PARADIGM BIOPHARMA

NWR Virtual Healthcare Conference

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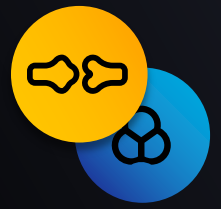
About Paradigm

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.

Recent Company Milestones

Osteoarthritis (OA)

- Phase 2 disease modifying OA data presentations at OARSI World Congress 2023.
- Parallel European Ethics and Regulatory approvals for phase 3 PARA_OA_002.
- Positive top-line results in phase 2 trial exploring disease modifying potential of iPPS.
- Successful formal Safety Review for PARA_OA_002 phase 3 trial.

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 American College of Medical Genetics and Genomics (ACMG) Conference.

Company

- Influenza ARDS data peer reviewed and published in Frontiers of Immunology
- Actively engaged in discussions with potential partners.

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]

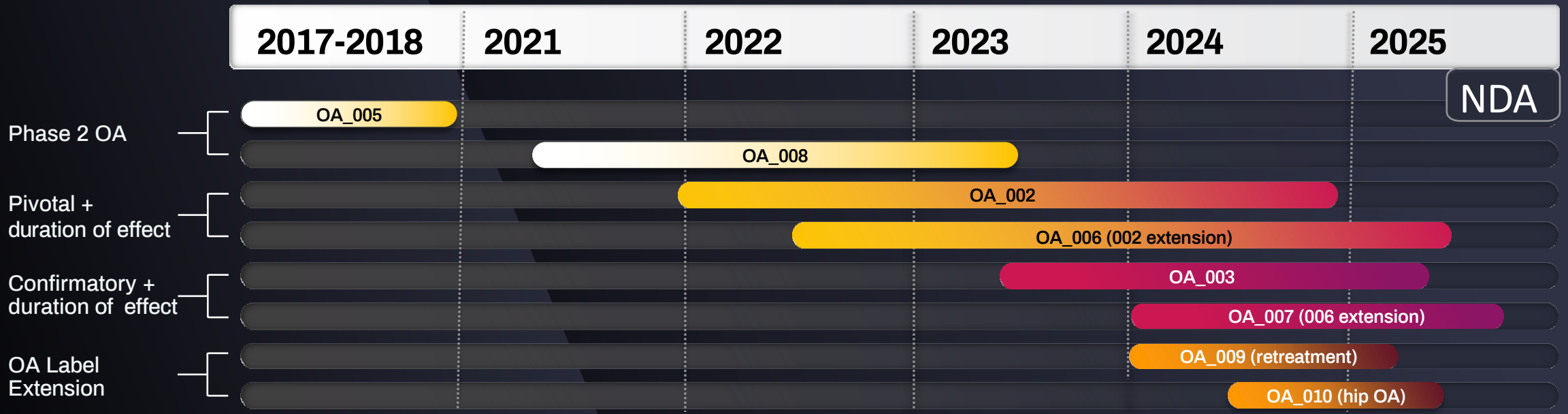
81%

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.

OA Clinical Development



Study	Objective	Status
005	To evaluate the effects of PPS on knee OA pain, function, and disease modification biomarkers at Day 53	Complete
008	To evaluate the effects of PPS on knee OA pain, function, and disease modification biomarkers up to Day 365	Ongoing
002 / 003	To provide evidence of effect for treatment of pain and improvement of function knee OA at Day 183	002 Enrolling
006 / 007	To evaluate the duration of treatment effect and safety up to 52 weeks from the last treatment in the parent study (002 / 003)	006 Enrolling
009	To establish efficacy and safety data to support repeat dosing in the label.	Planned
010	To establish efficacy and safety data to support adding Hip OA to the label.	Planned

6 weeks treatment duration in all OA studies

Timelines based on enrolment projections and may be subject to change.

