PARADIGM BIOPHARMA

ANNUAL GENERAL MEETING | 29 NOV 2023

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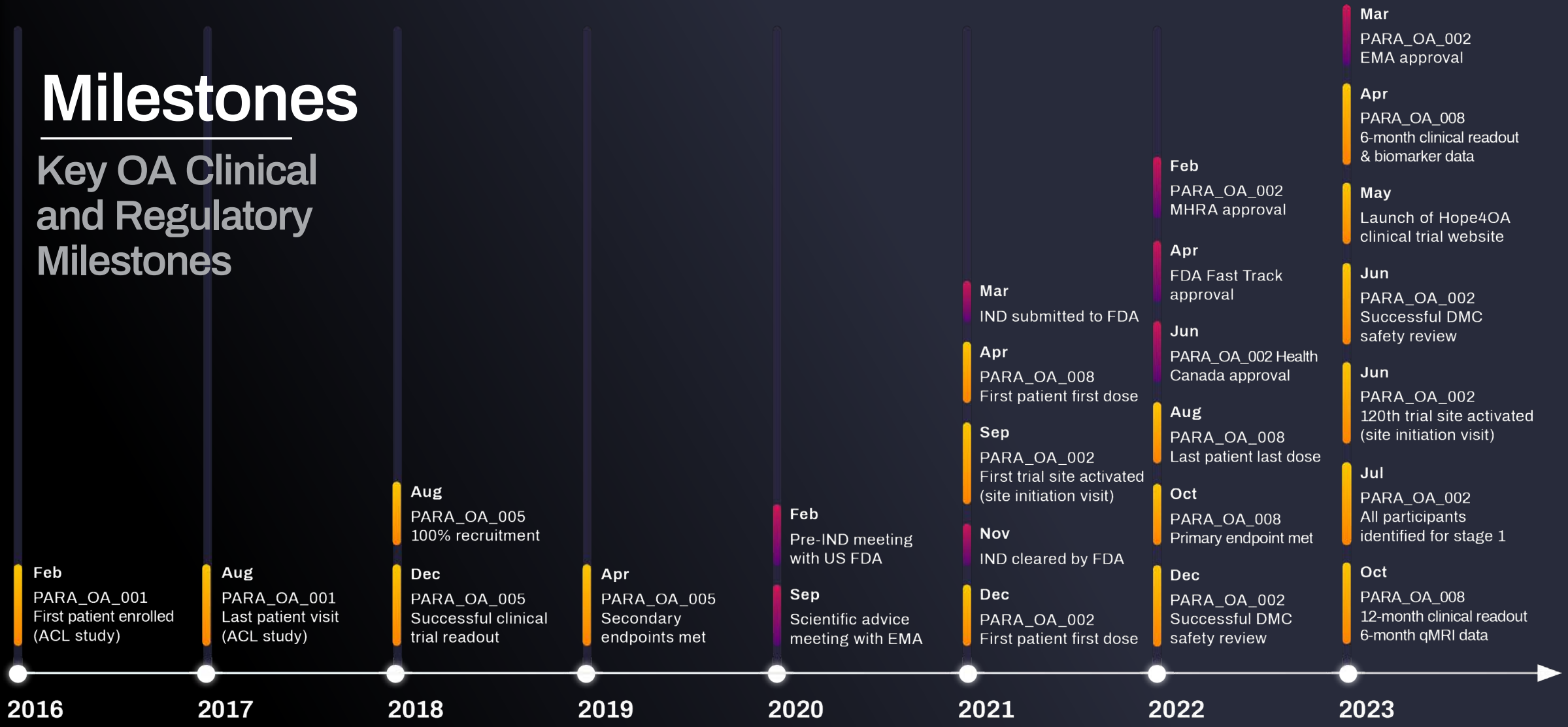
Milestones

Key OA Clinical and Regulatory Milestones



Legend: **DMC** = Data Monitoring Committee; **EMA** = European Medicines Agency; **IND** = Investigational New Drug; **FDA** = Food and Drug Administration (US); **MHRA** = Medicines and Healthcare Products Regulatory Agency (UK).

