PARADIGM BIOPHARMA

41st Annual J.P. Morgan Healthcare Conference

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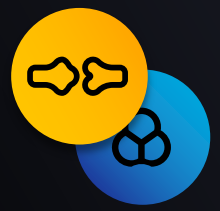
About Paradigm

Paradigm Biopharmaceuticals Ltd is an Australian public company founded in 2014 that listed on the Australian Stock Exchange (PAR.ASX) in 2015.

SAS – Special Access Scheme
EAP – Expanded Access Program
ADL – Activities of Daily Living
PGIC – Patient Global Impression of Change

Proven Molecule



Lead Programs

Established Safety & Efficacy

Pentosan polysulfate sodium for subcutaneous use (PPS, iPPS)

- PPS is a **non-opioid** with a 60-year track record treating pain, inflammation, and thrombosis in humans.

Osteoarthritis (OA) ZILOSUL®

- Zilosul® is a **phase 3 asset** being studied to treat pain & function, inflammation, and cartilage degeneration in OA.
- OA program granted FDA Fast Track.
- Globally harmonised protocol to secure simultaneous approval in all key jurisdictions.

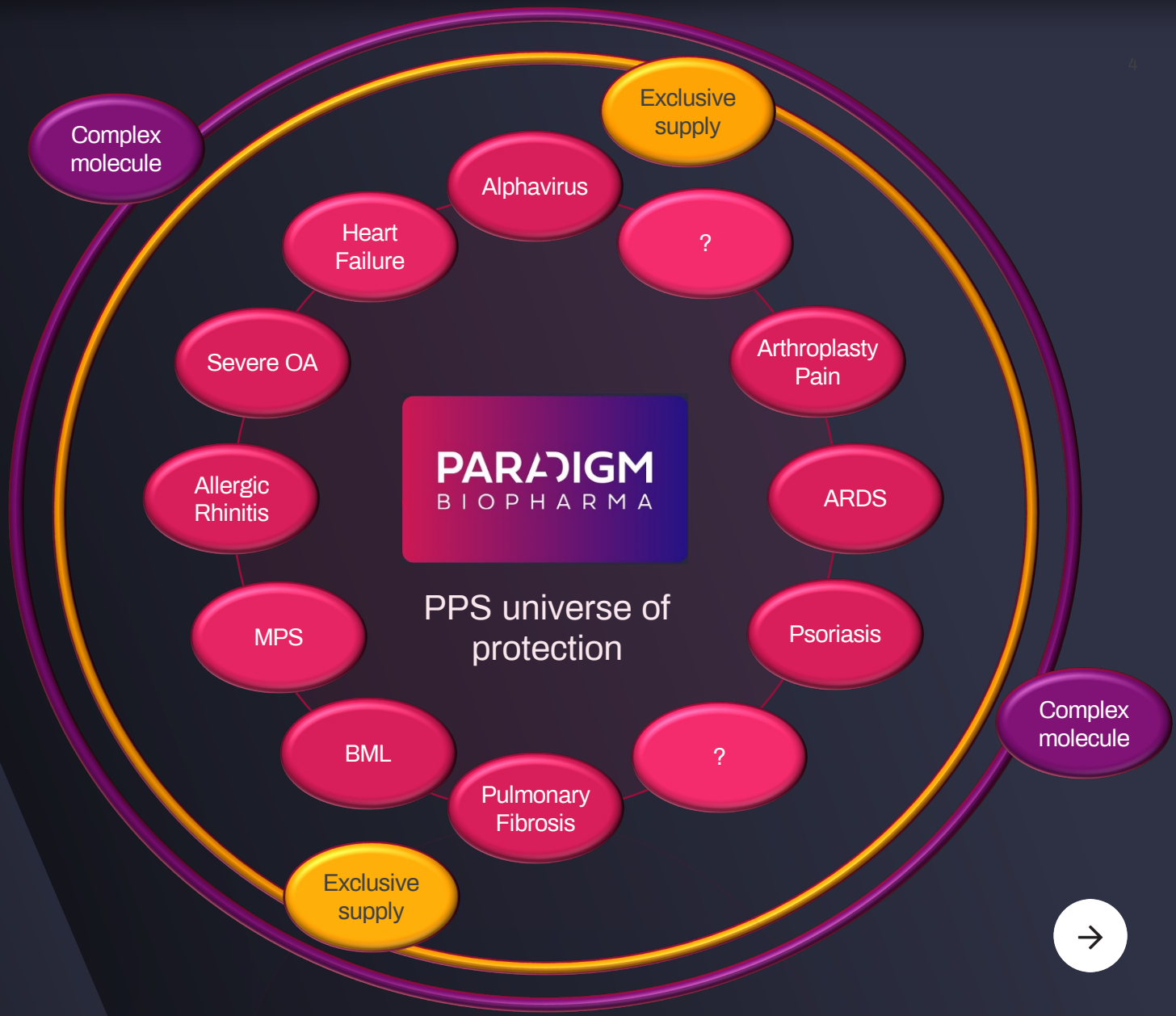
Mucopolysaccharidosis (MPS I & VI)