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

Top-Line Results

PARA_OA_008

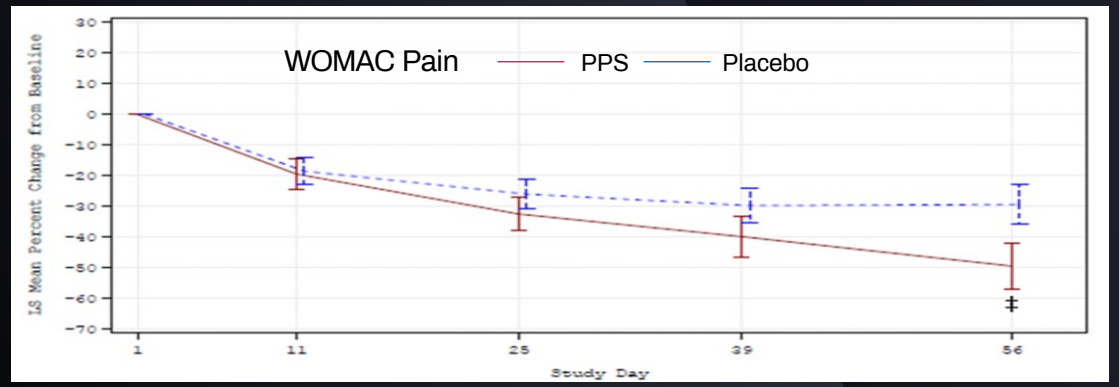
DAY 56 TOP-LINE RESULTS

Adjusted Percent Change in Synovial Fluid Biomarkers with Favorable Changes from Baseline

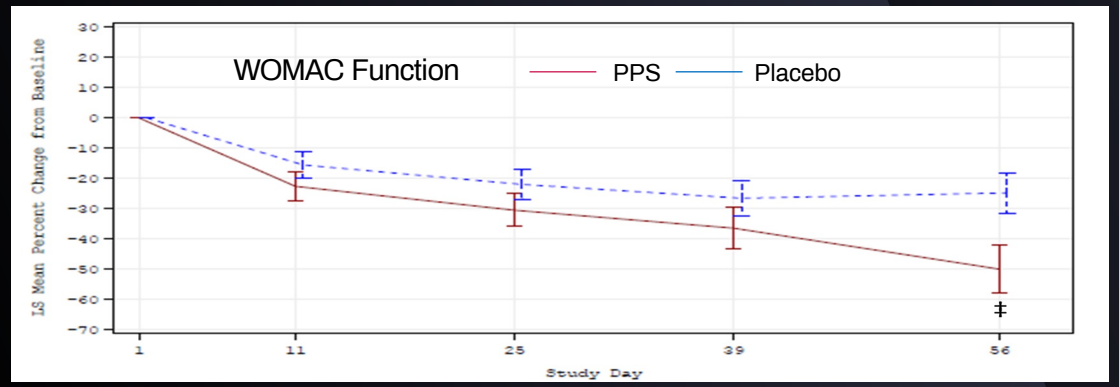
Biomarker	Statistics	PPS once-weekly N=17	PPS twice-weekly N=15	PPS pooled N=32	Placebo N=22
COMP (µg/mL)					
	LS mean change from baseline (95% CI)	-25.56 (-67.31, 16.19)	9.47 (-25.53, 44.47)	-4.67 (-33.04, 23.70)	26.17 (-3.14, 55.49)
	LS mean difference[1] (95% CI)	-51.73 (-100.62, -2.84)	-16.70 (-60.97, 27.57)	-31.42 (-70.42, 7.57)	
NGF (pg/mL)					
	LS mean change from baseline (95% CI)	5.33 (-72.58, 83.24)	51.12 (-5.70, 107.94)	35.10 (-10.29, 80.50)	60.33 (13.24, 107.43
	LS mean difference[1] (95% CI)	-55.01 (-141.70, 31.68)	-9.21 (-81.23, 62.81)	-26.47 (-88.31, 35.36)	
ARGS (ng/mL)					
