PARADIGM BIOPHARMA

INVESTOR UPDATE

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About Paradigm

Repurposing	FDA-approved drug with 60-year track record of treating inflammation, pentosan polysulfate sodium (PPS, ZILOSUL®).
Lead program	Osteoarthritis (OA) ~ Phase 3 asset with **72m addressable population** in key markets (US, EU5, AU, CAN). Estimated annual revenue potential >US$10B at 10% penetration of addressable market in Knee and Hip OA.
Proven Safety & Efficacy	Phase 2B trial provided encouraging evidence of meaningful treatment effects in responses to iPPS compared to placebo overall for pain, ADL and PGIC. Real world evidence via SAS and EAP.
IP	Strong portfolio of IP protection and patents on Zilosul – patents in all key markets from 2030 to 2040.
Manufacturing	Secured scalable manufacturing supply from only FDA approved manufacturer, bene pharmaChem – **exclusive agreement for 25 years** from date of marketing approval. Exclusive agreement covers all major markets

Executive Summary

IND clearance

- Interactions with the FDA reached agreement for a well designed, adequately controlled study to support registration.

De-risked Program

- Retained global harmony to achieve simultaneous registration in key jurisdictions.
- Paradigm completed 26 GLP non-clinical studies and a western population PK study as requested by the FDA.

Improving Value of Asset

- Clinical program will support broad label, maximise reimbursed price and market penetration from launch.
- Global market research indicates a price of between US$2,000 - US$3,000 p.a. in the US market is achievable for Zilosul for the treatment of pain and function in knee OA.
- Upside potential of US$6,000+ per course if disease modification (DMOAD) can be demonstrated.
- Development of pipeline indications has continued in parallel to OA program.
- Commenced partnering discussions.

Leadership transition

- Experienced team to drive clinical execution of all Paradigm's programs.
- Chairman focus on commercial discussions and strategic partnerships.
- Global search for new company CEO.


Paul Rennie, Chairman


Dr. Donna Skerrett, Interim CEO


Dr Ravi Krishnan, CSO


Justin Cahill, CFO

Development Pipeline

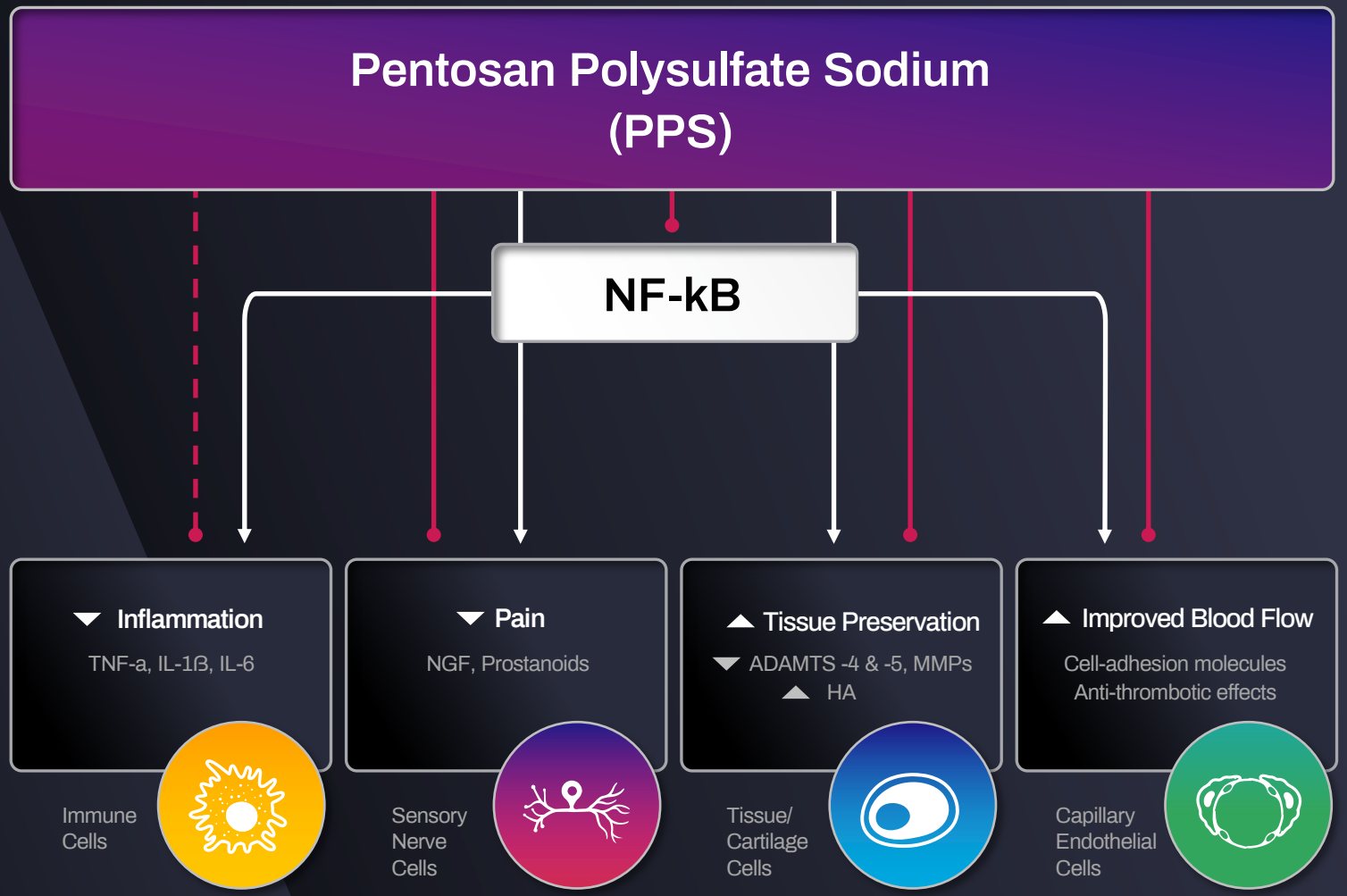
EMA = European Medicines Agency; HTA = Health Technology Assessment (funding authorities)

Mechanism of action

- Multiple modes of action
- Previous phase 2b, SAS and EAP experience

OA
MPS
ARDS
Heart Failure
Alphavirus induced arthralgia

Current proposed MoA



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.