- Phase 2 asset in ultra rare disease.
- PPS has demonstrated potential to treat residual musculoskeletal symptoms in MPS as adjunct to standard of care therapy.

- Phase 2 OA trial provided encouraging evidence of **meaningful treatment effects** compared to placebo overall for pain, ADL, and PGIC.
- Real world evidence with 700+ OA patients treated via SAS in Australia and EAP in the US.

Extensive market protection

- Molecular platform technology and a complex trade-secret manufacturing process make it extremely difficult to replicate.
- The starting material is extracted from a plant-based biological source and then chemically modified using a multi-step manufacturing process.
- Exclusive supply for 25-years post marketing and ongoing development agreements with the originator and the only FDA-approved API manufacturer for human use.
- Multiple method of use patents, continually refined and expanded with additional patents being pursued.



Recent Company Milestones

Osteoarthritis (OA)

- IND open for phase 3 clinical trial and Fast Track Designation granted by US FDA.
- Actively screening and enrolling participants in US, AU, UK, CAN.
- Phase 2 disease modifying OA data accepted for presentation at OARSI World Congress 2023.
- Positive top-line results in phase 2 trial exploring disease modifying potential of iPPS.

Mucopolysaccharidosis (MPS)

MPS VI

- Phase 2 clinical trial nearing complete enrolment evaluating the safety and tolerability of iPPS compared to placebo (2:1).