	LS mean change from baseline (95% CI)	25.16 (-32.54, 82.85)	23.02 (-23.12, 69.16)	23.82 (-13.69, 61.33)	79.96 (40.82, 119.10
	LS mean difference[1] (95% CI)	-54.81 (-123.44, 13.83)	-56.94 (-115.88, 1.99)	-56.15 (-108.32, -3.98)	
TNFα (pg/mL)					
	LS mean change from baseline (95% CI)	65.01 (-119.63, 249.65)	184.71 (44.57, 324.86)	142.44 (26.00, 258.87)	245.46 (125.81, 365.1
	LS mean difference[1] (95% CI)	-180.45 (-398.98, 38.09)	-60.75 (-238.57, 117.06)	-100.97 (-262.74, 60.79)	
IL-6 (pg/mL)					
	LS mean change from baseline (95% CI)	-9.29 (-119.35, 100.78)	97.86 (7.46, 188.25)	56.00 (-19.39, 131.40)	72.38 (-3.59, 148.34
	LS mean difference[1] (95% CI)	-81.66 (-211.33, 48.00)	25.48 (-89.36, 140.32)	-17.32 (-121.32, 86.68)	
TIMP-1 (µg/mL)					
	LS mean change from baseline (95% CI)	32.49 (-19.07, 84.04)	4.97 (-33.09, 43.03)	14.31 (-17.41, 46.04)	4.83 (-27.42, 37.08
	LS mean difference[1] (95% CI)	27.66 (-32.26, 87.58)	0.14 (-48.11, 48.40)	9.29 (-34.27, 52.85)	