Experience with iPPS in OA

Providing confidence for clinical success

Prior clinical and commercial experience exceeding 22,000 exposures demonstrates injectable PPS to be well tolerated. In osteoarthritis indications doses ranging from 1.7mg/kg to 3mg/kg once weekly and 2mg/kg twice weekly have been well tolerated and demonstrated meaningful effects.

Our phase 3 study will evaluate once and twice weekly regimens, covering total exposure ranges of 12-18 mg/kg in order to identify the best tolerated and effective regimen for commercialisation.

Clinical

- Paradigm's prior randomised controlled phase 2b trial demonstrated PPS improved pain, function and PGIC compared to control. Peak treatment effects for pain and function were 0.32 and 0.37 respectively.
- Ghosh et al (3mg/kg weekly x4) demonstrated improved pain, function and PGIC, with pain treatment effects of 0.3.
- Kumagai et al (2mg/kg weekly x 6) demonstrated improved pain and C2C, duration of effects up to 1 year.
- Paradigm sponsored pharmacokinetics informed of exposures and tolerance of once and twice weekly dosing.

Preclinical

- HED of canine PPS treatment is 1.7 mg/kg weekly x 6

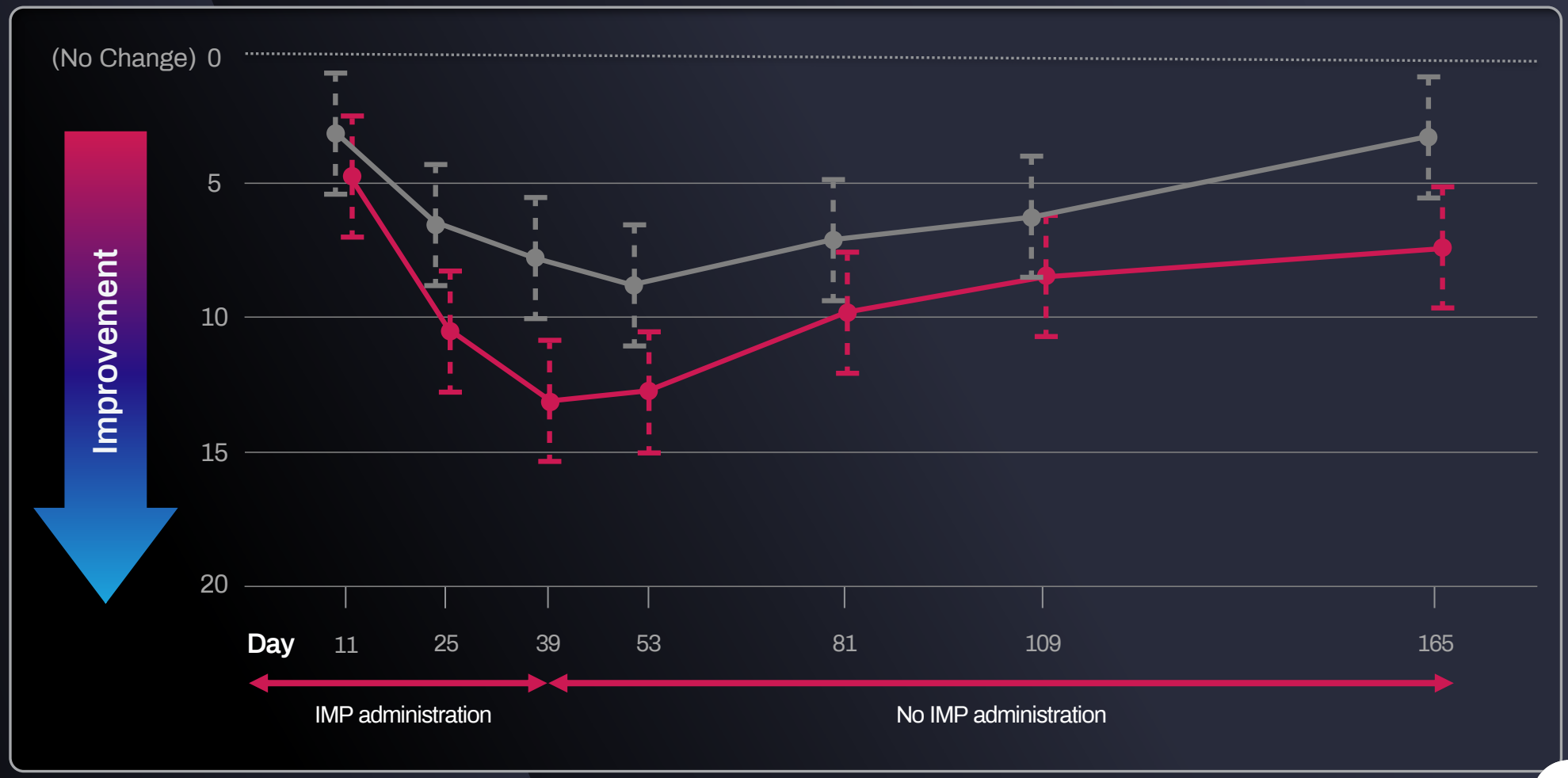
HED = Human Equivalent Dose

Phase 2b – Para_OA_005

Pain Reduction (KOOS)