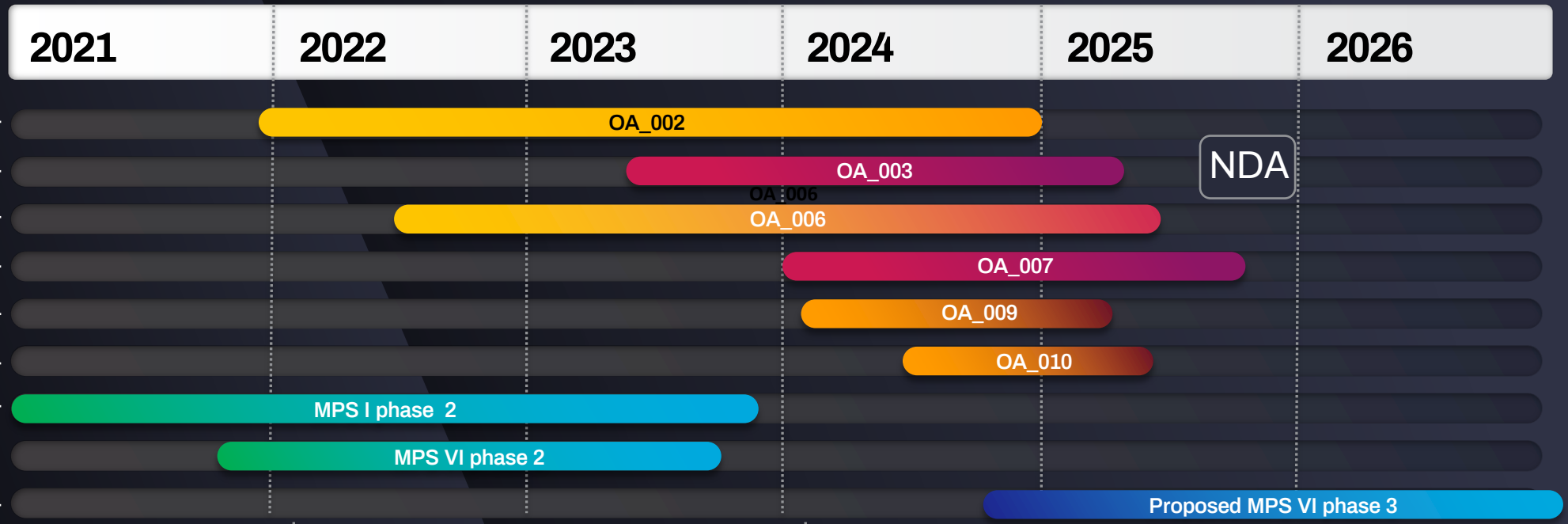
MPS I

- Presentation of interim 6-month data at the International Congress of Inborn Errors of Metabolism.

Company

- Additional IP protection with patent acceptance in the US to 2043.
- Partnership with NFL Alumni Health.
- Actively engaged in discussions with potential partners.

Lead Programs



002	OA NDA Pivotal	First subjects randomised Q4 2021, dose selection 1H CY2023
003	OA NDA Confirmatory	First subject randomised 1H CY2023
006 / 007	OA Establish durability of effect	Observational follow-up of pivotal and confirmatory studies
009	OA Retreatment	Timelines will be confirmed following dose selection Data will be incorporated into OA pain and function NDA
010	Establish safety and efficacy in Hip OA	
MPS I	Establish safety and efficacy in MPS I	Primary endpoint readout 2H 2023
MPS VI phase 2	Establish safety and efficacy in MPS VI	Primary endpoint readout 2H 2023
MPS VI phase 3	NDA Pivotal	TBA

** Timelines based on enrolment projections. May be subject to change.

Osteoarthritis

OA

Blockbuster market opportunity

Zilosul® aims to meet a significant unmet need in osteoarthritis.

Market size potential US$10B+ p.a.[4]

People affected by OA in 2020[3]

72m+

People affected by OA by 2030[3]

120m+

Markets: US, EU5, Canada and Australia.

In the US alone, OA is predicted to increase by 86% to 67 million by 2030.[3]

Knee and Hip (Global)

69% of all OA

OA patients dissatisfied with current treatments[1]

81%

Target uptake: 10% dissatisfied market[1]

Zilosul® indicative price: US$2500 per year[2]

