

PARADIGM'S MISSION STATEMENT

Paradigm's 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, aging or genetic predisposition.

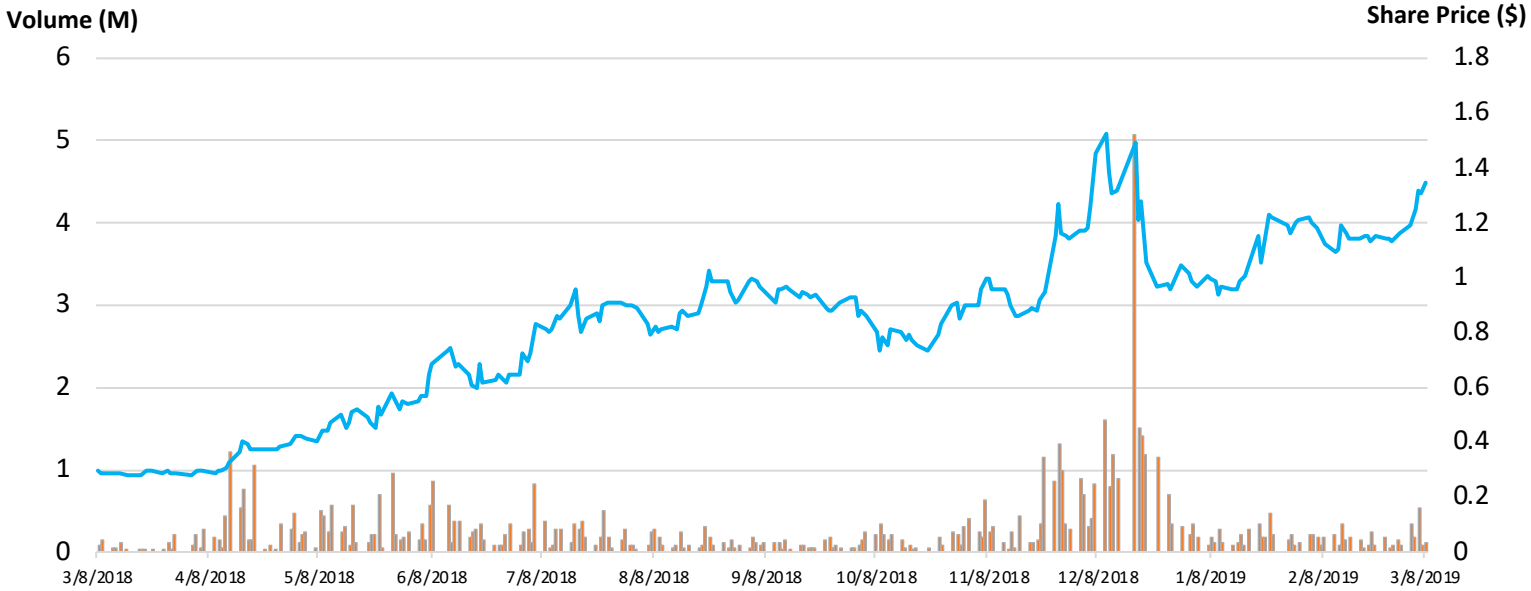
In achieving this aim, Paradigm will liberate human suffering from musculoskeletal pain, whilst creating shareholder wealth.

CORPORATE SNAPSHOT

- **Paradigm Biopharmaceuticals Ltd (PAR.ASX)** is an ASX-listed biotechnology company focused on repurposing Pentosan Polysulfate Sodium (PPS), an **FDA-approved drug** that has a **long safety track record** over sixty years.
- Initial focus is on repurposing PPS (under the name ZILOSUL®) to treat **Osteoarthritis (OA) – a Blockbuster market with over 31m sufferers in the US alone**
- **Company strategy is to execute partnerships with global pharmaceutical companies** that will assist with the final commercialization and registration of PPS as an OA pain treatment
- **Paradigm has completed on all the requisite components that Big Pharma require to execute a transaction**

Financial information	
Share price (08-March-2019)	A$1.35
Number of shares	140m
Number of Options	6.2m
Market capitalisation	**A$189m**
Cash (Dec 2018)	**~A$10m**

Top Shareholders	Shares (m)	%
Paul Rennie (Managing Director)	21.6	15.4%
Other Board and management	7.1	5.1%
Irwin Biotech *(technology vendor)*	6.3	4.5%
MJGD Nominees *(technology vendor)*	5.8	4.1%
J.P. Morgan Nominees Aust Pty Ltd	4.2	3.0%
Citicorp Nominees Pty Ltd	4.1	3.0%



SUCCESSFUL RE-PURPOSED DRUGS

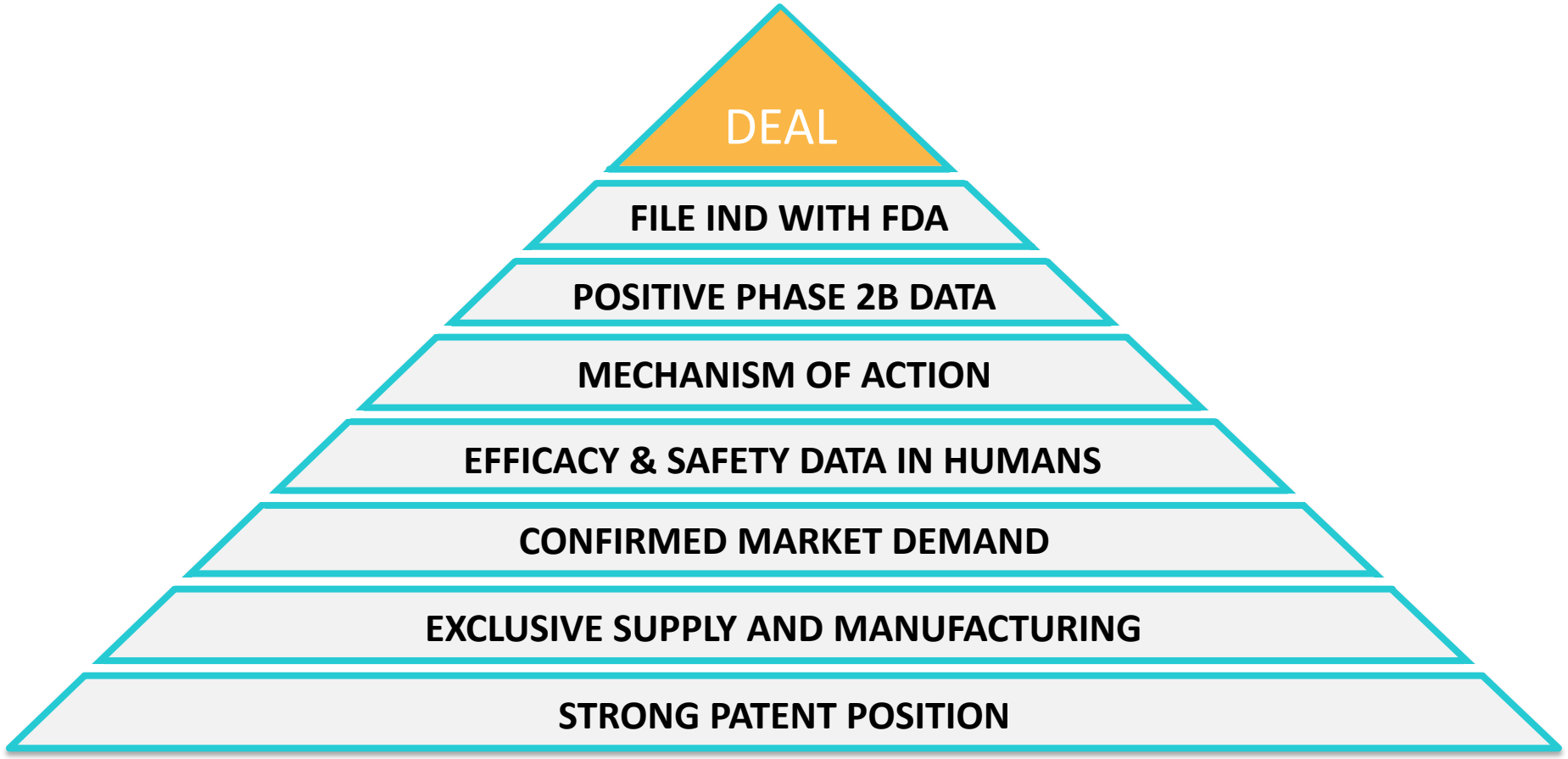
Re-purposed drugs have become true blockbusters

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

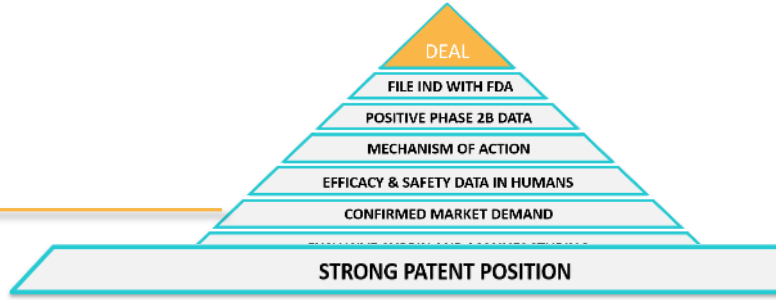
Source: Therapeutic Drug Repurposing, Repositioning and Rescue, Drug Discovery World Spring 2015; * Elmiron Use Patents ended in 2012, despite this no generic has been approved in US

FOUNDATIONS FOR SIGNIFICANT COMMERCIAL TRANSACTION

Paradigm is deal ready with all of the necessary 'building blocks' in place that a partnering pharmaceutical company would require to execute a transaction for OA