PARA_OA_008: Clinical Endpoints

Percentage Change from Baseline in WOMAC NRS 3.1 Index Pain and Function Subscale



‡ p = 0.050



‡ p = 0.017

DAY 56 TOP-LINE RESULTS – CHANGES IN WOMAC PAIN, FUNCTION AND STIFFNESS 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 responses in pain for iPPS-treated subjects are consistent with the clinical effects observed in this and prior studies of iPPS in osteoarthritis.

DMOAD Program

Osteoarthritis

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

PARA_OA_008

- Upcoming 6-month Data to be reported in Q1 will include:
  - Changes in one or more synovial fluid biomarkers;
  - Changes and correlation between synovial fluid, serum, and urine biomarkers and correlation with changes in clinical outcomes;
  - Changes in WOMAC pain, function, stiffness, and quality of life scores; and
  - MRI changes in the bone and joint.

Following the readout of the PARA_OA_008 6-month data, PAR intends to initiate discussion with the key regulatory agencies (FDA and EMA) to reach agreement on disease modification label pathways for iPPS.

Imaging Biomarkers

DMOAD Investigation

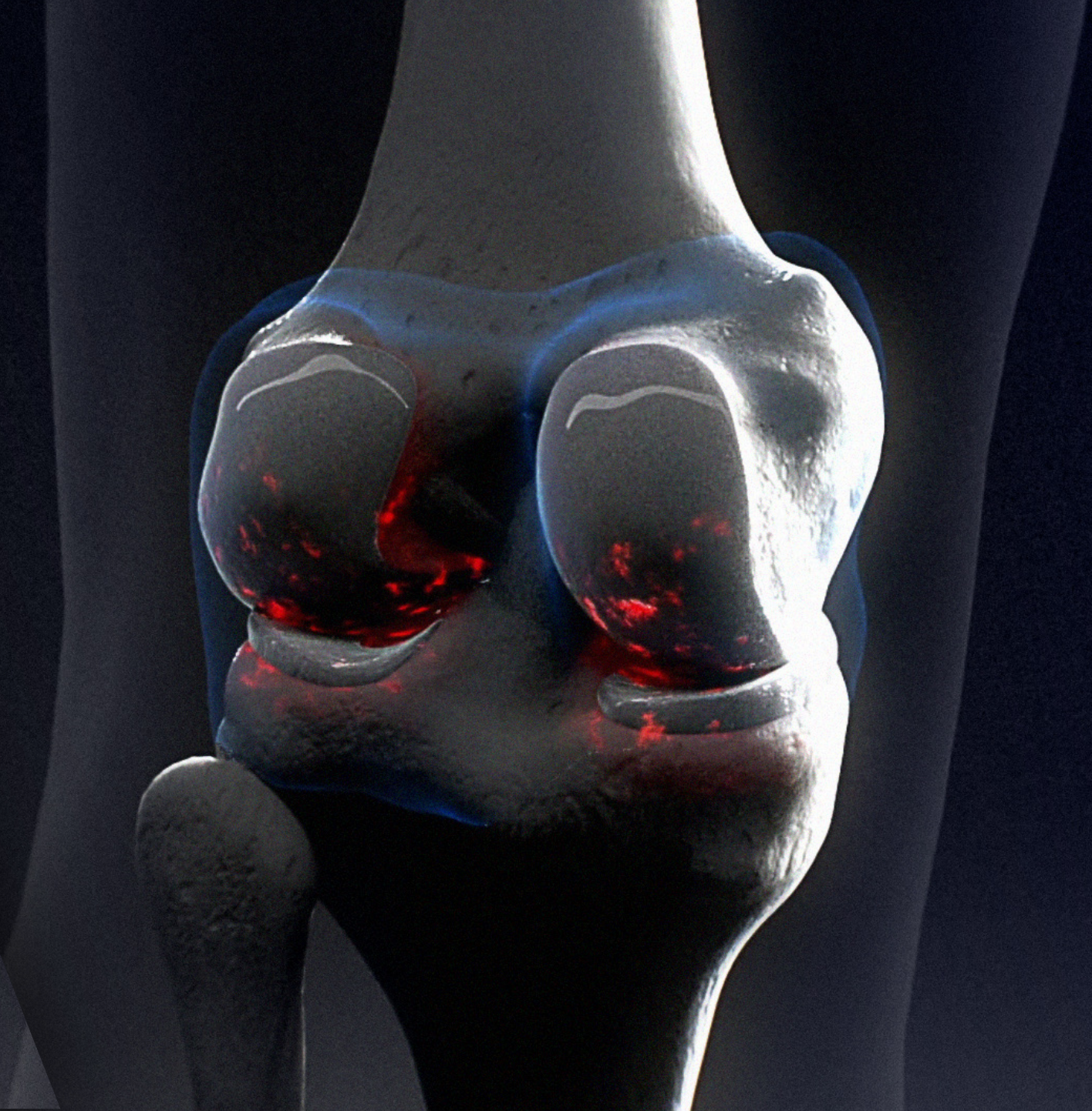
Structural imaging biomarkers for potential disease modifying treatments for OA

Biomarker	Evaluated	Biomarker Pathology
Subchondral BML area and volume	MRI	Pain and cartilage degeneration
Joint synovitis / effusion volume	MRI	Inflammation and pain
Cartilage thickness	MRI	Cartilage degeneration
Bone shape / osteophytes	MRI	Adverse bone remodelling
Joint space width	MRI & X-Ray	Adverse bone remodelling

