

## ASX Announcement

3 March 2021

### Regeneus Company Update Investor Webcast Presentation

**Regeneus Ltd (ASX: RGS) (Regeneus or the Company)**, a clinical-stage regenerative medicine company, today advises it has released an updated investor presentation.

The presentation will be delivered to investors by CEO Karolis Rosickas during Regeneus' Company Update Investor Webcast taking place at 11:00am Australian Eastern Daylight Time (AEDT) this morning via Zoom.

To register for the webcast, please follow this link:

[https://us02web.zoom.us/webinar/register/WN\\_YyKYF3USS0WusNbnBlafAQ](https://us02web.zoom.us/webinar/register/WN_YyKYF3USS0WusNbnBlafAQ)

*Registered participants will receive a confirmation email containing the Zoom access link and alternative phone dial-in details.*

**-ENDS-**

#### **About Regeneus**

Regeneus Ltd (ASX:RGS) is a Sydney-based clinical-stage regenerative medicine company using stem cell technologies to develop a portfolio of novel cell-based therapies. The regenerative therapies seek to address unmet medical needs in human health markets, focusing on neuropathic pain, including osteoarthritis and various skin conditions, with its platform technologies Progenza and Sygenus. Visit [www.regeneus.com.au](http://www.regeneus.com.au) for more information.

#### **Authorisation & Additional information**

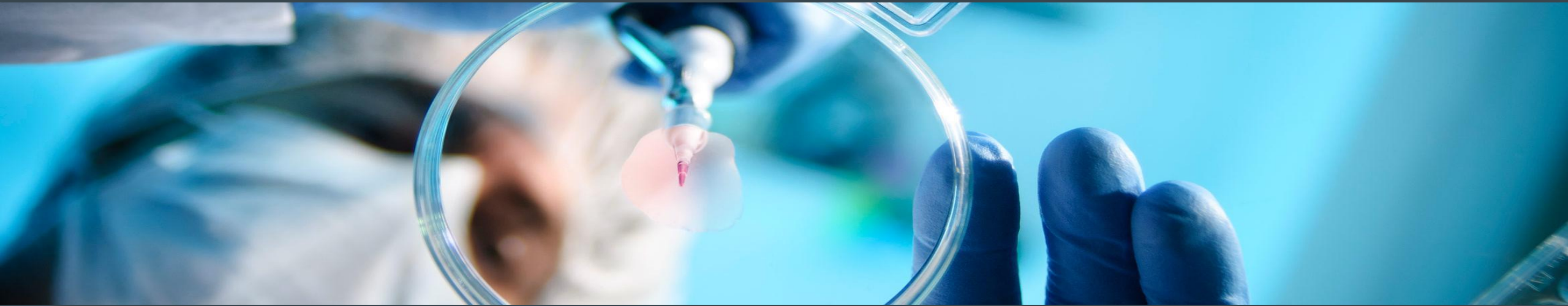
This announcement was authorised by the Board of Directors of Regeneus Ltd

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# Company update presentation

Developing next generation pain management and inflammation therapeutics

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# Company overview

## Background

- Regeneus (“RGS”) is a pioneer cell therapy company founded in Sydney in 2007
- The company went public (ASX:RGS) on the Australian Stock Exchange in 2013
- Two platform technologies leveraging proprietary IP in allogeneic adipose-derived mesenchymal stem cells (“MSC”) and their bioactive secretome (incl. cytokines, extracellular vehicles, miRNA)
- Successful Phase I trial of Progenza in knee osteoarthritis completed in 2017
- Signed Progenza collaboration and licensing partnership with Kyocera in Japan in 2020
- The company has filed or obtained over 80 patents in key geographies

## Financial information

Share price <a href="#">(02 Mar 2021)</a>	A\$ 0.115
Shares issued	300.3m
<b>Market capitalisation</b>	<b>A\$ 34.5m</b>
Cash <a href="#">(as of 31 Dec 2020)</a>	A\$ 4.1m
Debt <a href="#">(as of 31 Dec 2020)</a>	-
<b>Enterprise value</b>	<b>A\$ 30.4m</b>

## Experienced Board and management team



**Barry Sechos**  
Independent Chairman

- 20+ years experience as a director, business executive, and corporate lawyer
- Executive Director of Sherman Group