Clinical trial Regulatory

Key Milestones

Last 12 months

1. Secure funding to advance the development of Paradigm's programs.
   - Capital raising in November 2023 to fund the company through to mid CY25 (without additional licensing revenue).
2. PARA_OA_002 Stage 1, 100% recruitment.
   - Approximately 600 patients randomised into stage 1 of pivotal PARA_OA_002.
3. OA manuscript following Day 56 & Day 168 PARA_OA_008 readout, detailing biomarker and clinical outcomes completed for peer review and publishing.
   - Manuscripts being completed to include significant data recently released detailing structural improvement by quantitative MRI analysis.
4. Presentation of PARA_OA_008 data at major orthopaedic conferences.
   - Three presentations at the 2023 OARSI World Congress on OA.
   - Presentation of data at the American College of Rheumatology Conference 2023.
5. Activities implemented to accelerate phase 3 clinical trial recruitment.
   - Launch of dedicated phase 3 clinical trial website Hope4OA.com.
   - Activation of 40 additional clinical trial sites (120 total) across 7 countries.
   - Introduction of 1nHealth and SubjectWell to increase patient recruitment outreach.
   - NFL Alumni Health Research Partnership.
6. Commercial Transaction.
   - Binding offer received for regional license in MPS, ultimately rejected by Board.
   - Discussions with regional partners remain ongoing for both OA and MPS.

Osteoarthritis

OA



Lead Program Osteoarthritis

Global Phase 3 Achievements

Achievements FY23

PARA_OA_002 Stage 1

- 100% recruitment of stage 1 – 600 participants randomised.
- Interim analysis conducted by the DMC on 300 participants.
- Minimum effective dose of iPPS identified. 2 mg/kg twice weekly to be progressed into next stage of pivotal and confirmatory phase 3 trials.

Data Monitoring Committee (DMC)

- Two formal safety reviews conducted by the DMC for the PARA_OA_002 trial in December 2022 and June 2023. Recommended the trial proceed without modification.
- A third safety review conducted at the interim analysis, no new safety signals identified.

Activities Implemented to Accelerate Recruitment

- Launch of dedicated phase 3 clinical trial website Hope4OA.com
- Activation of 40 additional clinical trial sites (120 total) across 7 countries
- Introduction of 1nHealth and SubjectWell to increase patient recruitment outreach.
- NFL Alumni Health Research Partnership.

Optimal Dose

OA Program

iPPS optimal dose 2 mg/kg twice-weekly

- Extensive clinical experience with 2 mg/kg twice-weekly:
  - **PARA_005**, 121 participants total.
  - **PARA_OA_008**, 61 participants total.
  - **TGA Special Access Scheme** (SAS), >600 patients.
  - **US FDA** Expanded Access Program, 10 ex-NFL players.
- Regulatory authorities requested identification of minimal effective dose.
- Included a dose finding arm in the two-stage global placebo-controlled, randomised, adaptive **PARA_OA_002** phase 3 trial.
- Three non-clinical toxicology studies were completed after the commencement of **PARA_OA_002** concluding no adverse adrenal toxicity events at optimal dose of 2 mg/kg twice weekly.
- Program to proceed with dose of 2 mg/kg iPPS twice weekly for further development based on the above clinical experience and dose finding results.

Lead Program Osteoarthritis

Phase 2 PARA_OA_008

Exploring the durable effects of iPPS on pain, function & OA disease progression.

Biomarker study assessing change from baseline in multiple objective measures associated with disease progression of OA.

- 61 participants received iPPS once or twice weekly, or placebo.
- Follow-up period out to 12 months.

Outstanding top-line results:

- **Primary Endpoint Achieved** - change in one or more synovial fluid biomarkers associated with osteoarthritis disease progression at Day 56.
- **Statistically significant** improvements in pain and joint function at Day 56 (primary end point of the phase 3 OA program).
- **Significant improvements out to 12-months** in pain, function, stiffness, and overall WOMAC scores for twice-weekly iPPS compared to the placebo arm.
- **Positive structural changes** in the knee as measured by quantitative MRI analysis. At Day 168 iPPS treatment demonstrated:
  - increased cartilage thickness and volume indicating cartilage preservation
  - reduced bone marrow lesions
  - reduced synovitis

PARA_OA_008 | Summary of phase 2 randomised controlled clinical trial

iPPS demonstrated efficacy on both objective and subjective measures compared to placebo

OBJECTIVE DATA MEASURES	Day Reported
Improvement in synovial fluid biomarkers associated with OA disease progression	**56,168**
Improvement in structural changes in the knee determined by MRI	**168**

SUBJECTIVE DATA MEASURES	Day Reported
Significant improvement in mean change from baseline in WOMAC pain, function, and overall scores.	**56, 168, 365**
Significant improvement in Patient Global Impression of Change (PGIC)	**365**

Lead Program Osteoarthritis

Global Phase 3

Key Milestones FY24

Protocol Development for Next Stage of Phase 3

- Protocol submission to the FDA, Q1 CY24.
- 2 mg/kg twice weekly dose compared to placebo.
- Trial numbers likely to remain approximately 600 participants.