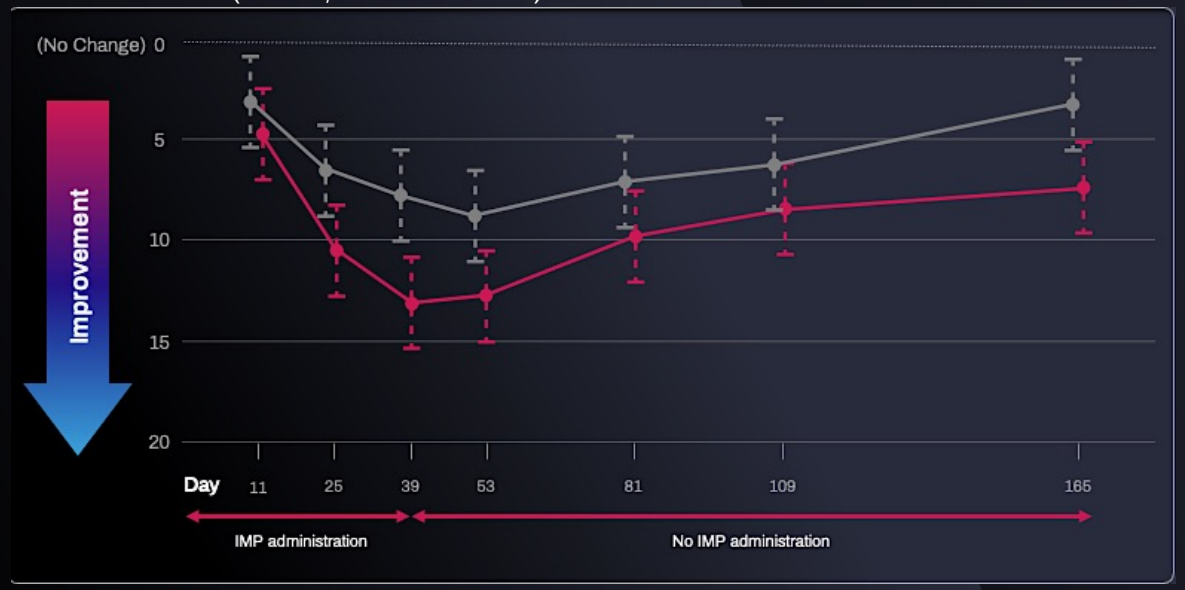
1. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.
2. Global Pricing Research conducted by Paradigm. EU5: Germany, UK, Spain, France, Italy
3. OARSI. Osteoarthritis: A Serious Disease, Submitted to the U.S. Food and Drug Administration December 1, 2016
4. Calculation based on 10% penetration dissatisfied patients with knee and hip OA in the 72m addressable market, at price of US$2500.

Phase 2b – PARA_OA_005 Results

PHASE 2B CONTROLLED STUDY CONDUCTED TO SUPPORT PARADIGM'S PHASE 3 OA PROGRAM

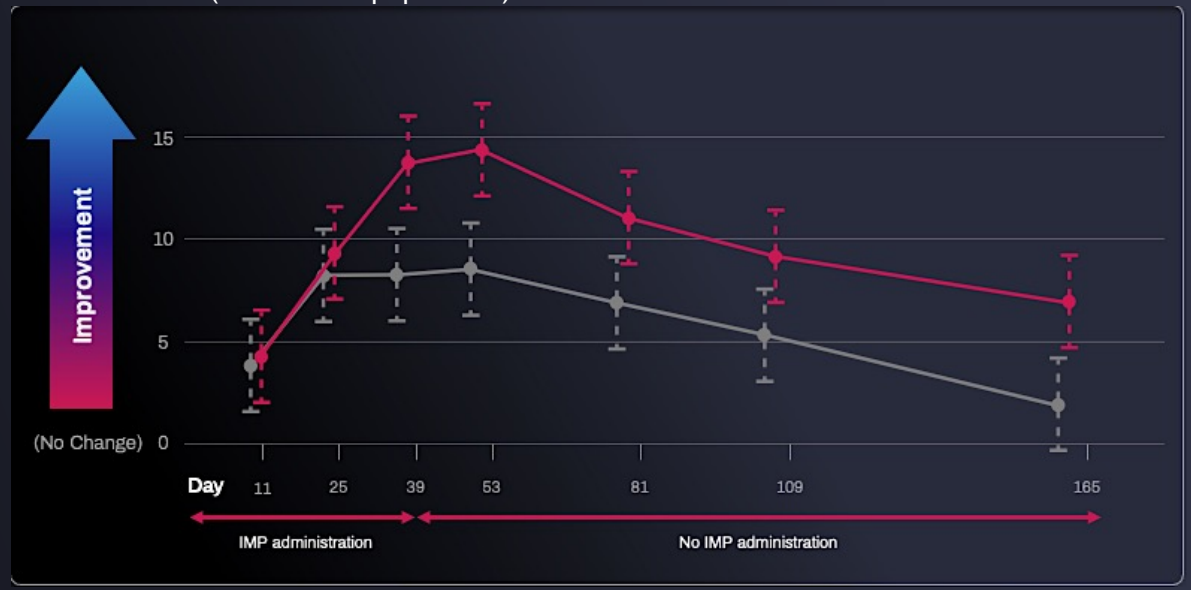
1 Pain Reduction (KOOS)