**Leo Lee**  
Non-Executive Director

- President, Novartis Japan
- 20+ years in pharma
- Former President of Allergan and Merck Japan



**John Chiplin**  
Non-Executive Director

- MD of Newstar Ventures
- Former CEO of three listed biotechnology, cancer immunotherapy and software companies



**Karolis Rosickas**  
Chief Executive Officer

- 17 years experience in healthcare and technology
- Co-founder and CEO of SingCell and OME Health
- VP at HSBC M&A in London



**Prof Graham Vesey**  
CSO & Executive Director

- Regeneus co-founder
- Co-founder of BTF, sold to BioMerieux in 2007
- Adjunct Professor at Macquarie University



**Dr Charlotte Morgan**  
Head of R&D

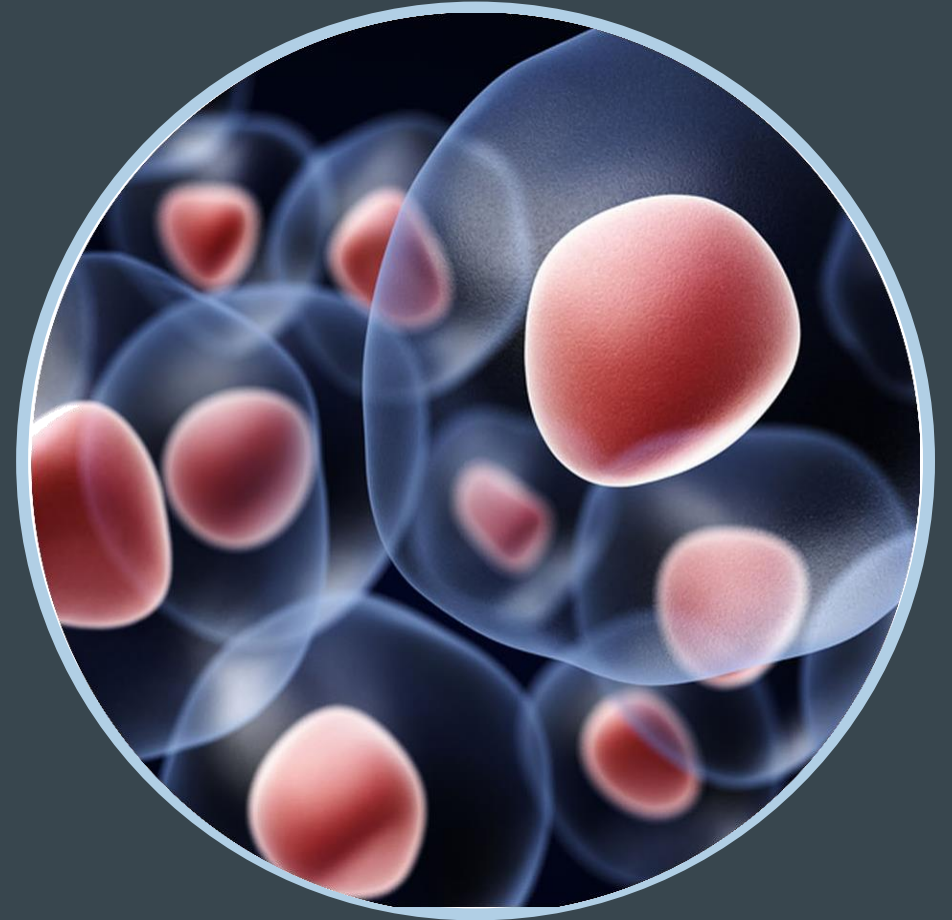
- 20+ years in managing product development and innovation
- PhD in microbiology
- Joined Regeneus in 2012



**Dr Sinead Blaber**  
Clinical Director

- 10 years experience in biotechnology industry
- Directed Progenza STEP Trial
- PhD in Biotechnology
- Joined Regeneus in 2009

# Technology and products



# Proprietary allogeneic mesenchymal stem cells and secretome platform

## Mesenchymal stem cells

- Multipotent stem cells, which perform multiple functions in human body including direct differentiation, activation of resident stem cells and secretion of bioactive molecules (secretome)



## Bioactive Secretome

- Bioactive molecules (cytokines, chemokines, growth factors, extracellular vesicles) secreted by MSCs
- Reduces inflammation and promotes tissue repair
- Improves functionality and viability of MSCs