Adjusted Mean Change From Baseline to Days 11, 25, 39, 53, 81, 109, and 165. (N=112) (1:1 randomised)

1



LS Mean Change +/- Standard Error

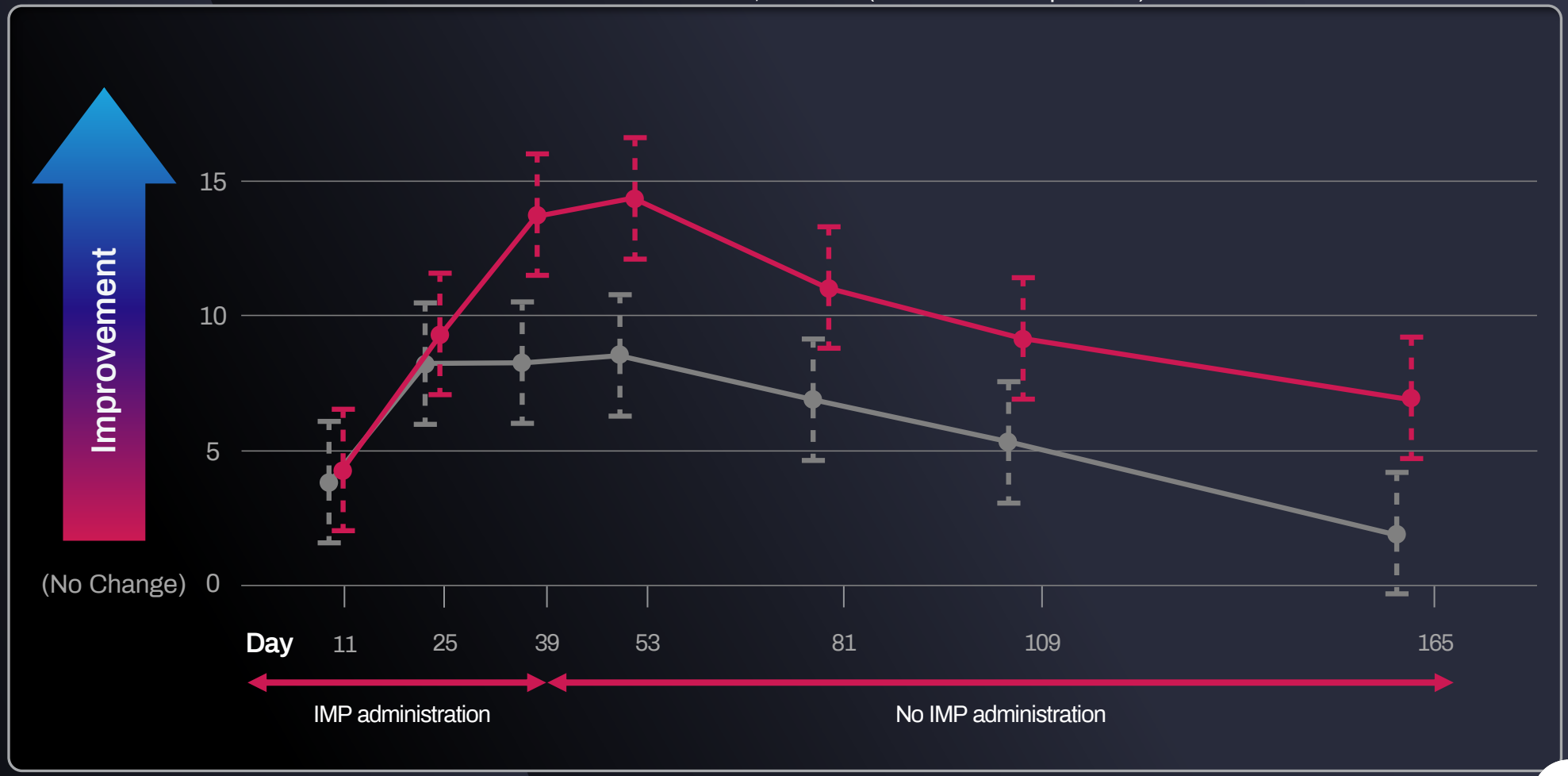
FAS = Full Analysis Set

Phase 2b – Para_OA_005

KOOS Function (ADL)

Adjusted Mean Change From Baseline to Days 11, 25, 39, 53, 81, 109, and 165 (Overall FAS Population)

2



LS Mean Change +/- Standard Error

FAS = Full Analysis Set

Patient Global Impression of Change (PGIC)

Para_OA_005

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

Special Access Scheme (SAS)

76% of patients reported on the PGIC scale a moderate to definite and considerable improvement (i.e., scores of 5 or higher) in their OA condition.

FDA IND Process

IND Submission and FDA Responses 2021

MAR 26

Paradigm submits IND application to US FDA.

Response due from the FDA within 30 days.

FDA response received toward the end of the 30-day review, stating the regulator required an additional 30-days

MAY 25

Paradigm receives FDA questions.

Company receives six questions from the agency principally relating to recently completed non-clinical studies.

JUL 30

Paradigm receives written response from the US FDA.

Agency accepted responses to five of the six questions received. FDA seek further clarification on one prior question

SEP 27

Paradigm receives written response from the US FDA.

Uncertain correlation between rat findings and humans, specified further monitoring of adrenal function and population exclusion related to prior immunosuppressive effects.