Adjusted mean change from baseline to days 11, 25, 39, 53, 81, 109, and 165. (N=112, 1:1 randomised)



2 KOOS Function (ADL)

Adjusted mean change from baseline to days 11, 25, 39, 53, 81, 109, and 165 (overall FAS population)

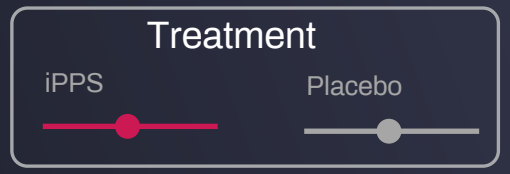


LS mean change +/- standard error

FAS = Full analysis set

Patient Global Impression of Change (PGIC)

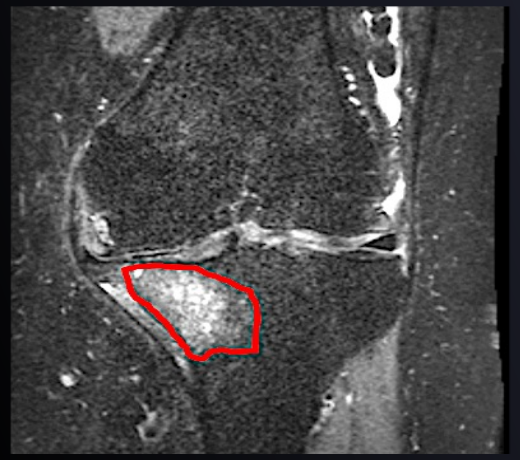
- Mean PGIC significantly higher in the iPPS group than placebo group at day 53 (4.42 versus 3.42, respectively; mean difference between iPPS and placebo 1.0 [95% CI 0.24, 1.8]; p=0.0106).



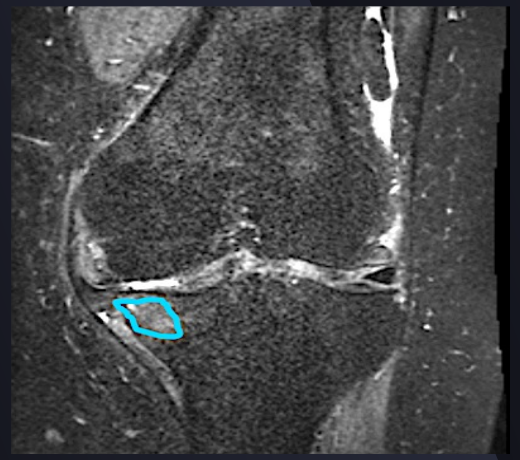
Phase 2b – PARA_OA_005 Results

- iPPS 2mg/kg SC twice weekly vs placebo.
- iPPS showed significant reduction in **bone marrow lesion** size as compared with placebo controls.