The combination of MSCs and the bioactive MSC secretome exerts a more powerful therapeutic effect

### Allogeneic cells

- Derived from a single donor
- Can be used in millions of patients

### Adipose-derived

- Adipose contains 500-1000x more MSCs than bone marrow or other sources

### Safe

- MSCs are immune-privileged cells, which escape patient's immune system without the risk of rejection
- No genetic modification of cells

### Established mechanism of action

- Immuno-modulatory properties of MSCs and bioactive secretome
- Direct cell differentiation
- Endogenous repair

# How Regeneus platform technology is different?

## MSCs / iPSCs only

- Generation 1.0 therapies
- ✗ Provide only limited functionality through differentiation and engraftment

## Extracellular vesicles (EVs)

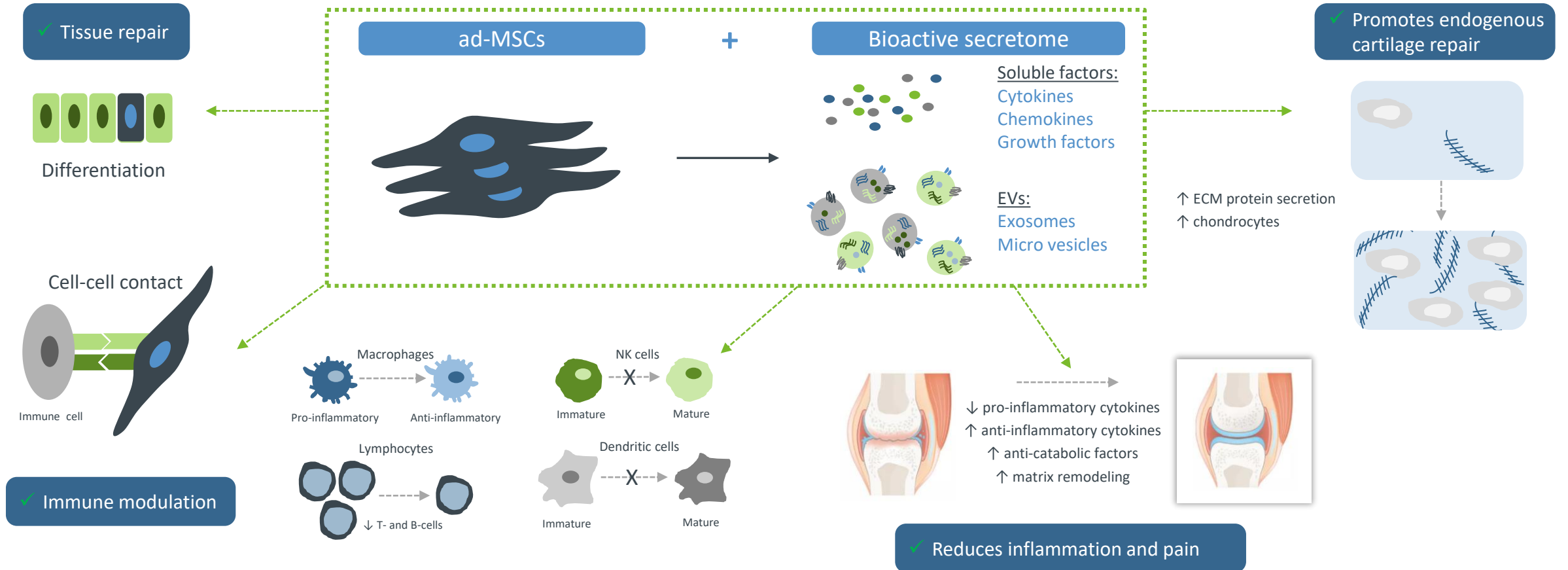
- Novel, early-stage modality
- ✗ Expensive isolation and purification process
- ✗ Manufacturing scalability not proven yet
- ✗ Still unknown mechanism of action of individual EVs
- ✗ Years away from regulatory approvals

## Progenza MSCs and Bioactive Secretome

- ✓ Secretome enhances viability and functionality of MSCs
- ✓ Secretome has independent immunomodulatory functions in inflamed environment
- ✓ Scalable and cost-effective manufacturing process