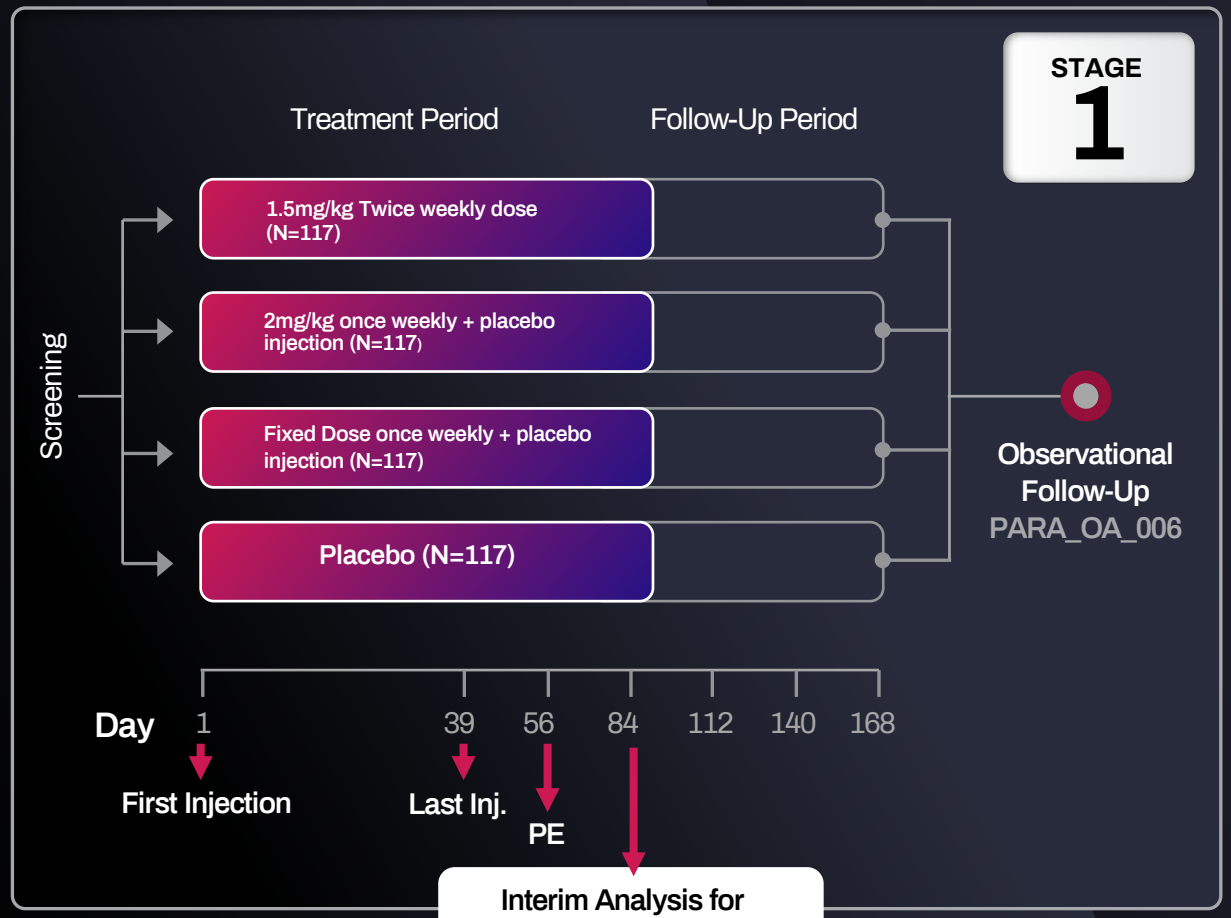
OCT 30

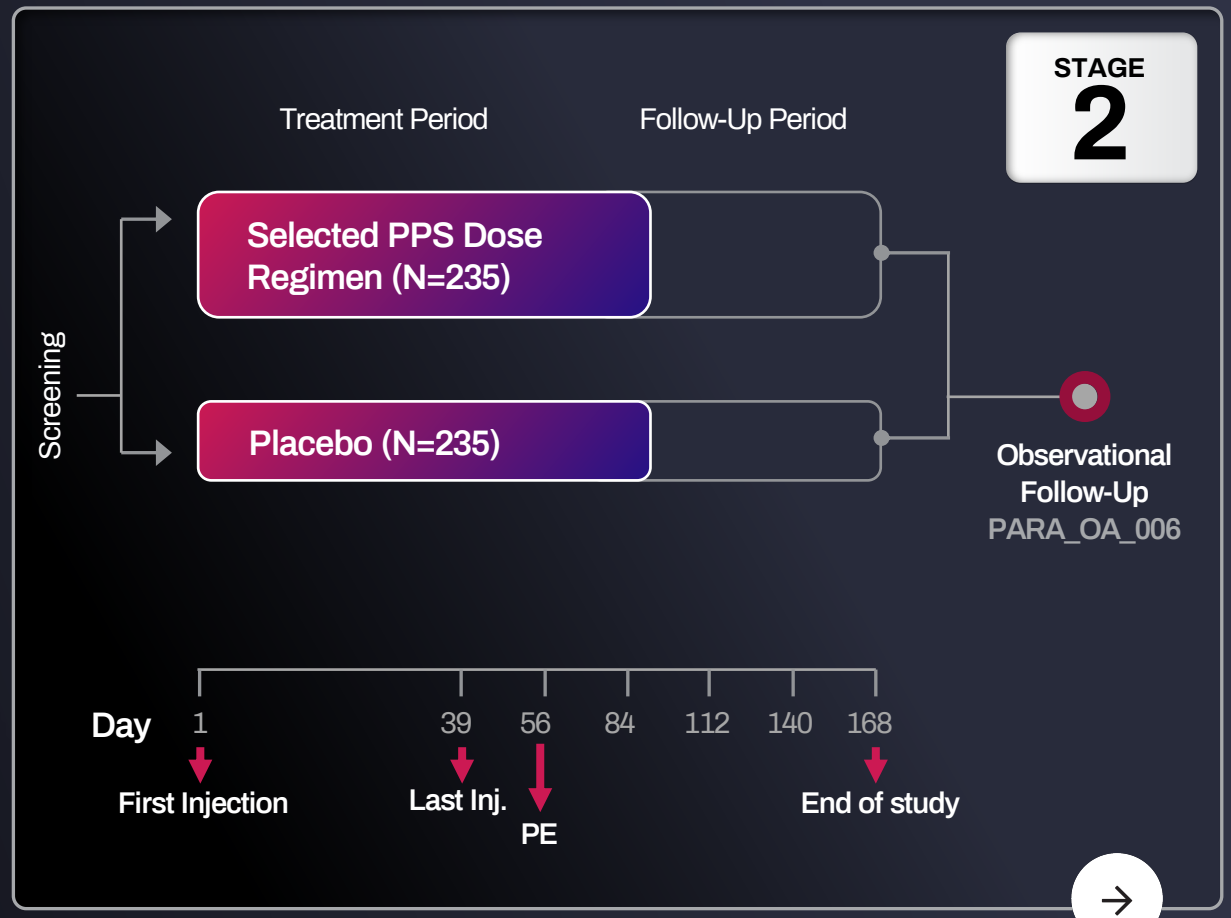
IND CLEARED BY US FDA TO PROCEED

To reach this agreement required multiple interactions as well as amendments to the originally submitted protocol. Paradigm have retained global harmony with these changes.

PARA_OA_002

Phase 3 Trial Design





PE = Primary endpoint

NB: Approximate recruitment numbers, may be subject to change.

Protocol amendment

Trial Design cont'd

At the request of the FDA the following amendments have been made:

- Study population exclusions for subjects with recent immunosuppressive therapy, recent heparin exposure, and drugs that interact with adrenal function or adrenal assessments
- Monitoring of platelets and testing for heparin induced thrombocytopenia (HIT) as indicated
- Adrenal monitoring for function of all three zones to rule out human translation of the uncertain rat findings - of note: no adrenal findings in dogs, and no adrenal suggestive events in over 20,000 prior PPS human exposures