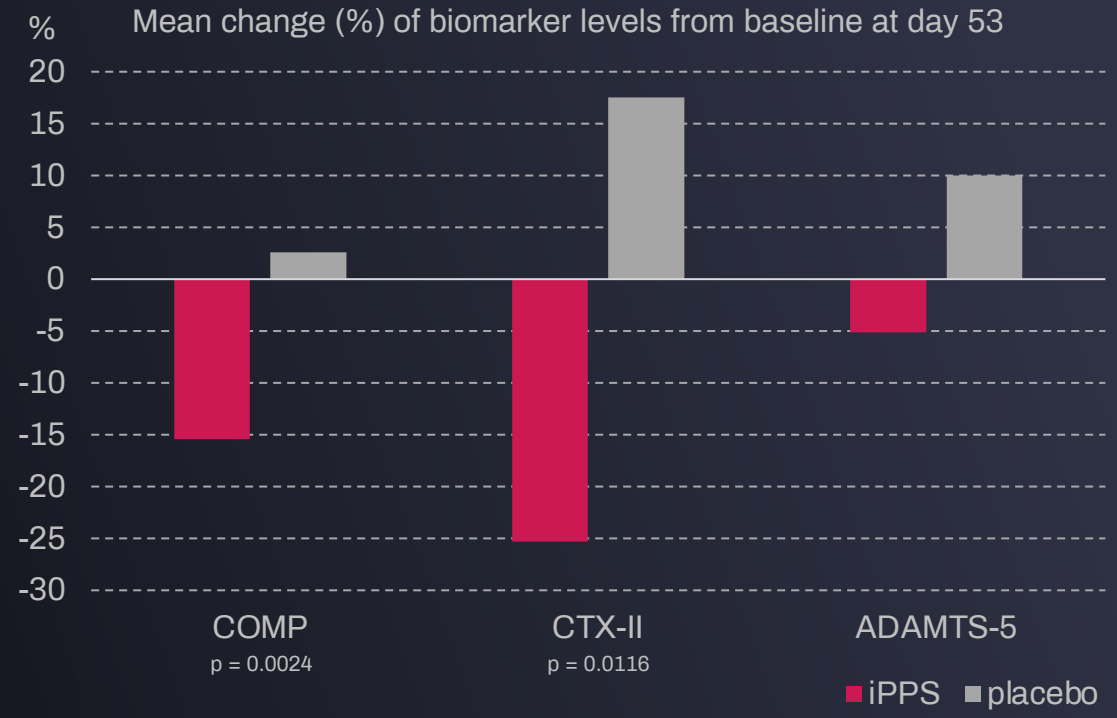
Grade 3 medial tibial BML at baseline



Grade 2 medial tibial BML at follow-up day 53



- iPPS showed significantly reduced serum levels of cartilage degradation biomarkers **COMP**, **ADAMTS-5** & urine levels of **CTX-II**.
- A single measurement of **increased COMP predicted subsequent cartilage loss on MRI** in symptomatic knee OA subjects (Hunter et al. 2007).



OA current and future clinical trials

PARA_OA_ 002

- Phase 2/3 dose vs treatment effect of iPPS for knee OA pain/function, compared to placebo.
- First stage (n=468) dose identification, Second stage (n=470) further treatment effect.
- 6-week treatment period, 18-week follow up.

PARA_OA_ 006

- Observational extension study from 002, continued safety/efficacy.
- Further 34-week follow up.

PARA_OA_003

- Phase 3 confirmatory trial, n=700.
- Safety/efficacy of iPPS for knee OA pain/function, compared to placebo.
- 6-week treatment period, 18-week follow up.

PARA_OA_007

- Observational extension study from 003, continued safety/efficacy.
- Further 34-week follow up.

PARA_OA_008

- Exploratory [randomised, double-blind] study of synovial fluid biomarkers after iPPS treatment in knee OA, compared to placebo.
- 6-week treatment period, 46-week follow up, n=61.