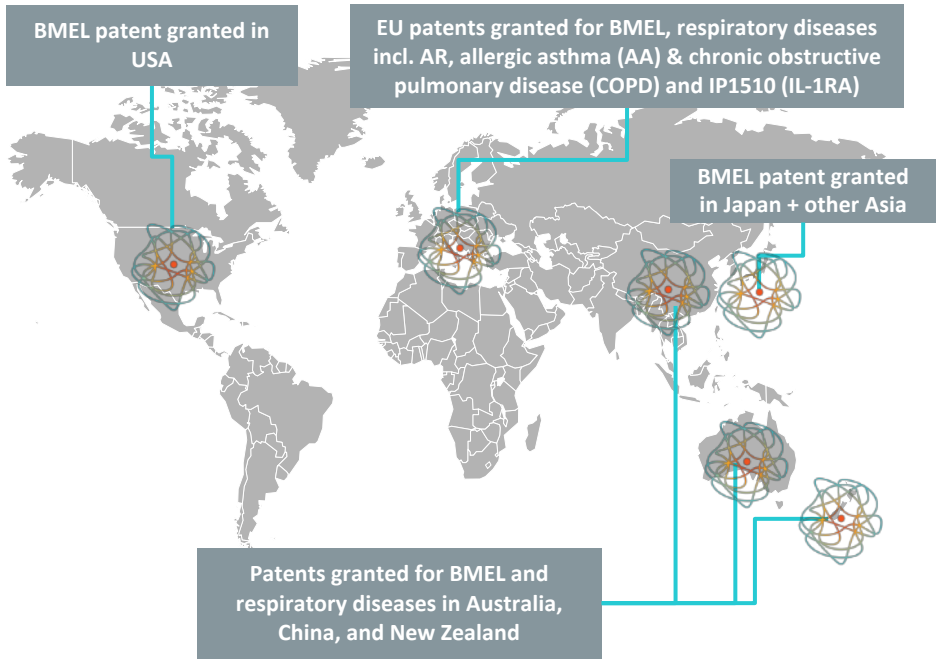
STRONG PATENTS & IP POSITION



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 - 2040**
- Established regulatory exclusivity and trademarks
- Patents for MPS (global ex Japan) + Orphan Status
- Patent applications for Ross River virus and Chikungunya virus
- Patent applications for osteoarthritis and concurrent BMEL
- Global patent for Heart Failure indication
- Prosecuting new patent applications

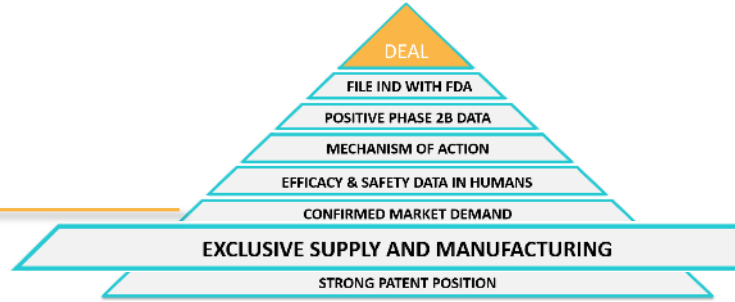


Secure **manufacturing** and supply

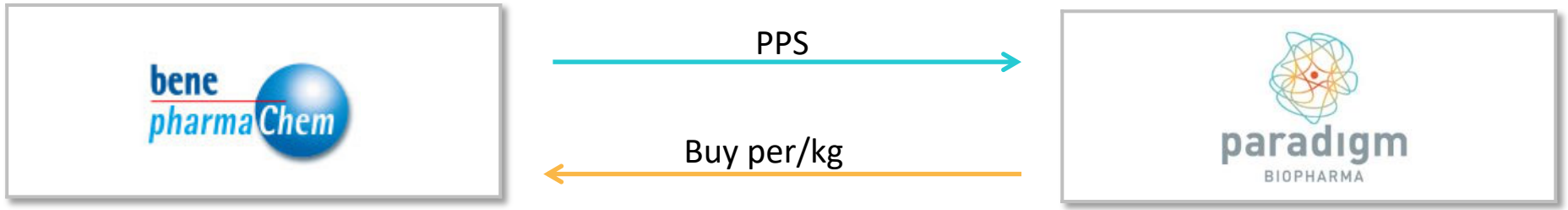
- Exclusive 20 year supply agreement with bene PharmaChem[1]
- bene pharmaChem makes the only FDA-approved form of PPS
- **Manufacturing methods are highly complex and a well kept trade secret**
- **bene pharmaChem has been exclusively supplying J&J for over 20 years or oral use**

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

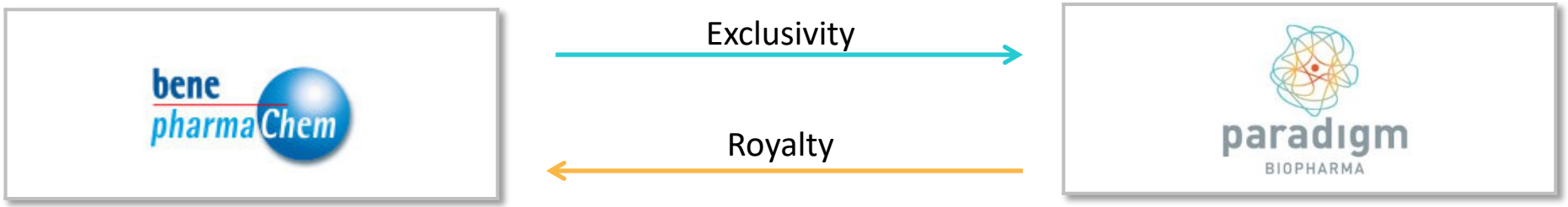
EXCLUSIVE SUPPLY & MANUFACTURING



Exclusive Supply

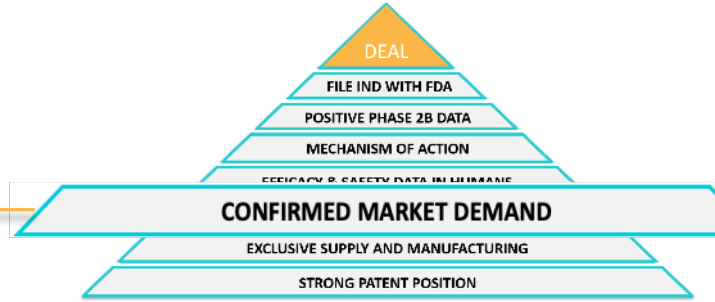


License



- **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
- Leading Big Pharma Co (J&J) source their PPS from bene.
- 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

MARKET DEMAND – OSTEOARTHRITIS WITH BMEL



Osteoarthritis - A blockbuster indication with no effective treatments

- **Blockbuster market -** Osteoarthritis is the most common form of arthritis, affecting over **31 million people** in the United States, with over 36 million outpatient visits and 750,000 hospitalisations p.a.[1]
- **No effective treatment –** ineffective NSAIDs and dangerous opioids are typical treatments
  - Current types of treatments under development have limited efficacy (Platelet-rich Plasma, Stem Cells, Viscosupplementation, Orthokine) and/or present significant adverse events (anti-NGFs)

Osteoarthritis and the link to Bone Marrow Edema Lesions (BMEL)

- **BMEL are commonly associated with OA** and have been **linked to early onset of OA** and joint cartilage degeneration. [2]
- BMEL sustains inflammation and the release of MMP's and ADAMTS-5 enzymes, causing cartilage degeneration
- iPPS promotes the resolution of the BMEL, **reducing inflammation and promoting joint health**

The established safety and clinically meaningful effect of iPPS combined with the strong demand via the TGA Special Access Scheme support iPPS as a commercial treatment

OA Market Facts:

Potential US market for iPPS:

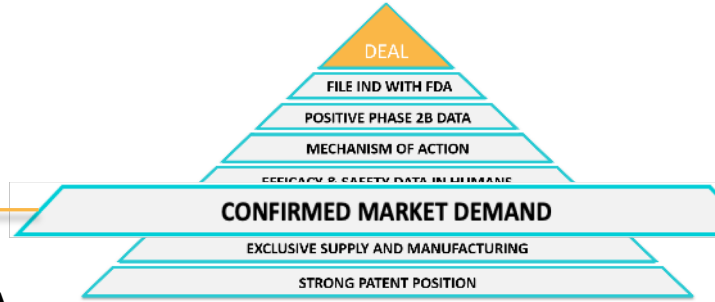
US$15bn[3]

Cost to US Economy:

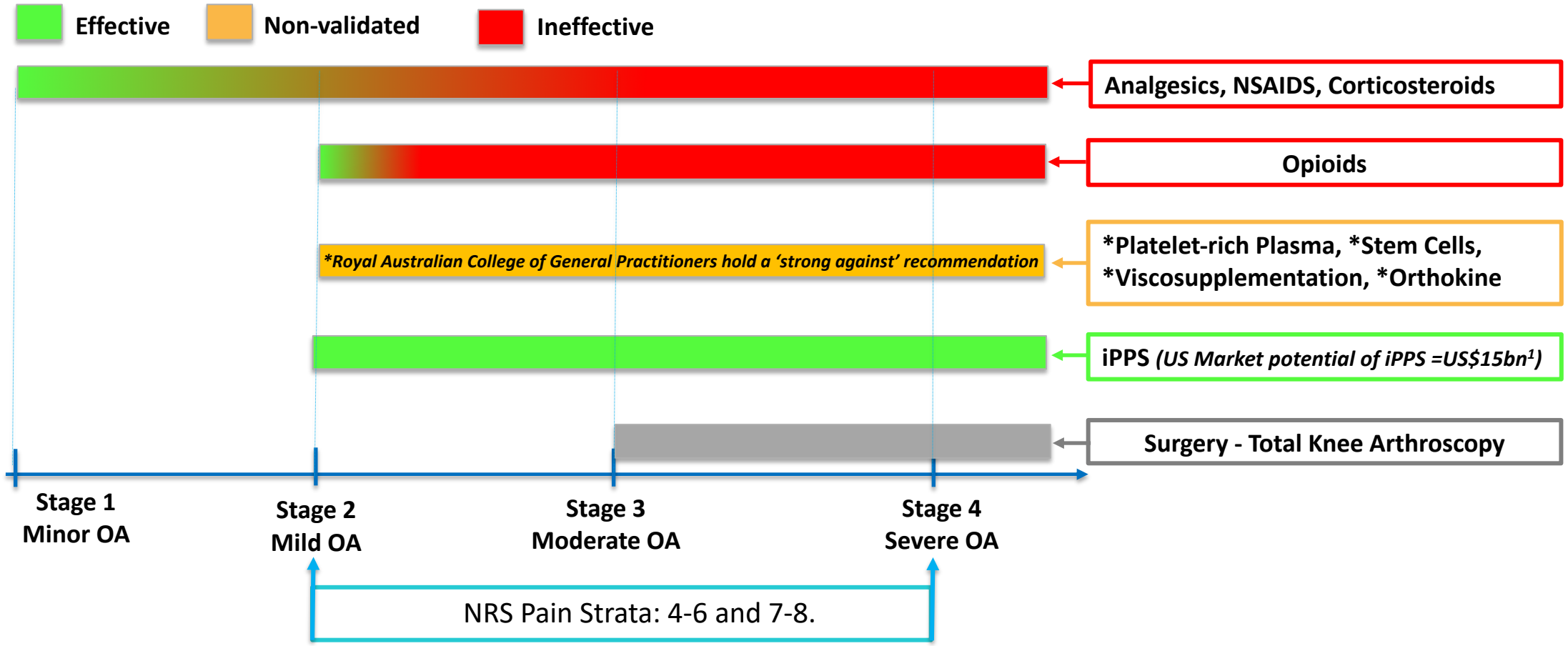
>US$128bn pa[4]

Source:
1. The occurrence and progression of BMELs 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. 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
4. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.