- Monitoring for pigmentary maculopathy - rarely seen with long term oral PPS therapy - not previously seen with injectable PPS

Phase 3 Asset

Global Harmonised Pivotal Trial – PARA_OA_002

United States

- FDA clears IND application investigating pentosan polysulfate sodium (PPS) for the treatment of pain associated with knee osteoarthritis.
- Approximately 56 sites have been selected.
- Lead investigator confirmed.
- Central Ethics approval received.

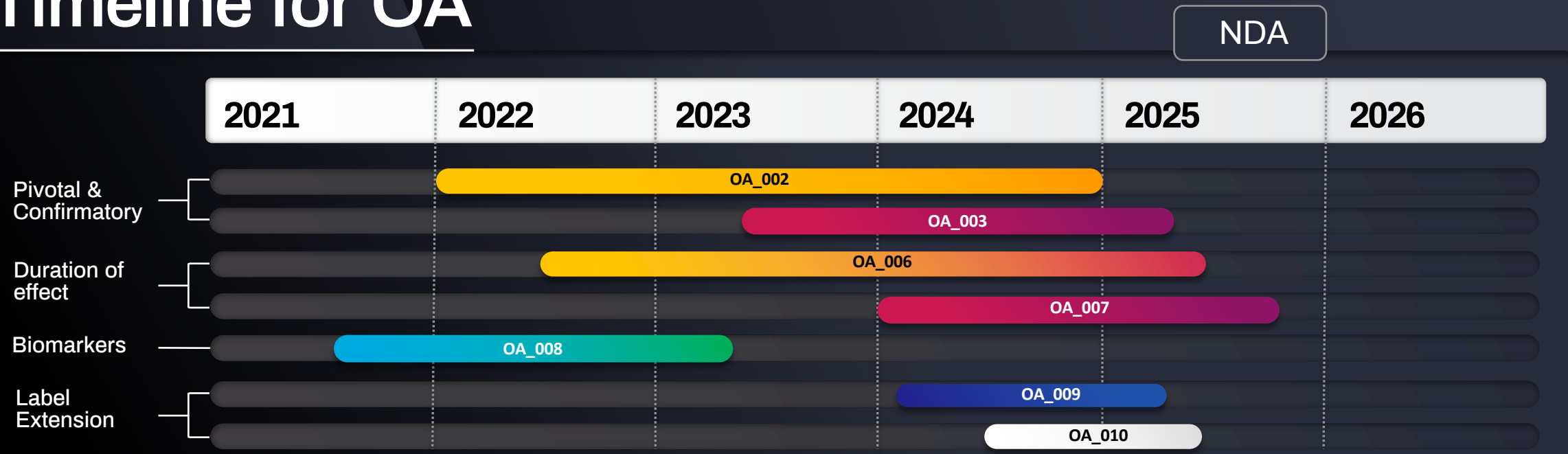
Australia

- Eight (8) sites have been selected.
- Protocol has received ethics approval.
- Paradigm has begun contracting sites in WA, VIC, NSW, SA and QLD.
- First 5 sites in Australia have initiated screening participants
- Lead investigator confirmed.

Europe and UK

- Twelve (12) sites to be initiated.
- UK Lead Investigator Confirmed .
- EU Lead investigator being finalised.
- Site initiation and screening to commence in CY2022.