Osteoarthritis - Global Phase 3

Harmonised clinical protocol to achieve simultaneous registration in key jurisdictions

PARA_OA_002 Global Progress

United States

- Fast Track Designation
- 50+ sites activated
- Enrolling participants

Australia

- 8 sites activated
- Enrolling participants

UK and Europe

- 12 sites selected
- UK reg & ethics approval received
- First UK site activated and commenced enrolling participants

Canada

- Regulatory and ethics approval received
- Up to 10 sites to be activated
- First subjects in screening

DMOAD Program

Osteoarthritis

EXPLORING THE POTENTIAL OF iPPS AS A DISEASE MODIFYING OA DRUG (DMOAD)

PARA_OA_008

- Biomarker study assessing change from baseline in multiple objective measures associated with disease progression of OA.
  - 60 participants received iPPS 2 mg/kg once or twice weekly, or placebo.
  - Follow-up period out to 12 months.

- Outstanding top-line results reported at day 56:
  - iPPS impacted multiple biomarkers measured in the synovial fluid.
  - iPPS treatment showed statistically significant improvements at day 56 in pain, function, stiffness, and overall WOMAC scores for twice-weekly iPPS compared to the placebo arm.

Top-Line Results

PARA_OA_008

DAY 56 TOP-LINE RESULTS – CHANGES IN SYNOVIAL FLUID BIOMARKERS

In all cases, the synovial biomarker changes in iPPS-treated subjects at day 56 were favourable compared to placebo control.

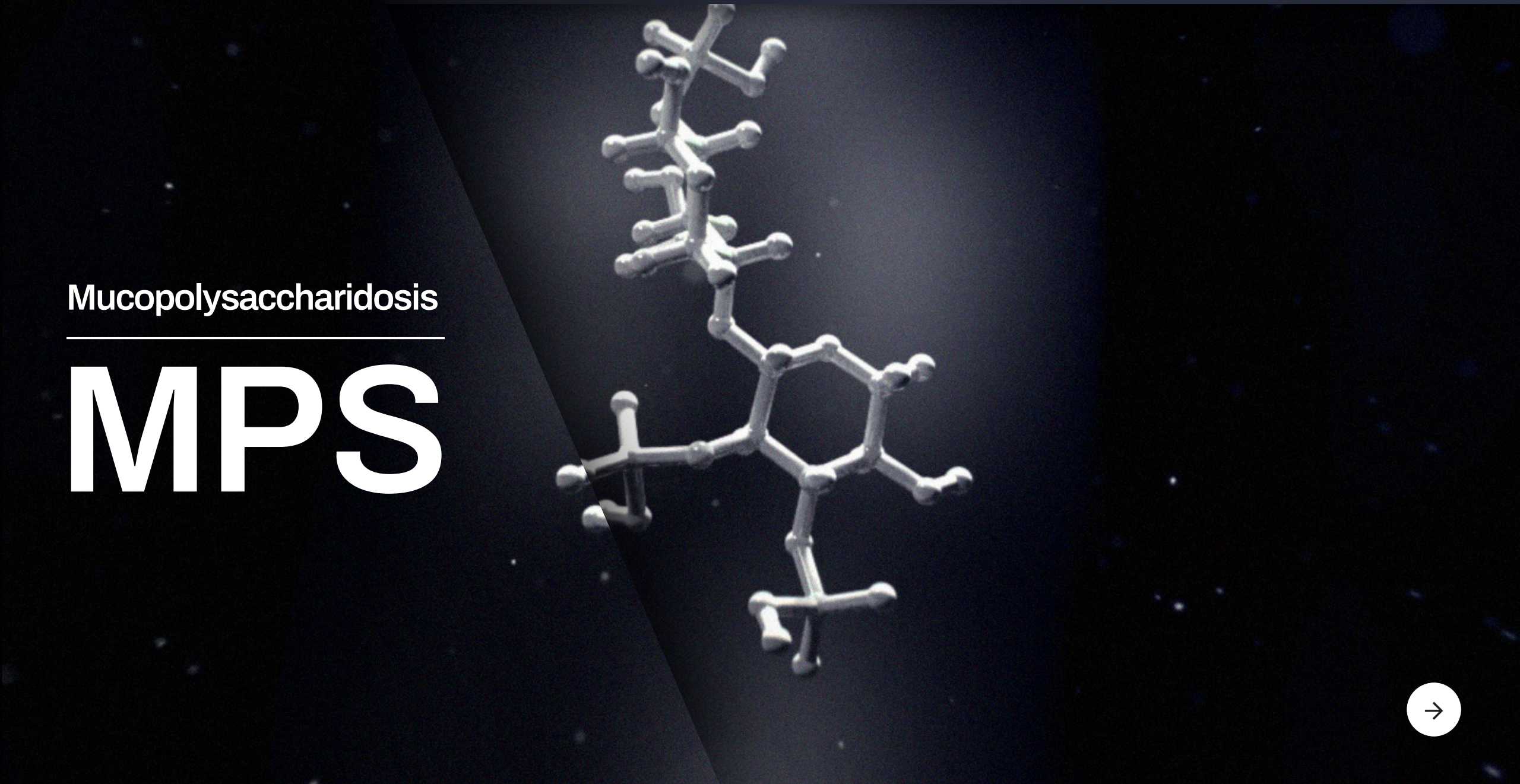
Synovial Biomarker	iPPS compared to placebo	Biomarker Function
NGF	Reduced	Pain mediator
IL-6	Reduced	Pro-inflammatory cytokine
TNF-α	Reduced	Pro-inflammatory cytokine
COMP	Reduced	By-product of cartilage degradation
ARGS	Reduced	By-product of cartilage degradation
TIMP-1	Increased	Endogenous inhibitor of cartilage degradation