TGA Provisional Approval Application

- Clinical development plan.
- PARA_OA_008 Manuscript.
- Literature Comparison Manuscript of PPS vs other pharmacologic OA treatments.

Next Stage of Phase 3 Enrolment Commencement

- Sites activated in PARA_OA_002 remain on standby for next stage.
- Recruitment initiatives previously implemented.



Mucopolysaccharidosis

MPS

MPS Achievements

Phase 2 Asset in rare pediatric disease assoc. with inflammation and ongoing musculoskeletal pain – PPS has FDA and EMA orphan designation for MPS



MPS I - Australia

- Open label trial dosing subjects weekly SC for 12-weeks, then every other week for a total of 52-week.
- Interim top-line data reported PPS was well tolerated, demonstrating reduction in pain and GAGs and improvement in function.
- Changes in biomarker profiles at 49 and 73 weeks of iPPS treatment suggest that iPPS has the potential to modulate the biomarkers that are associated with joint degeneration and arthralgia.

MPS VI - Brazil

- A double-blind placebo-controlled trial with 13 subjects. Dosed weekly SC for 24-weeks.
- Primary endpoint is safety, key secondary endpoints are pain and function.
- Principal Investigator is Dr Roberto Giugliani being conducted in 2 sites in Brazil. Dr Giuliani is considered the leading expert on MPS in LATAM.
- Attractive to pharma companies as:
  - limited requirement for marketing/ training – Patients are known due to the current standard of treatment enzyme replacement therapy needs.
  - Higher penetration rate of iPPS due small community of patients and highly engaged patient advocacy groups.

Rare Disease Program

MPS I & VI

Key Focus FY24

Following the completion of the two phase 2 studies in MPS I and MPS VI, Paradigm's clinical expenditure has concluded with the rare disease program to focus on:

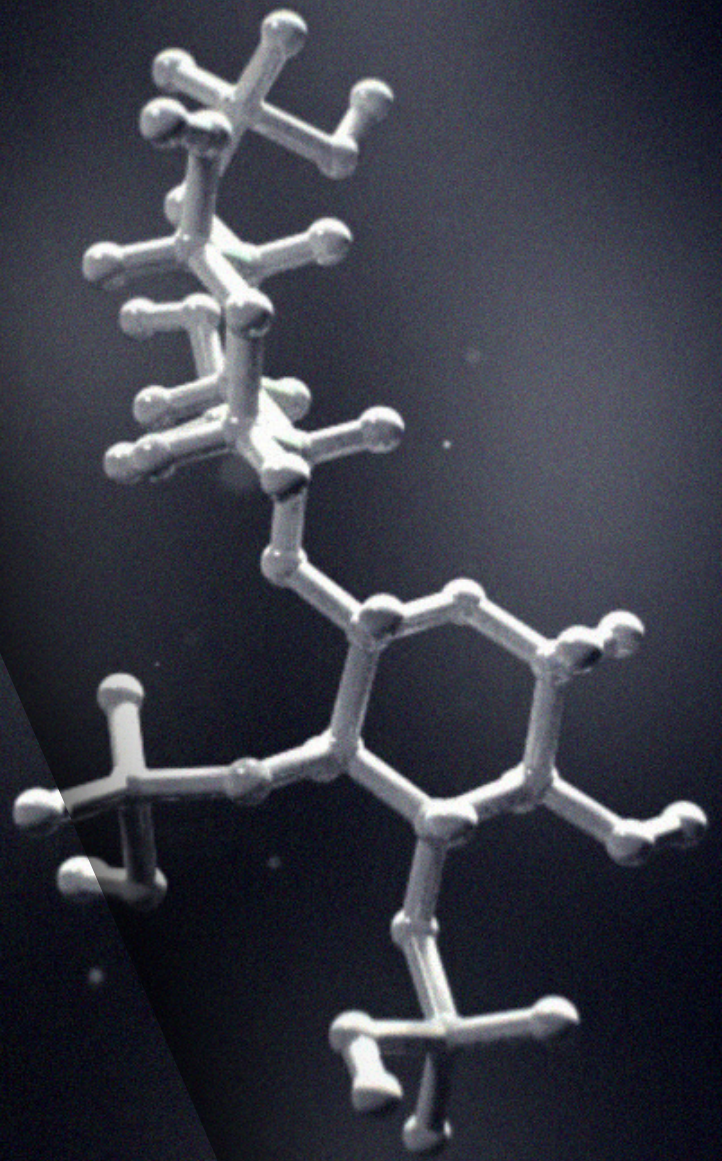
- Top-line data for MPS VI readout,
- Potential expedited or provisional approval submissions (Brazil, Australia),
- Continued discussions with potential partnering companies to progress this rare disease asset through to commercialization,
- Manuscript completion for MPS I and MPS VI for peer review and publishing.