MARKET DEMAND – OA STAGES AND TREATMENTS

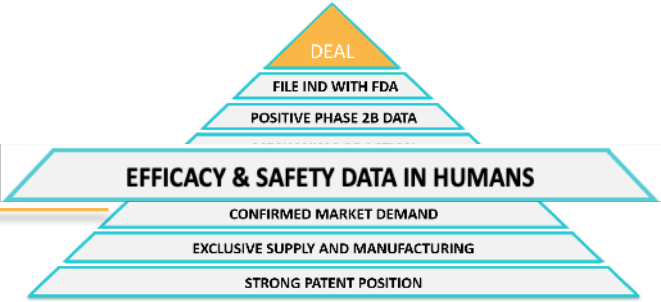


There are no effective treatments for Moderate to Severe OA



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

EFFICACY & SAFETY IN HUMANS – POSITIVE SAS DATA



TGA Special Access Scheme – Real World Evidence – 183 patients treated

All 183 patients reported on (median age of 56.4 years - range 18 to 84 years) had pain and failed current standard of care - analgesics, NSAIDs or corticosteroids.

At six weeks post PPS treatment:

Pain

- **162 out of 183 patients (88.5%)** showed a reduction in pain with the **average pain reduction** being **clinically meaningful at 51.4%** compared to pre-treatment

Function

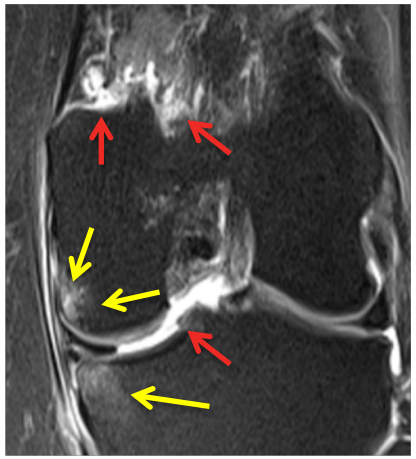
- **167 out of 183 patients (91.2%**) showed an **improvement in knee function** with the average improvement in knee function **being clinically meaningful at 60.8%** compared to pre-treatment function

Patient A MRI – Pre PPS Treatment

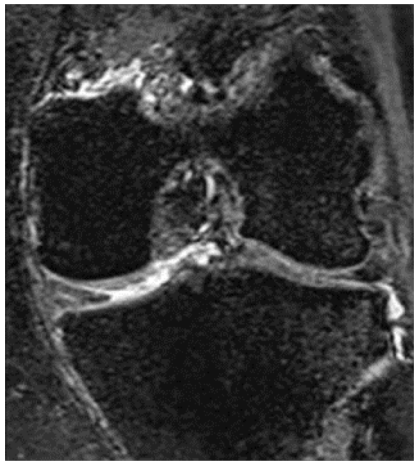
Pre treatment Scores

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

BME Lesions
Joint Space Effusions



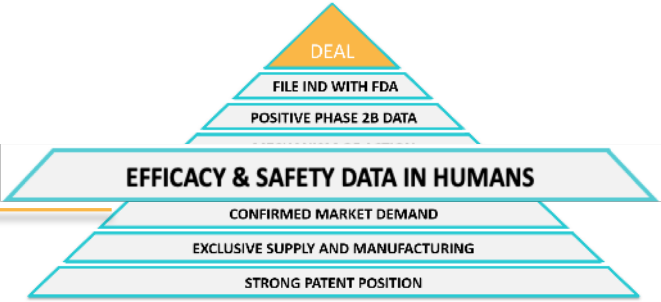
Patient A MRI – Post PPS Treatment



Post Treatment Results

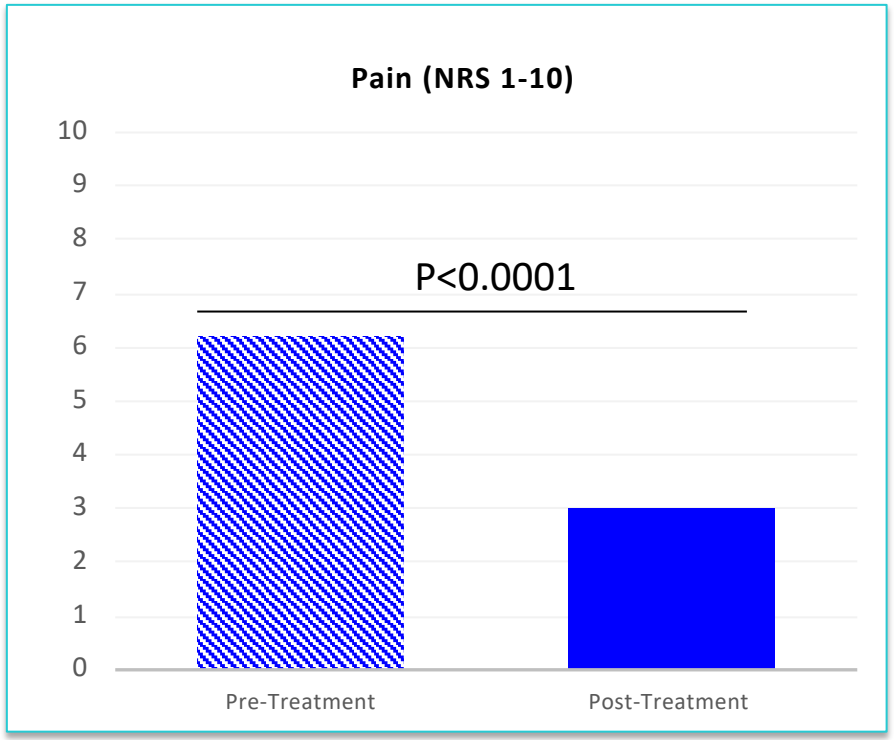
- **Complete resolution** of BMEL lesions and effusions
- Pain NRS = **0 (pain resolved)**
- Lysholm Score: **65 (Fair knee function)**

EFFICACY & SAFETY IN HUMANS – POSITIVE TGA SAS DATA



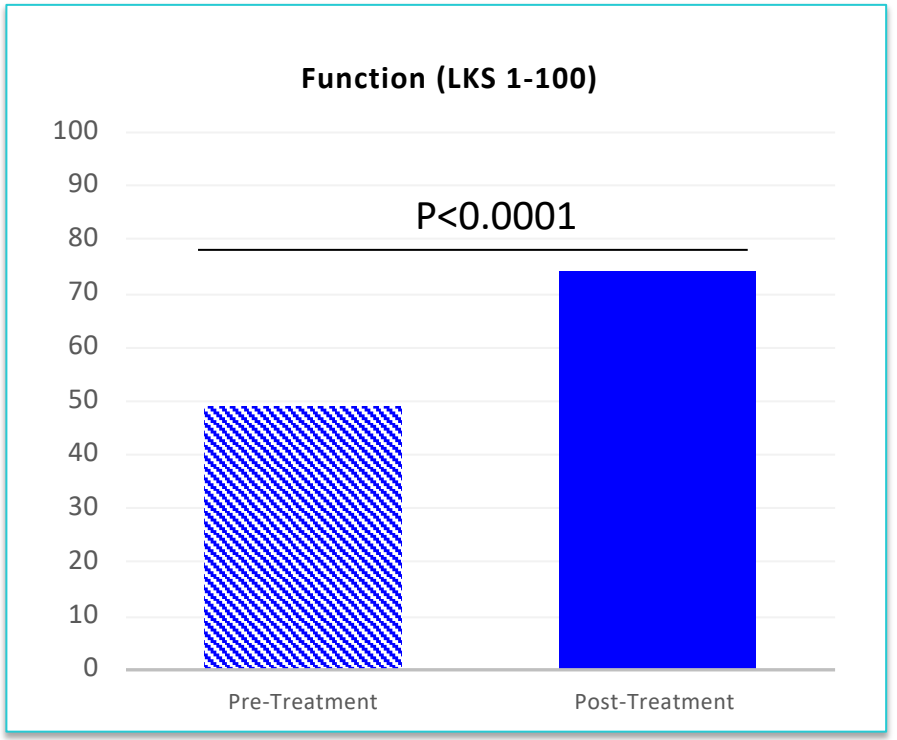
Pain (NRS) Before – After = 3.2 p<0.0001

51.4 % reduction in knee pain



Function (LKS) Before – After = 25.1 p<0.0001

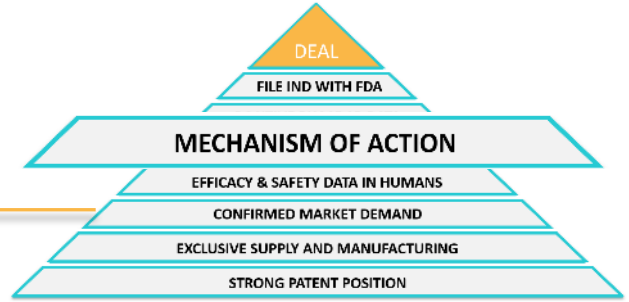
60.8% improvement in knee function



PPS's excellent and well known safety profile was re-confirmed by Paradigm in the treatment of 500+ TGA SAS Patients and 71 patients via PAR's Phase 2a BME and 2b OA clinical trials

***After = Results taken from patients six weeks post final treatment, i.e. twelve weeks (84 days) from first dose**

MECHANISM OF ACTION (MoA)



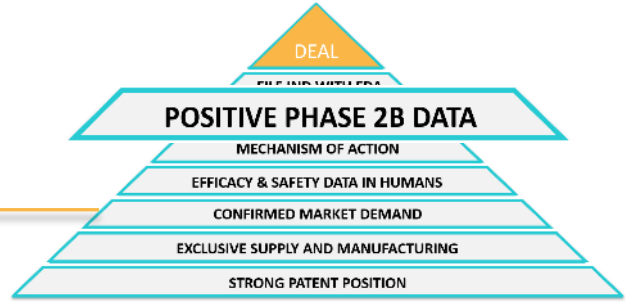
New Mechanism of Action – PPS role of in reducing pain

- Paradigm's has conducted a non-clinical study to demonstrate the pain reduction MoA of PPS
- The study is complete and the manuscript has been sent for **peer-review and publication**
- The manuscript is entitled: **"Human osteocyte expression of Nerve Growth Factor (NGF): the effect of Pentosan Polysulphate Sodium (PPS) and implications for pain associated with knee osteoarthritis"**
- Paradigm has registered patent protection on this new discovery and believe this further understanding around the MoA will be instrumental in the commercial development of PPS in OA and other indications
- Demonstrating that PPS can act to not only treat pain but reduce the effect and onset of OA is a medical breakthrough that gives paradigm strong commercial viability