Clinical Outcomes

PARA_OA_008

DAY 56 TOP-LINE RESULTS – CHANGES IN WOMAC PAIN & FUNCTION FROM BASELINE

- Participants in the study were asked to provide baseline pain scores using the WOMAC Osteoarthritis Index.
- iPPS treatment showed statistically significant improvements at day 56 in pain, function, stiffness, and overall WOMAC scores for twice-weekly iPPS compared to the placebo arm.
- The proportions achieving ≥30% and ≥50% improvement in pain were 73% and 60%, respectively.
- The reduction in pain for iPPS-treated subjects are consistent with the clinical effects observed in this and prior studies of iPPS in osteoarthritis.



Mucopolysaccharidosis

MPS

Mucopolysaccharidosis (MPS)

Phase 2 asset in rare disease associated with inflammation & ongoing musculoskeletal pain: iPPS has FDA & EMA orphan designation for MPS

MPS I - Australia

- Open-label trial SC dosing subjects weekly for 12 weeks, then every other week for a total of 52 weeks.
- Primary endpoint is safety, key secondary endpoints are pain and function, as well as PK.
- Interim top-line data presented at ICEIM 2021 by primary investigator Dr Drago Bratkovic showed iPPS is well tolerated, demonstrating reduction in pain and GAGs, and improvement in function.

MPS VI - Brazil

- A double-blind placebo-controlled trial with 12 subjects. Dosed weekly SC for 52 weeks.
- Primary endpoint is safety, key secondary endpoints are pain and function.
- Safety Monitoring Physician confirmed two successful safety reviews in participants aged 9 to 16 and in the 16+ cohort, with the clinical trial now assessing the youngest cohort (aged 5 to 9 years).

Summary

Phase 3 asset in blockbuster indication

- Actively screening and enrolling participants globally in P3 Knee OA clinical trial.
- Obtained regulatory feedback for a harmonised clinical protocol to achieve simultaneous registration in key jurisdictions.
- Clinical program will support broad label, maximise reimbursed price and market penetration from launch.
- Disease modifying potential

Promising Pipeline

- Development of pipeline indications with unmet needs in parallel to OA program for:
  - Mucopolysaccharidosis (MPS)
  - Respiratory
  - Heart Failure
- Paradigm has extensive preclinical dossiers on PPS supporting multiple indications.

For more information please visit:
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