Key Activity

Regulatory Program

Reg meetings	Agency / program	Program	Topic / Purpose	Timeline (CY)
Provisional determination application	TGA	OA	Indication: Pain and function • TGA to assess whether data from 008 satisfactorily meet the 5 criteria to be eligible for the provisional approval pathway.	Q1 24
Type D	FDA	OA	Adrenal Meeting • Review of non-clinical and clinical data	Q1 24
Protocol Review	FDA	OA	Protocol Review for next stage of phase 3 program	Q1 24
Type C/D	FDA EMA	OA	Biomarker/DMOAD • Establish a regulatory pathway	Q2 24
Pre-submission meting	TGA	MPS	To discuss with TGA whether data from MPSVI-001 and MPSI-001 satisfactorily meet the 5 criteria to be eligible for the provisional approval pathway.	Q2 24
End of Phase meeting	ANVISA	MPS	• Presentation of nonclinical data • Presentation of Phase 2 data • Proposed Phase 3 Synopsis • Registration pathway feedback	Q2 24

Company UPDATE





Partnering Update

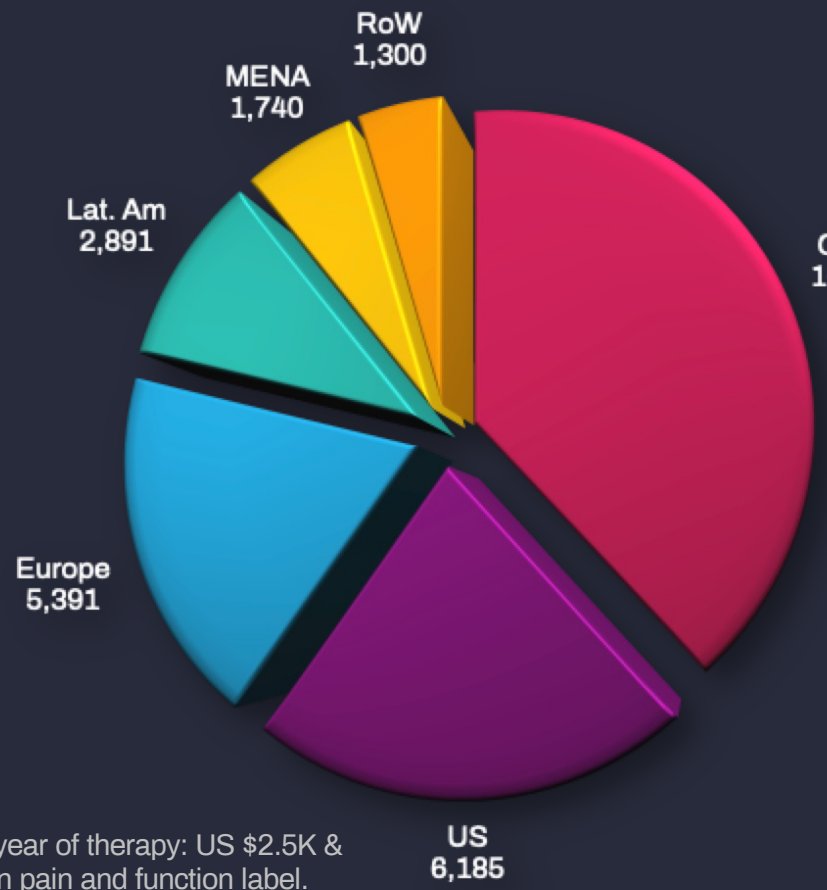
Beverley Huttmann
Head of Business Development

Commercial strategy for iPPS via partnerships

- Global or regional companies to achieve the best value for shareholders, for example
  - MPS regional – due to geographic distribution of people with MPS.
  - China OA – major opportunity.
- Paradigm attends major partnering events and has engaged the services of two consultancies to assist with partnering activities:
  - Plexus Ventures globally except China.
  - Yafo Capital (Shanghai) for China.
- Key data releases influence interest and activity.
  - 12-month clinical durability and 6-month quantitative MRI data for osteoarthritis.
  - Phase 2 data for MPS VI.
- Paradigm is on track to secure a licensing agreement in one or multiple regions by the end of FY24.