Established Mechanism of Action - PPS role in joint structural improvement

- Appendix 3 reports the previously published Mechanism of Action (MoAs) of the drug, pentosan polysulfate sodium (PPS)

POSITIVE PHASE 2B OA/BMEL DATA



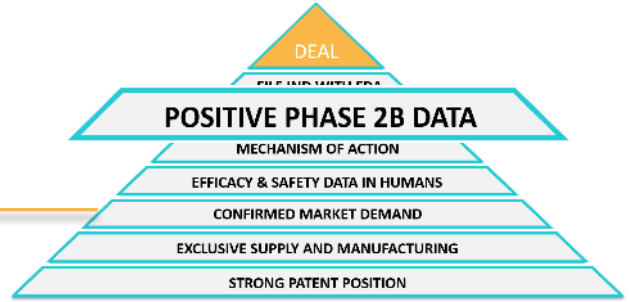
In its Phase 2b clinical trial Paradigm demonstrated clinical efficacy five different ways

- **Clinical trial met the primary endpoint with a change in the Knee Injury and Osteoarthritis Outcome Score (KOOS) from baseline. Clinical efficacy was demonstrated in five ways:**

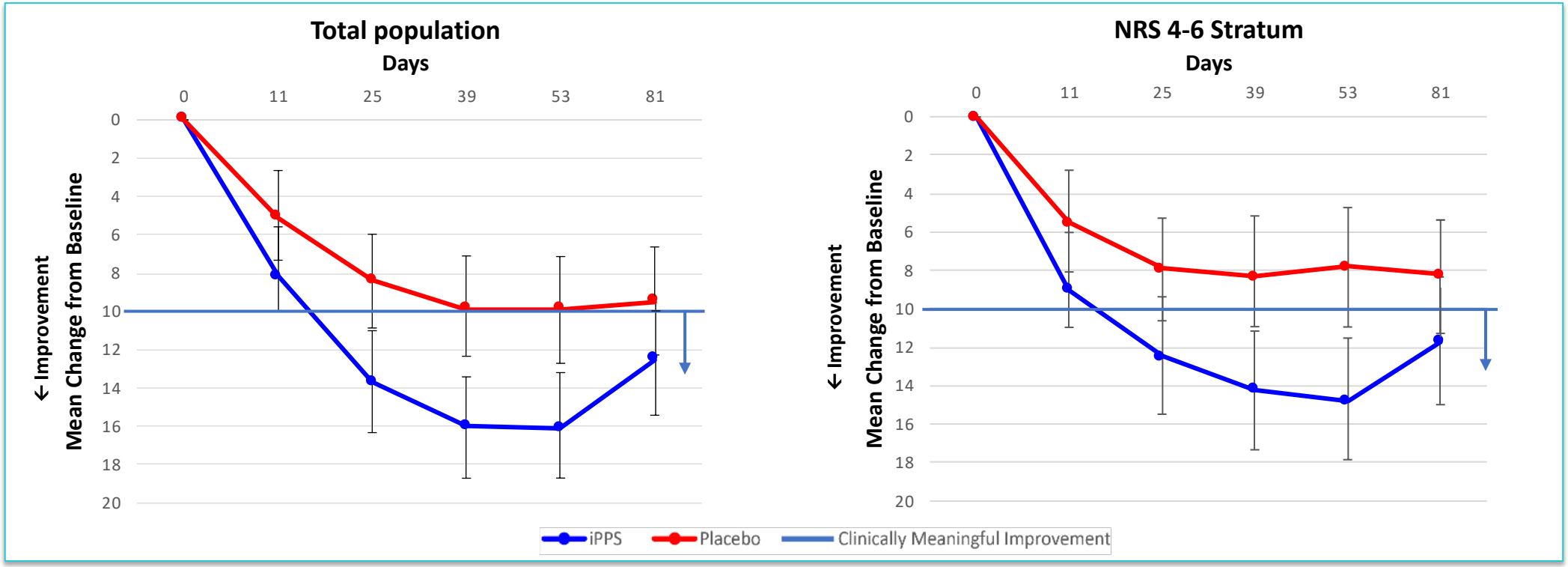
1. **A mean change from baseline greater than 10 on KOOS scale.** See chart on slide 15
2. **Mean percentage change from baseline in NRS pain.** See chart on slide 17;
3. **Number of trial subjects (both iPPS and Placebo) that had a greater than 50% reduction in KOOS Pain from baseline.** See chart on slide 16
4. **Number of trial subjects (both iPPS and Placebo) that had a greater than 50% reduction in NRS Pain from baseline.** See chart on slide 16.
5. **Patient Global Impression of Change (PGIC).** Note this is a secondary endpoint but it does measure clinical efficacy.

What is the PGIC? The self-reported measure Patient Global Impression of Change (**PGIC**) reflects a patient's belief about the efficacy of treatment. The PGIC is a standardized, self-reported tool that **measures** the change in a patient's overall status ranging from "very much improved" to "very much worse". **Participants in the Paradigm trial who were treated with the drug (iPPS) reported a very much improved efficacy which was highly statistically significant over placebo at p=0.0062.**

POSITIVE PHASE 2B OA/BMEL DATA

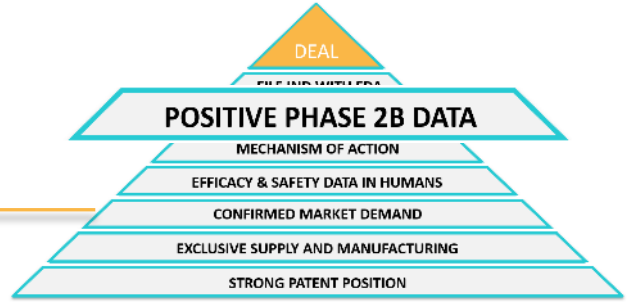


Mean Change in KOOS Pain From Baseline

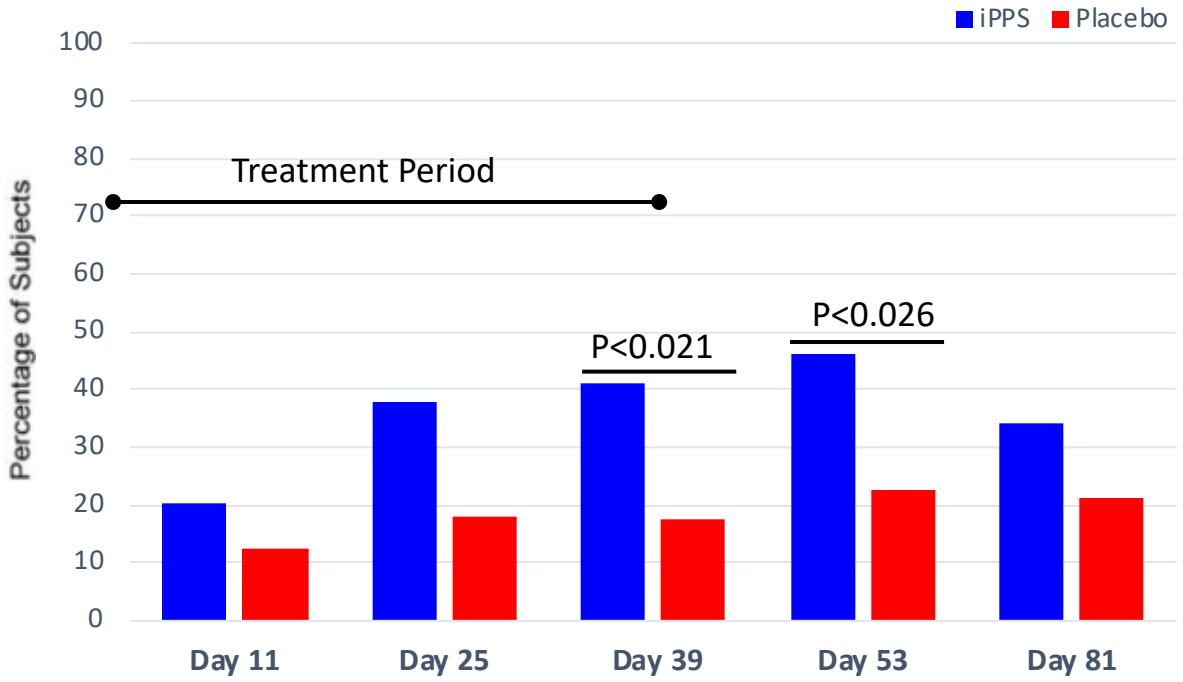


- In the **Total Population and NRS 4-6 Stratum** Paradigm demonstrated a statistically significant mean change in KOOS Pain from Baseline versus Placebo at day 39 and day 53
- **A mean change in KOOS Pain from Baseline greater than 10 is considered clinically meaningful** this was achieved the Total Population and NRS 4-6 Stratum from day 25 onward

POSITIVE PHASE 2B OA/BMEL DATA

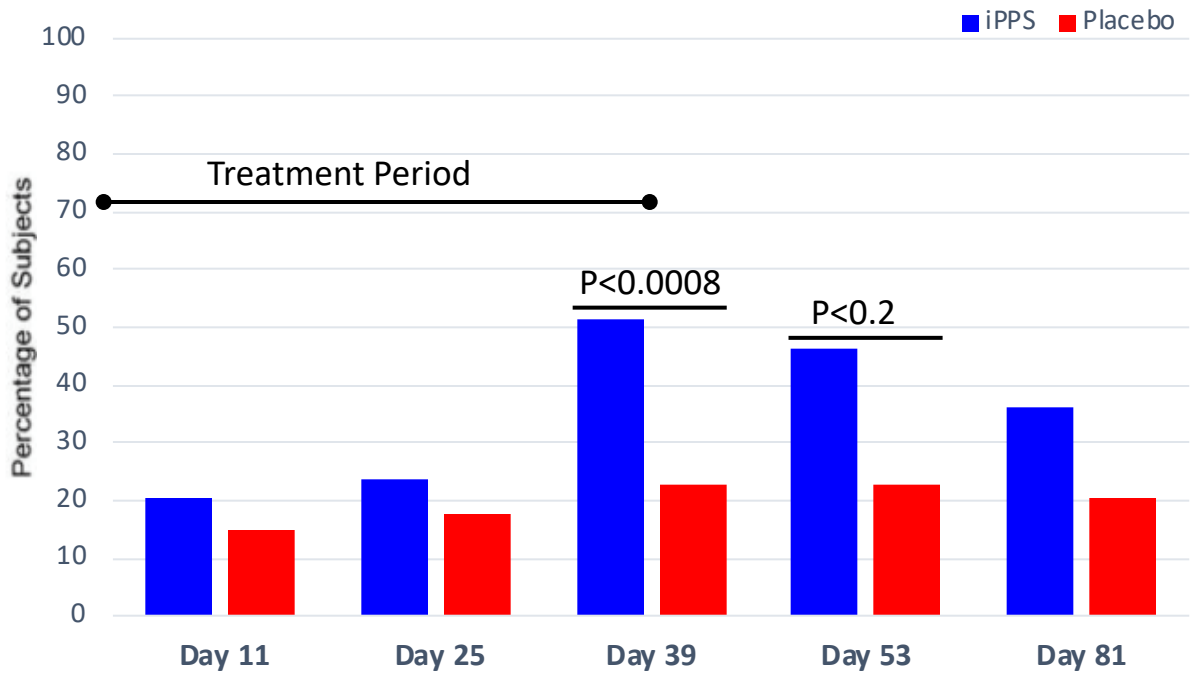


Number of Subjects with a >50% Reduction from Baseline in KOOS Pain Score at Days 11-81 – NRS: 4-6 Stratum