Timeline for OA



Study	Objective	Key Milestone
002	NDA Pivotal	Dose Selection - 1H CY2023
003	NDA Confirmatory	First patient Randomised 1H CY2023
006 / 007	Establish durability of effect	First patient enters 006 observational study 2H CY2022
008	DMOAD	Primary Endpoint readout Q3 CY2022
009	Retreatment	Timelines will be confirmed following dose selection
010	Establish safety and efficacy in Hip OA	

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

Disease Modifying OA Drug (DMOAD)

Current programs to inform of Zilosul potential as a DMOAD

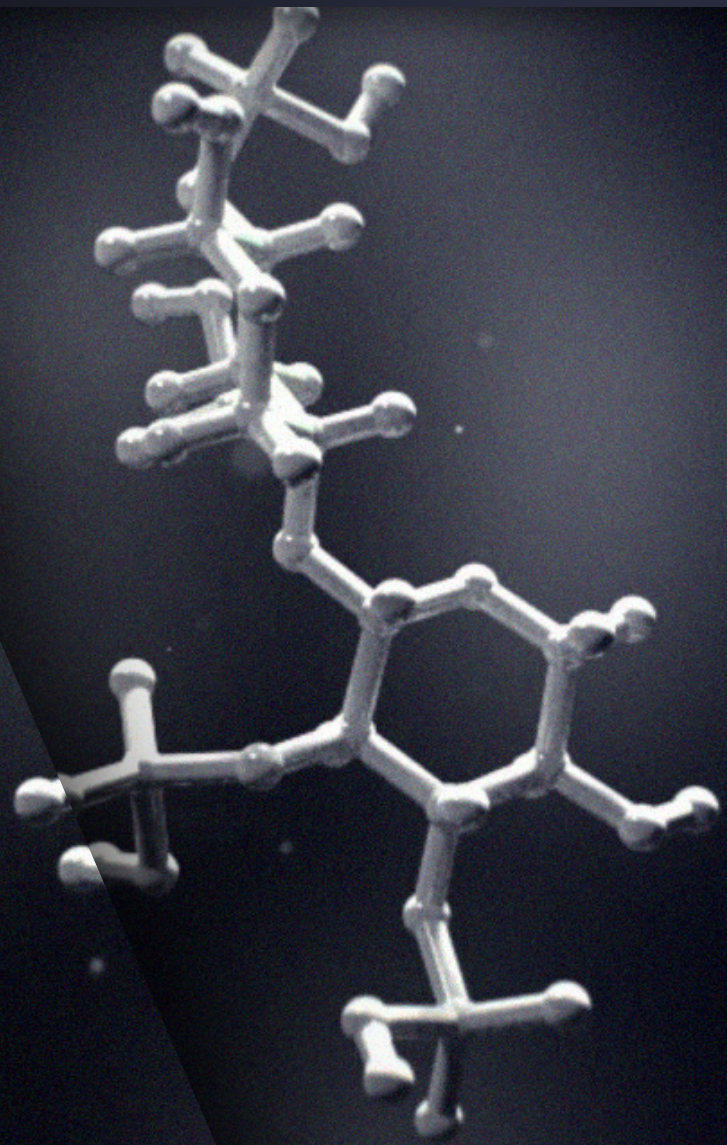
PARA_OA_008 - Australia

- Biomarker study assessing change from baseline in multiple objective measures associated with disease progression of OA.
- Study will randomise 60 participants to receive PPS or Placebo.
- To date the exploratory clinical trial is >50% recruited.
- Protocol amendments include once weekly dosing regimen, second trial site initiated, extended follow-up period to 12-months.
- Interim read out Q3CY22.

Canine OA Study

- Dogs with OA of the stifle (knee) joint are treated with PPS at a dosing of 3mg/kg (1.7mg/kg human equivalent) weekly for 6-weeks.
- Pain and function will be assessed together with structural changes from baseline as determined by the global OA score measured by X-ray and bone marrow lesions and cartilage volume by MRI.
- Serum samples will also be taken to measure biomarker levels associated with inflammation, cartilage degradation and pain.
- 20 weeks follow-up period (equates on average to a period of 3 years in human lifespan)

Commercial



Partnering Strategy

Preference is to partner

- Maintain optionality to bring Zilosul to market ourselves

De-risked phase 3 asset with globally accepted trial design in key markets

Increased inbound interest in partnering OA since open IND

- Global / regional partnerships preferred
- Option to partner pipeline indications to a single partner, or partner by indication
- Open process underway to appoint advisory firm to assist with partnering process

Exclusive Supply & Manufacture

Supply chain ready to partner

bene pharmaChem

Exclusive supply of raw Active Pharmaceutical Ingredient (API) to Paradigm.

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- Paradigm produce the final injectable solution of PPS.
- Important to control quality & cost of supply.

Commercial Partner

Purchases final PPS injectable product from Paradigm.