Why China?

Knee OA at 10% uptake (USD $27B)

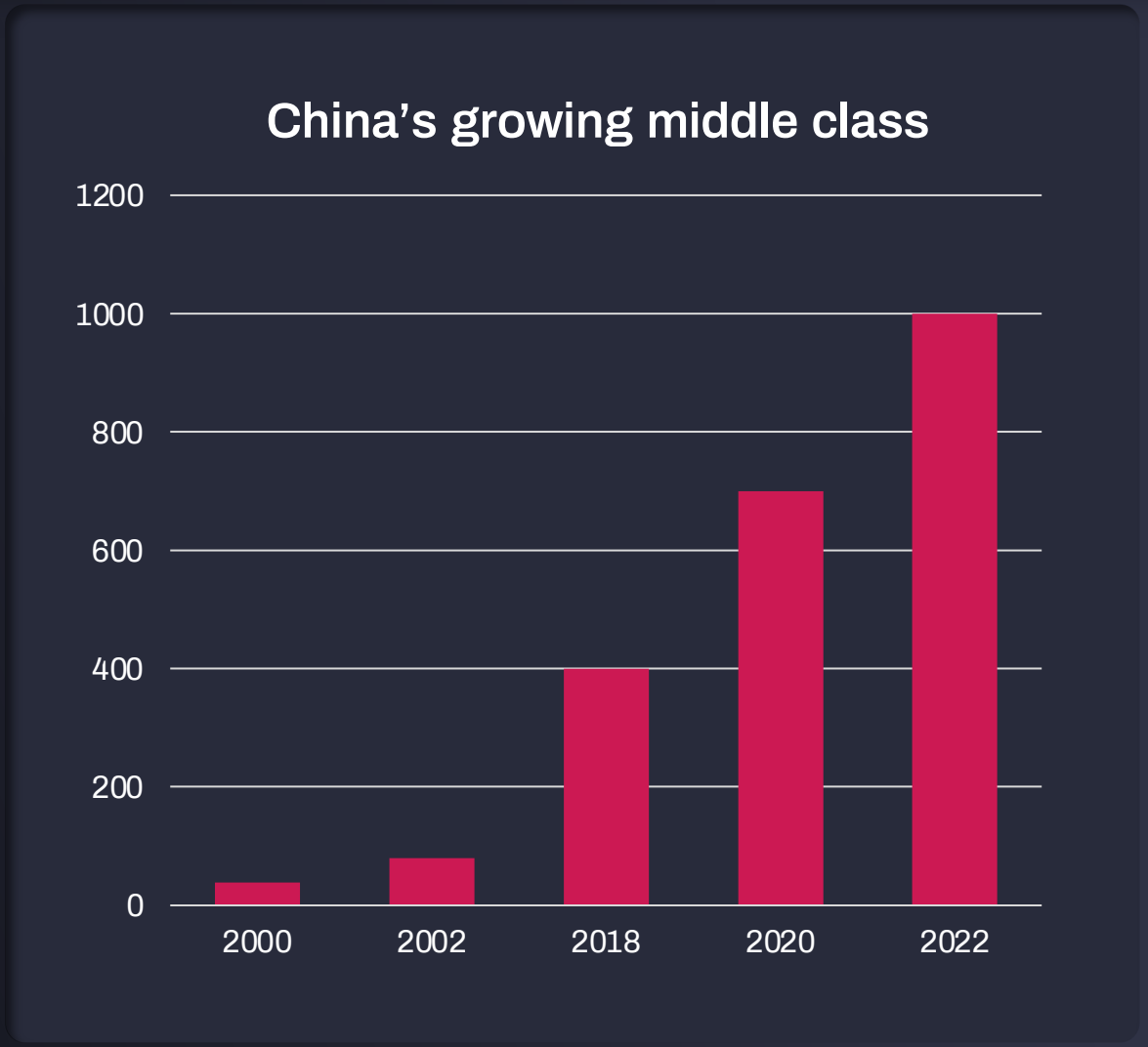


Assumed price per year of therapy: US $2.5K & $1K* ROW based on pain and function label.
*Pricing to be confirmed in ex-US regions.