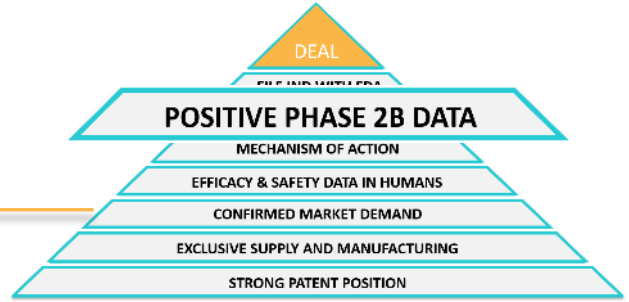
- Statistically greater proportions of subjects with >50% reductions in pain from Baseline after iPPS as measured by **KOOS Pain subscale** (chi-square analysis)
- >50% pain reduction corresponds to high reduction in pain (OARSI definition)

Number of subjects with a >50% Reduction from Baseline in NRS Pain Score at Days 11-81 – NRS:4-6 Stratum

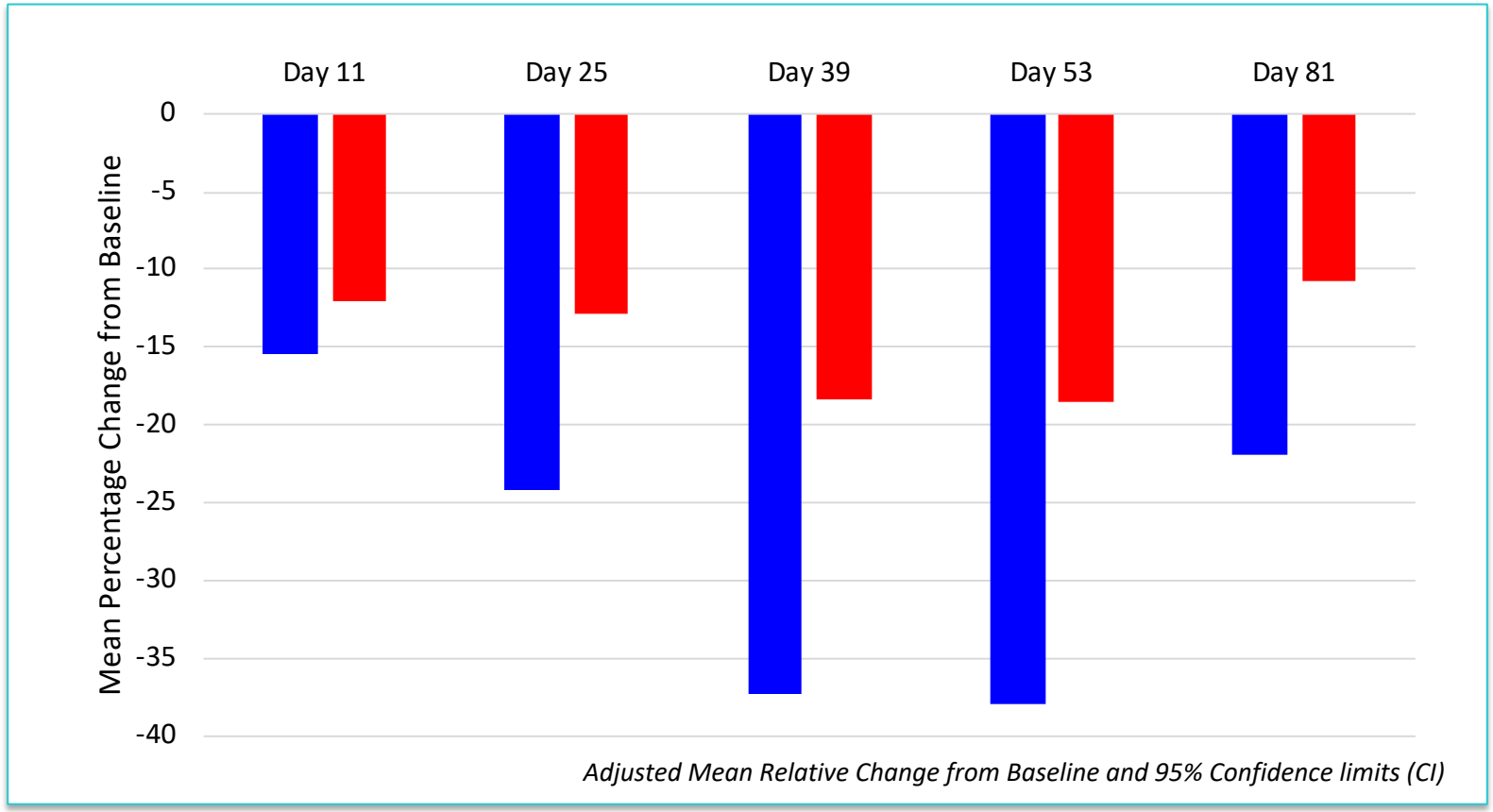


- Statistically greater proportions of subjects with >50% reductions in pain from Baseline after iPPS as measured **NRS pain score** (chi-square analysis)
- >50% pain reduction corresponds to high reduction in pain (OARSI)

POSITIVE PHASE 2B OA/BMEL DATA



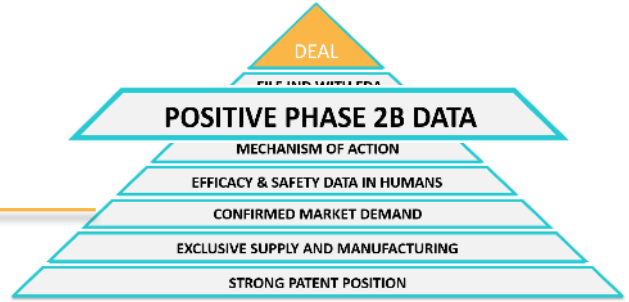
Mean Percentage Change in NRS Pain from Baseline – NRS:4-6 Stratum



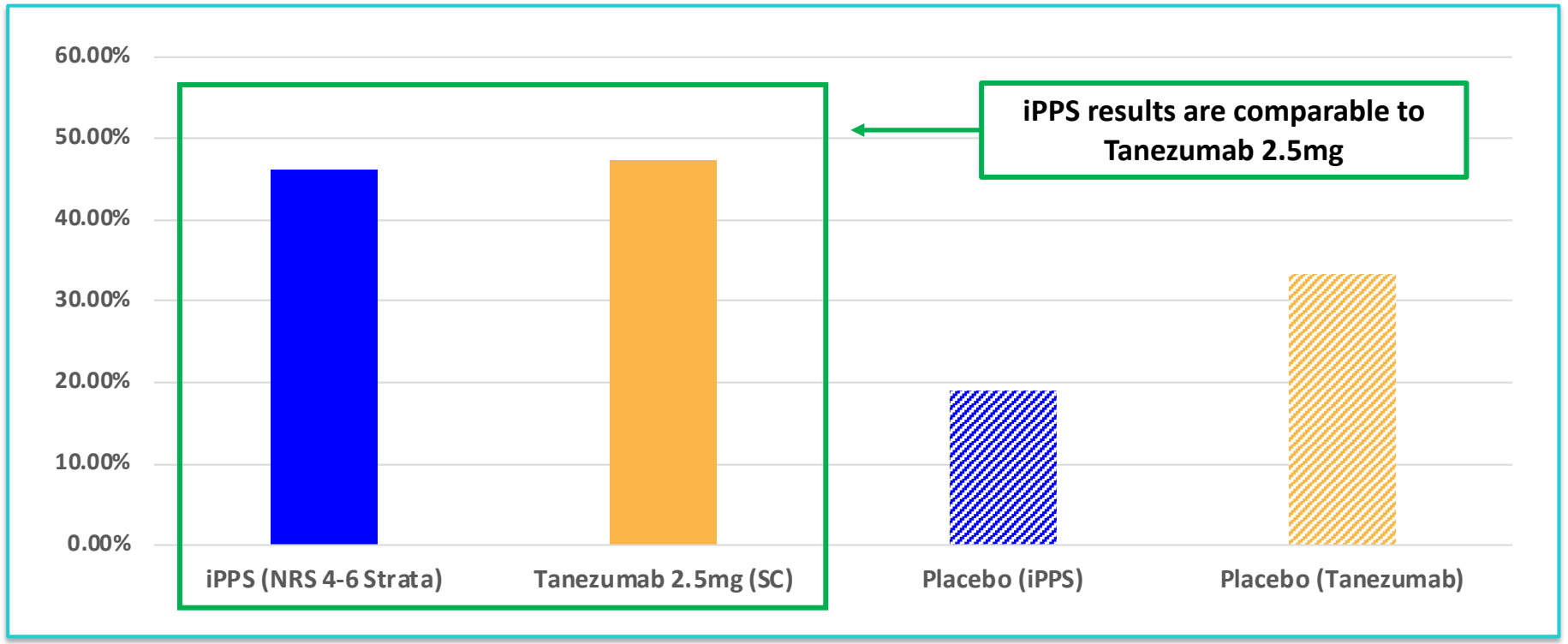
These data are consistent with the TGA SAS Results

- ***Day 39*** *PPS (**Blue**) vs Placebo (**Red**) p=0.028*
- ***Day 53*** *PPS (**Blue**) vs Placebo (**Red**) p=0.039*

IPPS VS TANEZUMAB (PFIZER/ELI LILLY - ANTI-NGF)



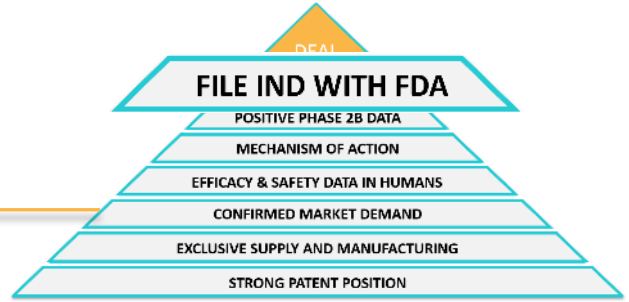
Percentage of subjects with >50% improvement in KOOS/WOMAC pain score at day 53