Scalable Model to accommodate Future Indications

Product Development Dynamic

Value vs Time

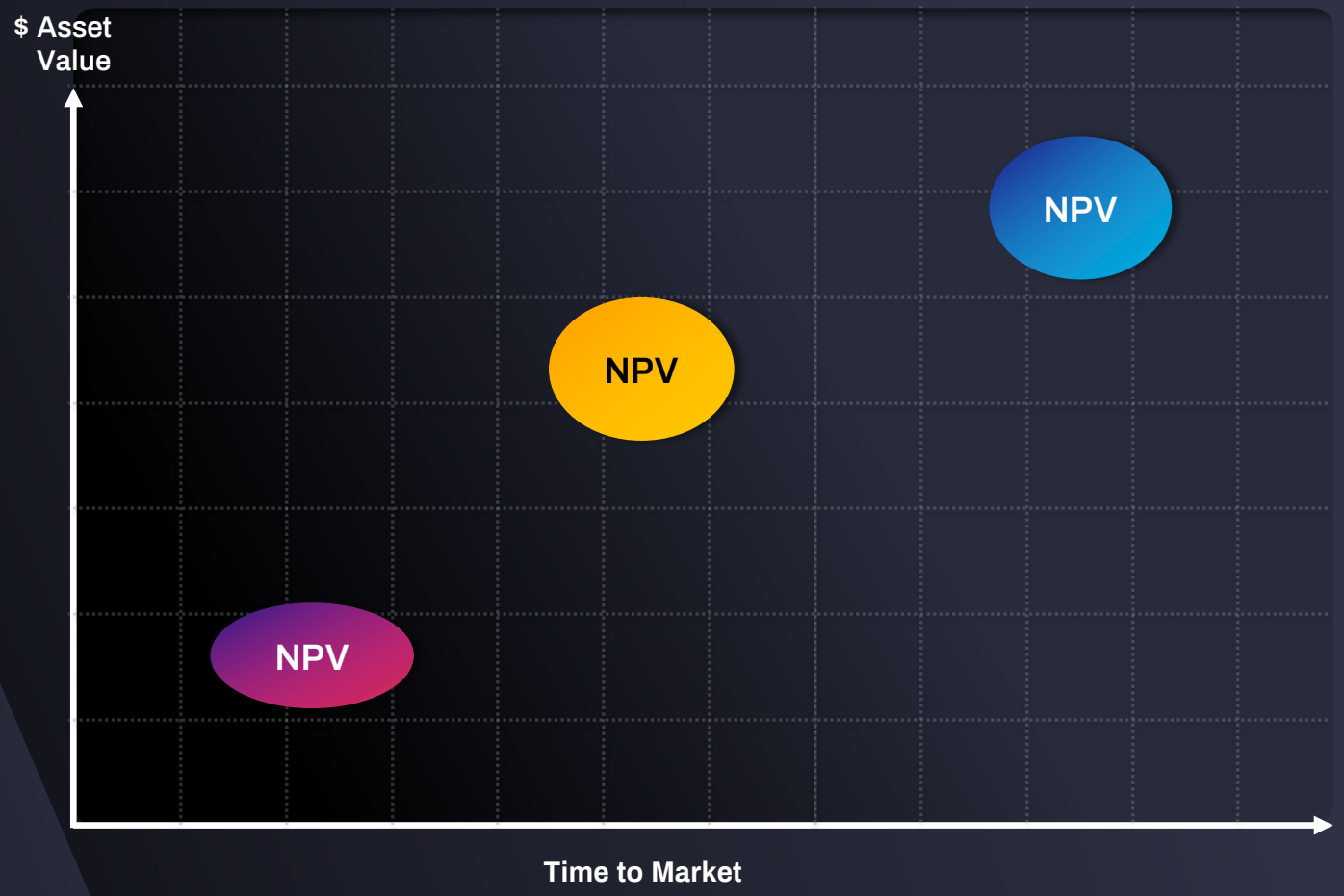
Decisions made along the product development cycle will determine the value of the asset under development and the time & cost it takes to develop.

PAR's development strategy is focused on maximising the value of our asset for the benefit of:

- Patients suffering from disease with high unmet needs
- Potential Commercial Partners
- PAR Shareholders

This is what's driven our scope of clinical development and our timelines.

** NPV is illustrative



PAR is taking the longer-term view with decisions to maximise value creation from iPPS

Improving value of the Asset

Clinical and commercial activities to improve Zilosul label

- 006 & 007 determine long term durability of effect
  - Differentiate from current therapies and improve cost effectiveness for payers.
- 009 retreatment study
  - Establish safety and efficacy of repeated dosing for regulatory bodies and payers.
- 010 OA in Hip (approx. 19% of the OA market, potential $3B value based on market size and indicative price of Zilosul)
  - Expand label with selected dose from 002

All studies to support label claims, registration and funding in reimbursed markets

- Seeking to align clinical studies to maximise product launch value to mitigate against further studies for pain and function after launch.
- Delivery device for patient & prescribing physician convenience.
- Market Access Strategy (by Region / Country) under development to streamline market access post registration

Activities are occurring in parallel to clinical program

Decisions taken in the short term to drive long term value

Current Cash Runway

Opening Cash FY22 of $71MAUD, key activities for FY22:

- Clinical OA
  - PARA_002
  - PARA_006
  - PARA_008
- Clinical MPS
  - Continue MPS I and MPS VI phase 2 clinical studies
- R&D
  - OA Canine model to inform approach for DMOAD
  - Heart Failure - awaiting Q4CY21 update and determine next steps in development
  - MoA & Mechanistic study
- Regulatory
  - Various activities for NDA preparations, including Pharmacology, Pharmacodynamics and Toxicology studies to support product registration (multi year studies)
- Commercial
  - Development of delivery device
    - Multi year project
  - External advisory costs to assist with partnering opportunities

Further capital will be required in future to commercialise Zilosul

- Company will continually monitor funding required to complete all programs
- Multi year / Multi trial / Multi currency effort
- Maintain optionality for sources of Capital - Partnering / Equity / Debt Conversion to Equity

Sensitivities influencing rate of spend:

- COVID
  - Site and Lab capacity
- Recruitment rate for clinical programs
- AUD:USD

Global Market Research

- In 2021 Paradigm conducted market research in major global markets, with physicians, funding decision makers (payers) and patients to better understand willingness-to-pay and willingness-to-prescribe Zilosul for osteoarthritis of the knee (kOA)
- The research centred around 3 key questions in two scenarios:
  1. Zilosul registered for pain and function (P&F) only
  2. Zilosul registered for pain, function and disease modification (DM).

1

How is Zilosul perceived by physicians & public payers?

2

How will Zilosul fit in the Tx algorithm & how would physicians use it?

3

How much would public payers and patients pay for Zilosul?