PARADIGM

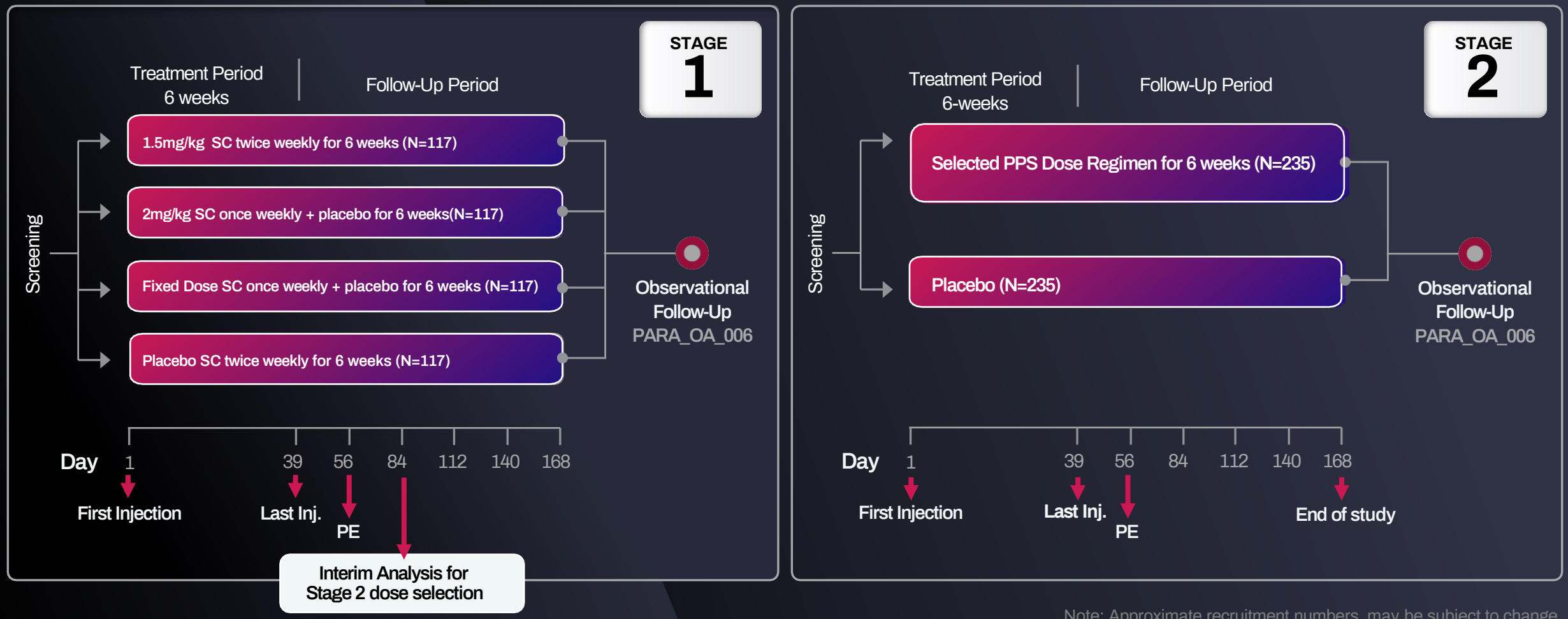
Phase 3 Program

OA



PARA_OA_002

Phase 3 Trial Design –Primary Endpoint: WOMAC Pain, Secondary: WOMAC Function



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

Osteoarthritis - Global Phase 3 Enrolment

Harmonised clinical protocol to achieve simultaneous registration in key jurisdictions

120+ sites planned across the US, EU, UK, Canada and Australia

PARA_OA_002 Global Progress

USA
- Fast Track Designation
- 76 active sites
- 14 sites selected
- US enrolling

Australia
- 5 active sites
- 12 sites selected
- AU enrolling

UK and Europe
- 1 active site
- 12 sites selected
- UK enrolling

Canada
- 5 active sites
- 6 sites selected
- CA enrolling

Next 6 months

Expected Key News Flow Events

- PARA_OA_008 – 6-month data March CY2023
- Canine OA model – 20-week follow-up (3-year human equivalent) data Q2 CY2023
- PARA_OA_002 – Stage 1 100% recruitment 1H CY2023
- Discussions with key regulatory bodies (FDA/EMA) on Disease Modification pathway for label
- Progress commercial discussions on MPS asset

For more information please visit:
paradigmbiopharma.com