- iPPS results are comparable to Tanezumab 2.5mg (46.20% vs. 47.30%)
- Tanezumab clinical trials have been plagued by significant Adverse Events (rapidly progressive osteoarthritis and osteonecrosis (a loss of blood to the bone that causes the bone to die)
- iPPS has an excellent safety profile, established over the past 70 years

Results from Tanezumab Phase 2b OA Clinical Trial

FILING OF PIVOTAL STUDY WITH AGENCY (IND)



Filing of Investigative New Drug (IND) application with Regulatory Agency

- Preparation of Phase 3 Clinical Trial protocols
- Design Phase 3 Clinical Trial
- Meet with the FDA re trial design and end-points (pre-IND meeting)
- Incorporate FDA feedback (if any) into trial design

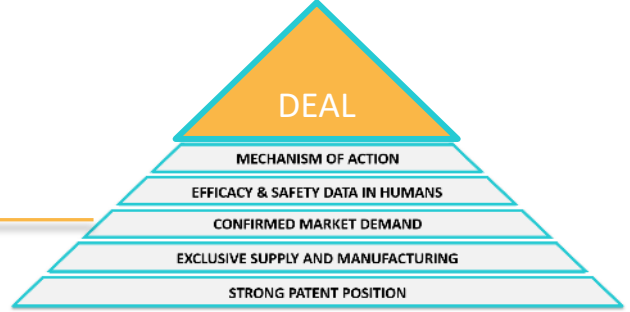
The IND application must contain information in three broad areas:

1. Animal Pharmacology and Toxicology Studies
2. Manufacturing Information (CMC & GMP)
3. Clinical Protocols and Investigator Information – soon to be achieved

- Lodge IND application with FDA
- FDA will generally respond within 30 days – if they do not the company are free to commence the clinical trial

Filing an IND and commencing the pivotal Phase 3 clinical trial is not required to execute a Pharma transaction but will often enhance transaction metrics when dealing with a US Pharma

DEALS – GLOBAL BIG PHARMA INTEREST IN OA



Safety Issues

Recent transactions highlight big pharma interest in OA

COMPANIES	COMPOUND	REGION	UPFRONT	TOTAL VALUE	STATUS
Pfizer / Lilly	Anti-NGF	Global	US$200m	US$1.8bn	Phase 3
REGENERON / teva	Anti-NGF	Global	US$250m	US$1.25bn	Phase 3
flexion / SANOFI	Corticosteroid	Global	Take-over*	US$1.0bn*	Commercialised
AMGEN / janssen	Anti-NGF	Global (ex Japan)	US$50m	US$435m	Discontinued
	GLOBAL AVERAGE		**US$166m**	**US$1.12bn**	
Galápagos / SERVIER	ADAMTS-5 Inhibitor	EU	Unknown	US$346m	Phase 1
TissueGene, Inc. Cell Technologies / Mitsubishi Tanabe Pharma	Gene therapy	Japan	US$24m**	US$434m**	Handed Back
TissueGene, Inc. Cell Technologies / mundipharma	Gene therapy	Japan	US$27m	US$591m	Phase 3
REGENERON / Mitsubishi Tanabe Pharma	Anti-NGF	Asia	US$55m	US$325m	Phase 3
	REGIONAL AVERAGE		**US$35m**	**US$424m**	

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

Rare Diseases – Deal Ready

LEADING MPS TREATMENTS

MPS presents a significant opportunity for Paradigm

	YEAR APPROVED	COMPANY AT APPROVAL	CONDITION	2017 REVENUES (USD MILLION)
Aldurazyme™	2003	BioMarin Pharmaceuticals	MPS I	$90.02[1]
Elaprase®	2006	Shire Pharmaceuticals	MPS II	$615.7
Naglazyme®	2005	BioMarin Pharmaceuticals	MPS VI	$332.2
VIMIZIM®	2014	BioMarin Pharmaceuticals	MS IVA	$413.3
Mepsevii™	2017	Ultragenyx Pharmaceuticals	MPS VII	$5.43[2]

The FDA attached further post-marketing requirements
1. The bulk of Aldurazyme® revenues are reported by its co-developer Sanofi-Genzyme, which were €207m (USD235.4m) in 2017
2. Q1 to Q3 FY18. Product only approved in November 2017
Source: Company SEC Filings

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)[1]

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

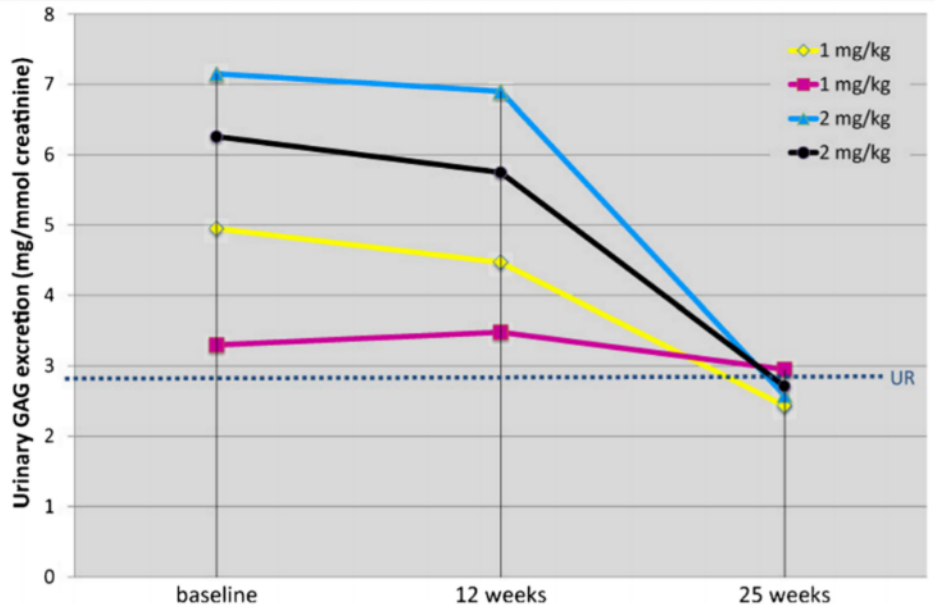
MPS RESULTS – PARADIGM/HENNERMANN ET AL.

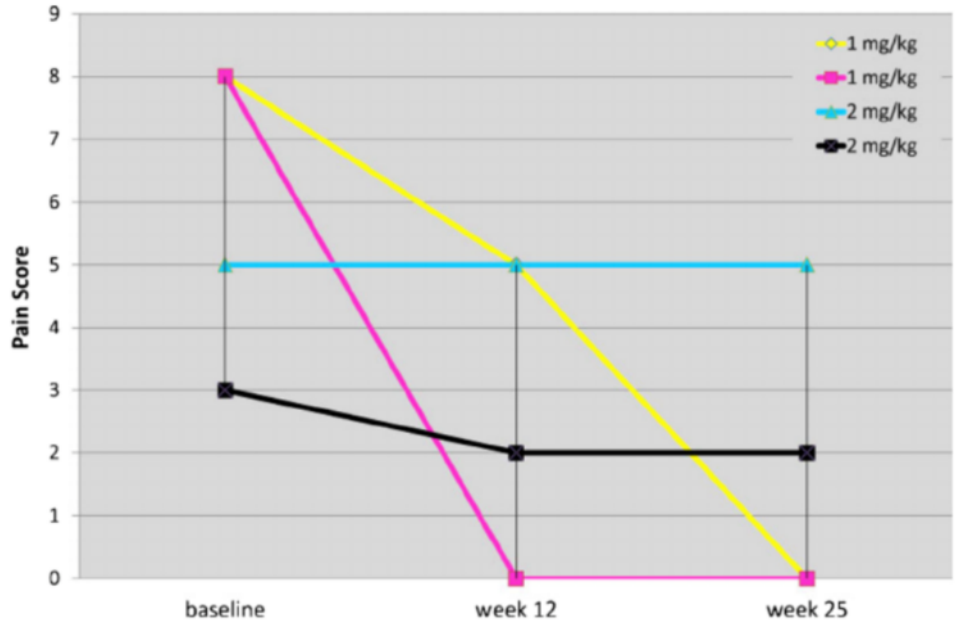
Paradigm acquired highly valuable Phase 2a clinical trial data

Type	Phase 2a – Open Label
Number of Patients	4
Dosing Range	1mg/kg – 2mg/kg
Treatment Length	24 Weeks

Primary Outcome	Safety
Secondary Outcomes	GAG levels
	Pain
	Mobility

Total Number of subject n=4.
(n=1 1mg/Kg Yellow), (n=1 1mg/Kg pink),(n=1 blue 2mg/Kg) and (n=1 2mg/Kg black)



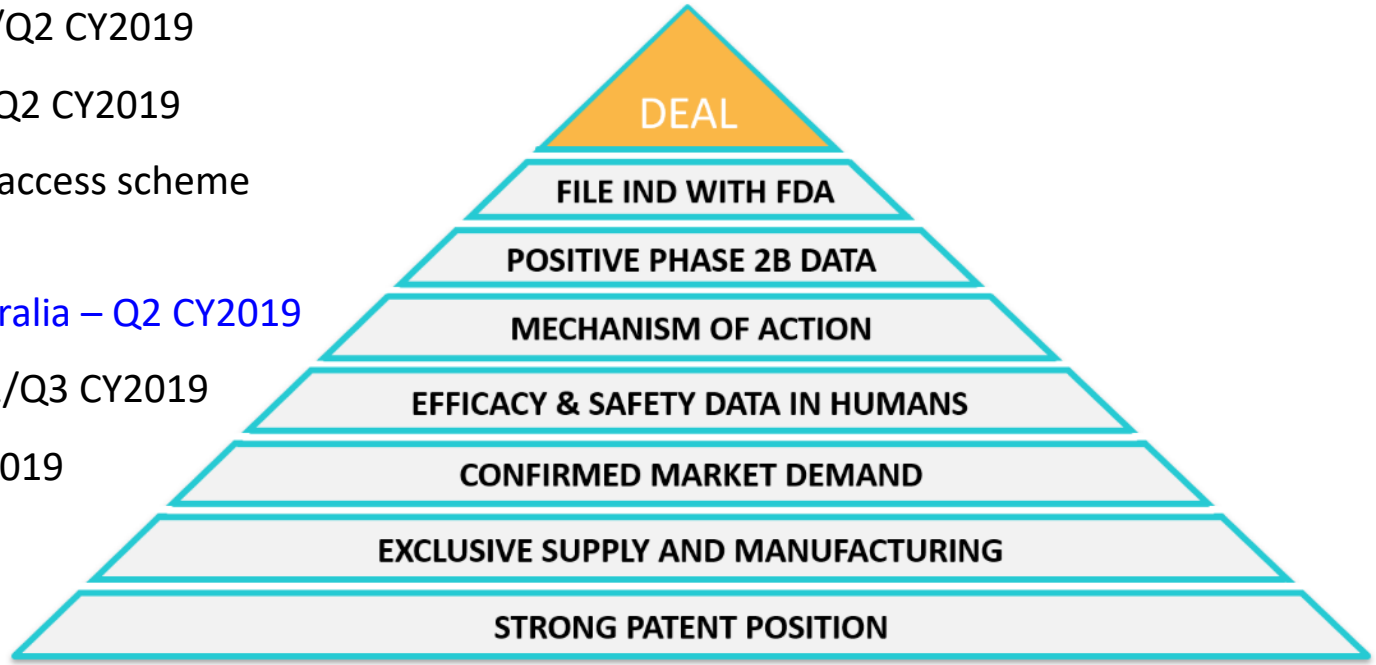


- MPS diseases are caused by a missing enzyme (α-L-iduronidase), which inhibits the body's ability to metabolise certain molecules called GAGs (Glycosaminoglycans). **The accumulation of GAGs causes inflammation that is akin to Osteoarthritis**
- **Trial Conclusion -** iPPS treatment was well tolerated (safe), resulting in a significant reduction of urinary GAG excretion and in an improvement of joint/mobility and pain above any beyond ongoing/existing ERT treatment.