Tx = treatment

Zilosul's proposed profile was regarded positively

Assuming sustained efficacy and robust safety data, physicians and payers believe Zilosul will provide high value to the treatment of kOA by covering some important unmet needs

ZILOSUL®

- New MoA
- ★ Favourable safety profile with no renal, GI, CV side effects or cartilage degradation
- ★ No drug abuse potential
- Meaningful pain reduction, functional improvement and potential DM effect ★
- Subcutaneous RoA vs. IA injections
- Convenient dosing regimen (6 week treatment) vs. daily intake

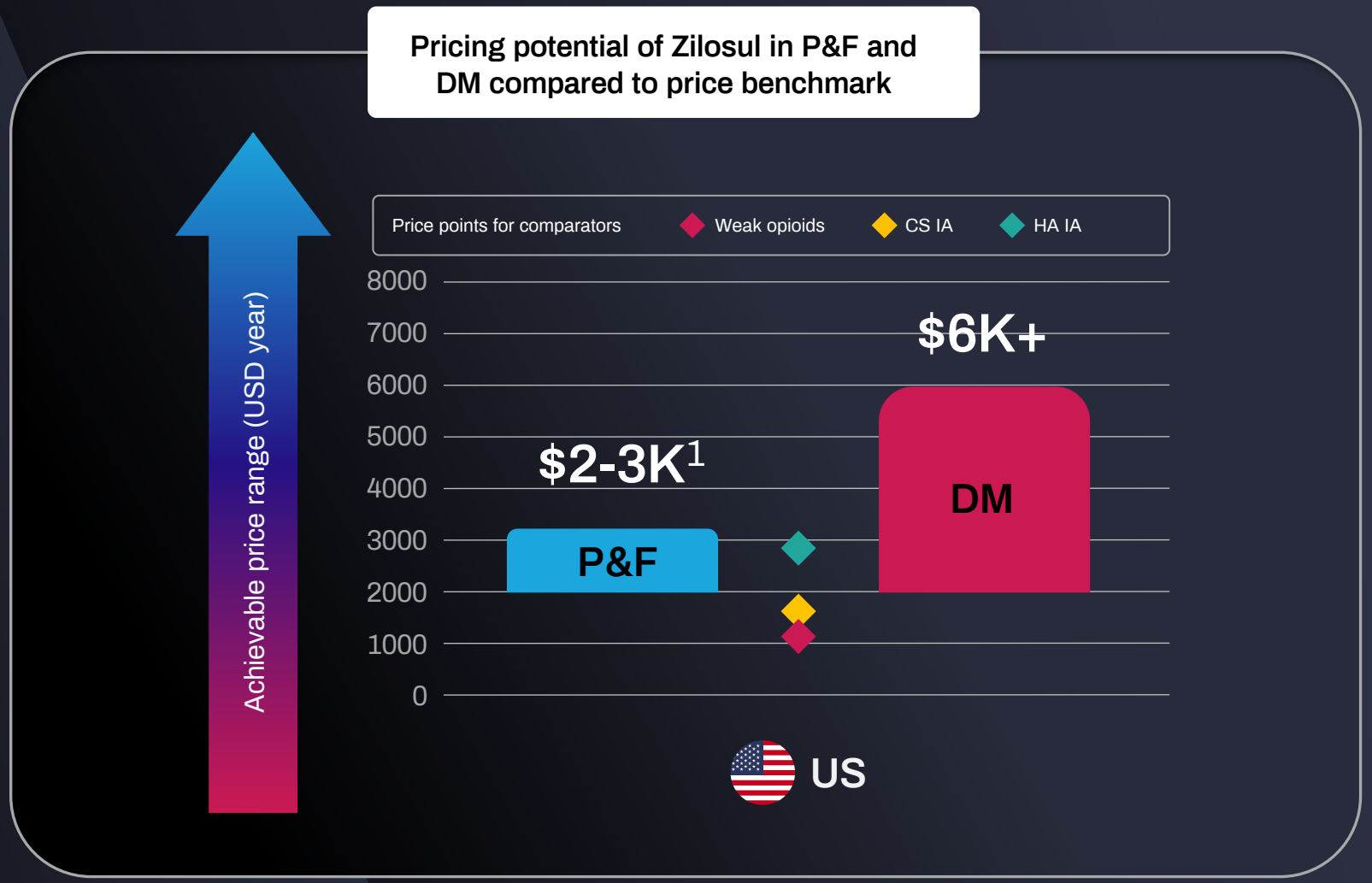
Zilosul is expected to cover the main residual unmet needs highlighted by physicians and payers as it will provide an alternative treatment to kOA patients that is well-tolerated and potentially preserving structural changes in kOA

CV = Cardiovascular; DM = Disease Modification; GI = Gastrointestinal; IA = Intra-articular; kOA = Knee Osteoarthritis; MoA = Mechanism of Action; RoA = Route of administration

★ *Zilosul addresses the key residual unmet needs identified by payers and KOLs*

Target pricing

- Achievable for P&F with PAR current clinical program
- A significantly higher price for DM



1. Reasonable price - higher prices may be achievable but will likely trigger restrictions on use by payers

Summary

De-risked phase 3 asset in blockbuster indication

- Actively screening patients.
- Harmonised clinical protocol to achieve simultaneous registration in key jurisdictions.
- Clinical program will support broad label, maximise reimbursed price and market penetration from launch.
- Global market research indicates a price of between US$2,000 and US$3,000 p.a for the treatment of pain and function in knee OA.

Upcoming news flow

- ✓ MPS I – Preliminary Data
- Para_OA_002 first patient dosing (AUS, US)
- Heart Failure proof of concept top-line data
- Para_OA_008 100% recruitment
- UK and EU site initiation
- MPS VI study progress (World*symposium* 2022)
- MPS VI publication of findings from focus group (Orphanet)
- **Para_008 Preliminary Data Readout**
- **Progress commercial discussions**

Questions

For more information please visit:
paradigmbiopharma.com
or email any queries to
investorrelations@paradigmbiopharma.com