Snapshot - China

>70% of the nation's 1.4 Bn population is employed, urban, professional middle class

- **36% of drug purchases** are fully or part funded by private health insurance.
- **72% of drug purchases** are fully or part funded by the patient.

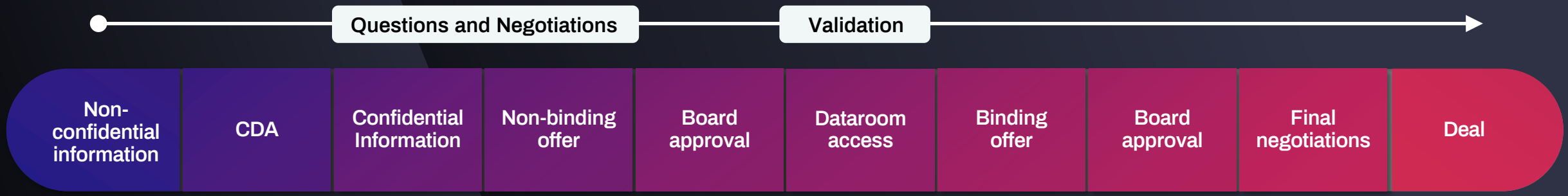


Health care in China

An evolving system

In the last decade, the Chinese healthcare market has evolved significantly & continues to do so.

- In 2018 the China National Drug Administration (CNDA) published new Guidelines for the Acceptance of Overseas Clinical Trial Data for Drugs.
- Prior to 2018 new drugs could not be sold in China without undergoing domestic clinical trials – this delayed market access to China.
- Now clinical trials conducted in other countries may be accepted providing a subset of the participants are ethnic Chinese. This allows faster access to the Chinese market with lower costs for pharmaceutical companies.
- Imported medicines may be registered and reimbursed in China.
- Registration in China does not rely on prior registration in other markets.



Partnering Process

Current Partnering Activity

Region	Indication(s)
China	OA
Latin America	OA, MPS
Gulf Corporation Countries (GCC)	OA, MPS
United States	OA
Europe	MPS

Finance

Funding Position

Recent capital raising of approximately A$30 million to fund the company through to mid CY25 (without additional licensing revenue), providing the company with:

- A$69.4m[1] pro forma cash balance post capital raising.
- A$103.2m[2] pro forma cash balance post capital raising (including Options exercise proceeds of A$33.8m).

- Potential partnering deals to provide material additional non-dilutive cash runway.

- Implementation of cost-reduction strategies to ensure capital spend is focused on progressing OA program through phase 3 program.

[1] Cash balance and R&D Refund provision as at 30 September 2023 and assumes A$28.5m capital raising (excluding costs of the Offer)
[2] Cash balance and R&D Refund provision as at 30 September 2023 and assumes A$28.5m capital raising (excluding costs of the Offer) and full exercise of all Options

FY24 Key Outcomes

1. Phase 3 OA program protocol acceptance from US FDA for progression with lowest effective dose (2 mg/kg twice weekly).
2. Regional licensing agreement(s) in OA and MPS.
3. Pivotal study next stage commencement of recruitment.
4. Confirmatory study start-up and recruitment initiation.
5. TGA provisional approval determination application submission.
6. Peer-reviewed publication of PARA_OA_008 phase 2 clinical trial in key scientific journal.

Expected Key Milestones | Next 18 Months

H1 | CY24

Phase 3 OA program
FDA protocol review for next stage of Phase 3 program

TGA Provisional Approval OA
Submission for next stage determination application

Phase 3 OA program
Next stage enrollment commencement, subject to regulatory agreement.

Regional licensing agreement(s) in OA and MPS

H2 | CY24

TGA Provisional Approval OA
Dossier Submission, pending determination application approval

PARA_OA_008
Manuscript peer reviewed and published in scientific journal

Phase 3 OA Program
Commencement of confirmatory phase 3 study

MPS program
Potential expedited or provisional approval submissions (Brazil, Australia)

MPS
MPS I & VI data manuscripts peer reviewed/published in scientific journals

H1 | CY25

Phase 3 OA program
100% recruitment of pivotal phase 3 study.

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