POTENTIAL SHARE PRICE CATALYSTS / NEWS FLOW

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

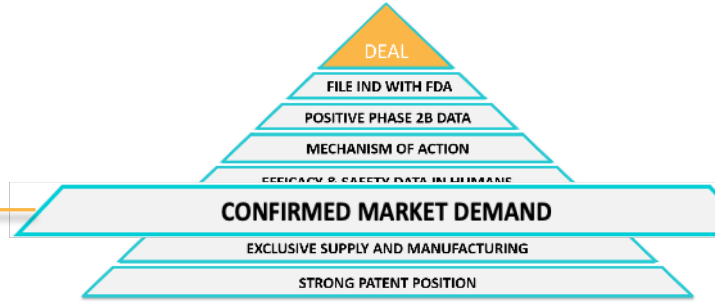
- OA Phase 2b trial results released. **Partnering Discussions Commenced**
- **Release Secondary End-point data front the OA Phase 2b trial** – Q1/Q2 2019
- **Potential to treat to MPS patients in Australia via the SAS** – Q1/Q2 CY2019
- **Up to 50 ex-NFL players in the US** to be treated with iPPS for OA pain - **Potential for significant media attention if treatment is successful** – Q1/Q2 CY2019
- **File IND for Phase 2/3 for Mucopolysaccharidosis (MPS)** - Q2 CY2019
- **Further release of patients OA data** under the TGA special access scheme throughout 2019
- **File TGA Provisional Approval** to sell ZILUSOL (iPPS) in Australia – Q2 CY2019
- **Ross River Phase 2a (safety study)** trial results release – Q2/Q3 CY2019
- **File IND and meet with FDA re Phase 3 trial in OA** - Q3 CY2019
- **Possibility of being granted "Fast Track status" for Phase 3 OA trial**



APPENDICES & ADDITIONAL INFORMATION

1. OPIOID EPIDEMIC
2. MECHANISM OF ACTION (MOA)
3. STAGES OF OA OF THE KNEE
4. MPS
5. VIRAL ARTHRITIS
6. CLINICAL PIPELINE
7. PEER COMPARISON
8. BOARD AND MANAGEMENT

1. MARKET DEMAND – OPIOID EPIDEMIC



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

- **Previous 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]

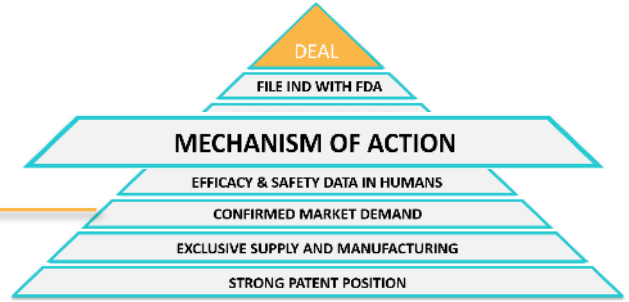
US$78.5 billion

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

Given PPS is non-addictive and possibly disease modifying, it may potentially receive FDA Fast-Track 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.

2. MECHANISM OF ACTION (MoA)



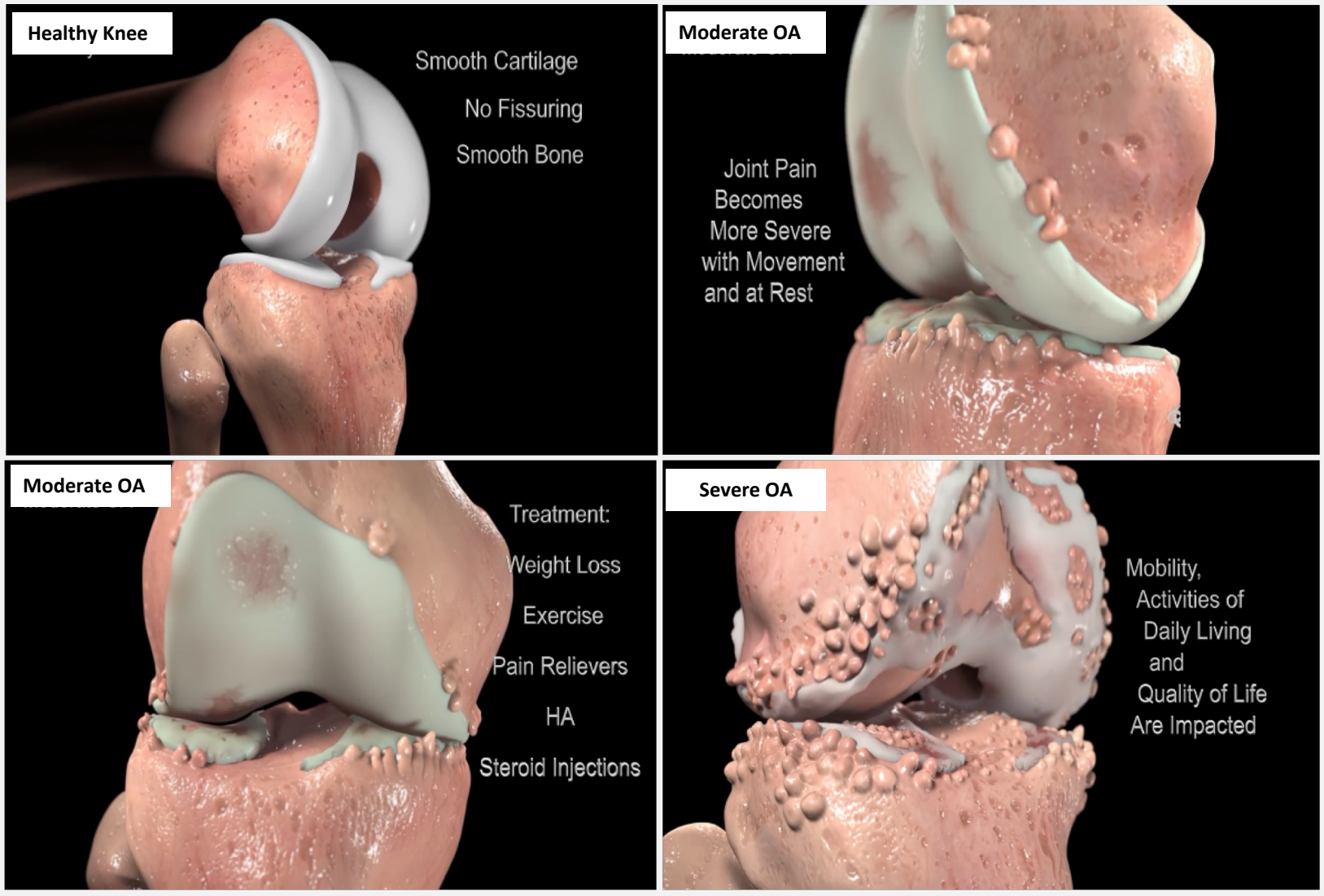
Mechanism of Action - PPS has demonstrated:

- The inhibition of cartilage degrading enzymes that are released post-acute injury;
- Anti-inflammatory effects, whilst blocking the effects of the pro-inflammatory cytokines TNF-alpha and IL-1;
- Antithrombic and antilipadaemic effects, which enhance micro-vascular circulation in the sub-chondral bone. Improving the micro-vascular circulation is believed to be a critical factor in resolving BMEL;
- ADAMTS-4, ADAMTS-5a and MMP-3 b inhibitor – Inhibition of these enzymes or reducing their levels by PPS prevents cartilage degradation in OA;
- **To be safe and well tolerated in patients** – 70 years safe use, >100m injections for DVT and >550 OA patients treated via TGA SAS and PAR clinical trials;

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

Paradigm is well advanced in proving PPS mechanism of action in relation to reducing the effect of Nerve Growth Factor (NGF) on KOA effected joint tissue – something that will be the subject of publication in an upcoming peer review publication.

3. STAGES OF OA – MINIMAL, MILD, MODERATE & SEVERE



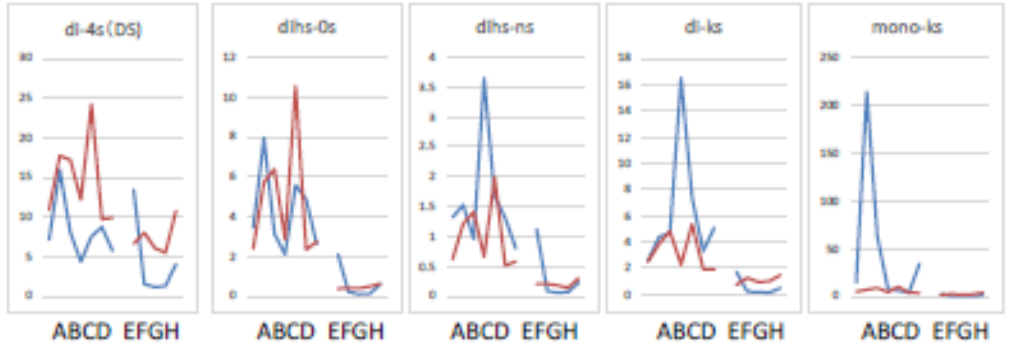
Source: Bioventus

4. MPS RESULTS – DR FURUJO

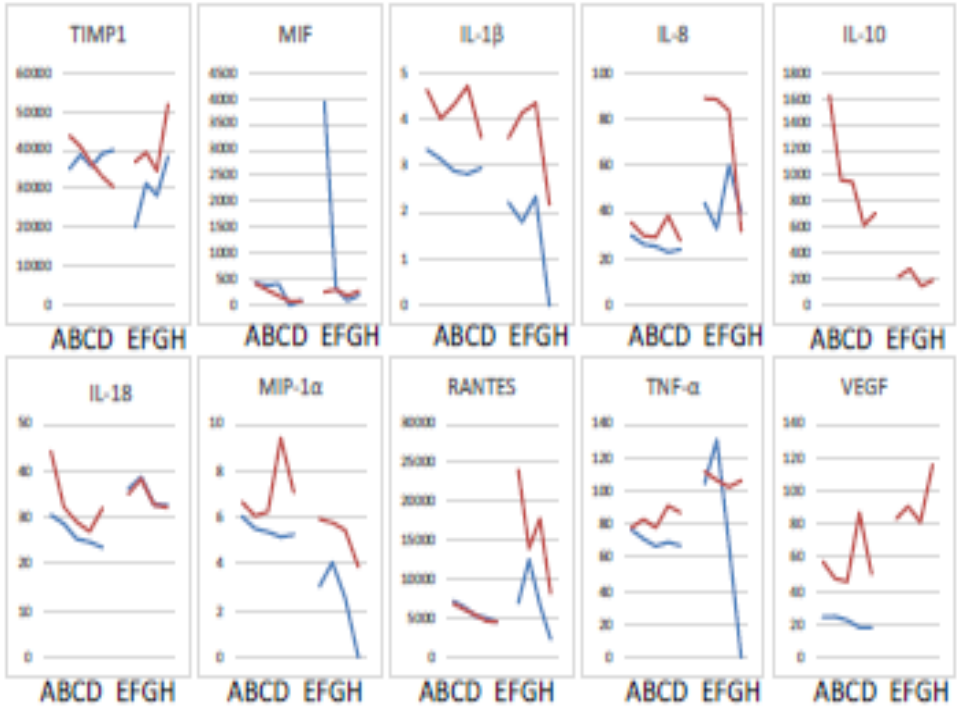
Paradigm's data supported by Dr Furujo's Findings

Type	Phase 2a – Open Label
Number of Patients	2
Dosing Range	0.5mg/kg – 1.5mg/kg
Treatment Length	17 Weeks
Primary Outcome	Safety
Secondary Outcomes	GAG & Inflammatory markers Pain Mobility

Urinary GAG Levels



Inflammatory Markers

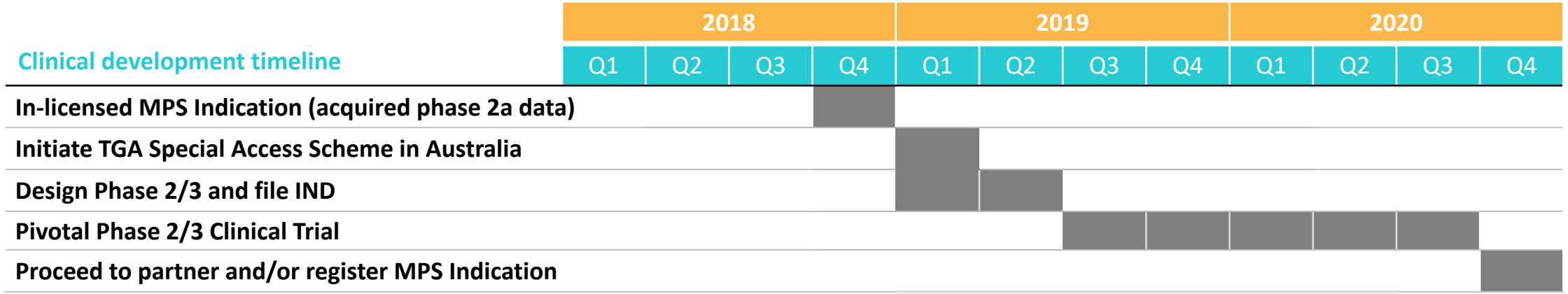


- **Trial Conclusion -** The preliminary findings of this open label study were encouraging, demonstrating a reduction in the inflammatory markers and urinary GAG levels with visible signs of improved joint function and pain reduction.
- Strong evidence that iPPS could be a very good adjunct (similar to combination) therapy for existing ERT treatments, enhancing the attractiveness of this program to large pharma companies currently serving the MPS market with ERT treatments, like BioMarin Pharmaceuticals (BMRN.NASDAQ,, Mkt Cap US$17bn).

4. MPS: CLINICAL TIMELINE

MPS - An Orphan Indication with near term commercialisation potential

- **Animal model data demonstrated** that PPS was able to reduce the levels of Glycosaminoglycans (GAGs) (accumulation of GAGs leads to joint pain and dysfunction) and inhibit inflammatory responses due to TLR-4 signaling by the accumulated GAGs.
- **Phase 2a open label data demonstrated** that PPS treatment was well tolerated (safe) and resulted in a significant reduction of urinary GAG excretion and in an improvement of joint and mobility and pain.
- **Paradigm to initiate treatment of MPS patients in Australia via the TGA Special Access Scheme in Q1 CY2019** (data to be released 3-6 months post initiation of treatment)
- **Paradigm plans to submit an IND application** to the US FDA for a pivotal Phase 2/3 MPS trial in Q2 CY2019.
- **Paradigm is confident that a single successful Phase 2/3 clinical trial will enable PPS to be registered as a treatment for certain MPS indications.**
- **MPS is classified as an Orphan Indication/Designation in the US and EU,** which will accelerate the regulatory approval process and provide a minimum 7 years (10 for EU) market exclusivity.



4. MPS, RARE DISEASES AND ORPHAN DRUGS

- **7,000+ rare diseases** (defined as conditions that affect fewer than 200,000 Americans)
- The **1983 Orphan Drug Act in the US,** and other such laws internationally incentivise pharmaceutical companies to develop medicines for rare diseases – "orphan drugs" – that would otherwise not be commercially viable.
- The **incentives on offer** include:
  - **Seven years of market exclusivity in the US**, and ten years in Europe (which may be further extended for paediatric use);
  - **Reduced or waived regulatory fees and tax credit**;
  - an opportunity **to generate clinical safety and efficacy data on limited number of subjects per trial** (some pivotal clinical trials have less than 50 subjects and cost a fraction of typical trials); and
  - **Full cost of treatment covered** by PBS (Aust), NHS (UK) and US Insurers/Govt

Pharmaceutical companies with marketing authorization for orphan products are more profitable than those without.

"large pharmaceutical firms watched smaller drug-makers develop drugs for orphan diseases that reached hundreds of millions or even billions in sales and followed suit". In 2011, for example, pharma giant Sanofi-Aventis paid US$20 billion to buy orphan drug maker Genzyme"

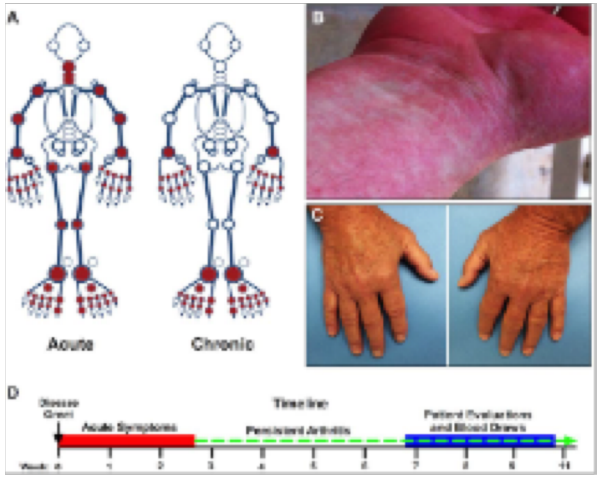
Source: http://theconversation.com/how-pharmaceutical-companies-profit-from-drugs-for-rare-diseases-

5. VIRAL ARTHRITIS - ALPHAVIRUS

No approved treatment for severely debilitating viral infection

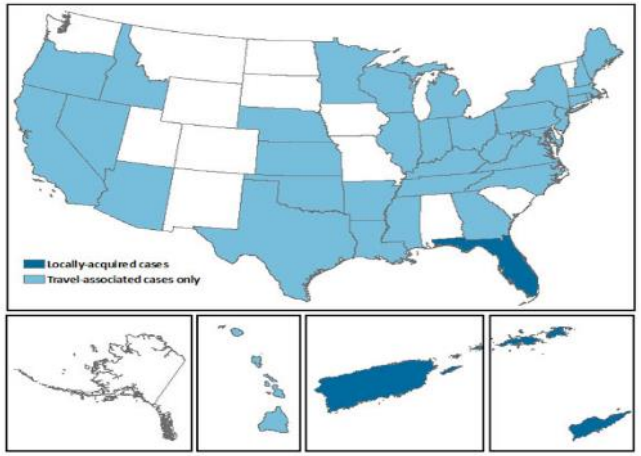
Viral Arthritis

- 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



Chikungunya cases ,USA

5. 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 (safety study) treating RRV induced arthritis and arthralgia **– 100% recruited – Read-out Q2 CY2019**
  - Phase 2 clinical trial in CHIKV-induced arthritis and arthralgia to be initiated post RRV read-out

	2018				2019				2019			
Clinical development timeline	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Proof of concept study under SAS (n=30)	Completed CY2016											
Phase 2a Clinical Trial Ross River (n=20)												
Plan for a Phase 2 Clinical Trial - Chikungunya												

6. 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	▪ Heart 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

7. 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
BIOMARIN	BMRN.NASDAQ	~23.4Bn	World leader in developing and commercializing innovative biopharmaceuticals for rare diseases driven by genetic causes. 7 drugs in market. Leader in ERT for MPS diseases.	7 Drugs in market/commercialisation	US$5.0Bn+
flexion Transformative Medicine... Where It Matters	FLXN.NASDAQ	704	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.	In market/Commercialisation	US$4.6Bn+ (~7.8m ppl receiving IA corticosteroid injections in USA)
AXSOME THERAPEUTICS	AXSM.NASDAQ	384	Developing novel therapies for the management of central nervous system disorders, focusing on treatment of BMEL	Phase III	US$2.5Bn+[2]
Medical Developments International	MVP.ASX	280	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+
paradigm BIOPHARMA	PAR.ASX	189	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, entering Phase III/II	US$37Bn+[4]

Source: Bloomberg, company filings

1. Market data as at 08 March 2019, exchange rates of AUDGBP 0.56 and AUDUSD 0.70 **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)

8. 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)

THANK YOU