# Established mechanism of action

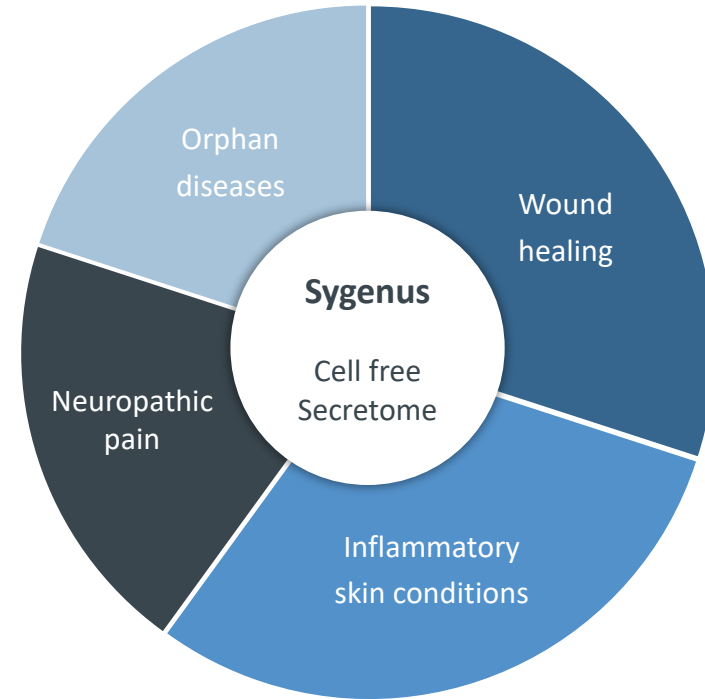
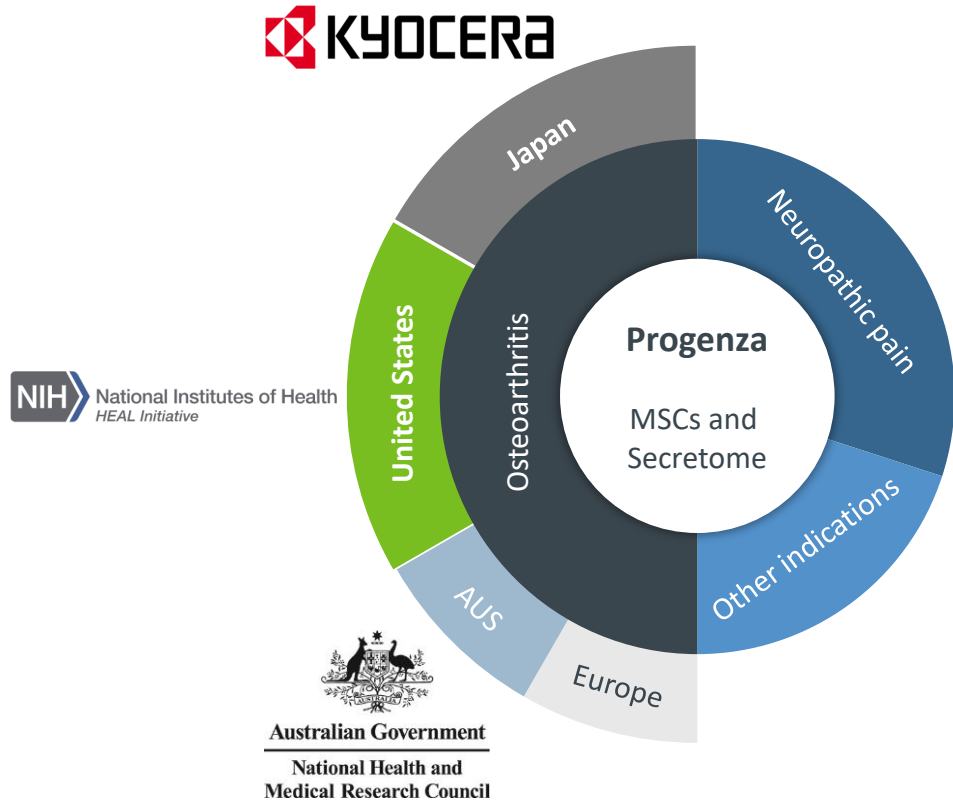
## PROGENZA



The combination of MSCs and the bioactive MSC secretome in Progenza exerts a powerful therapeutic effect via repair and regeneration of endogenous joint tissues, reducing inflammation, modulation of the immune system and pain relief

# Scalable product platforms

Multiple opportunities in pain and inflammation focused indications

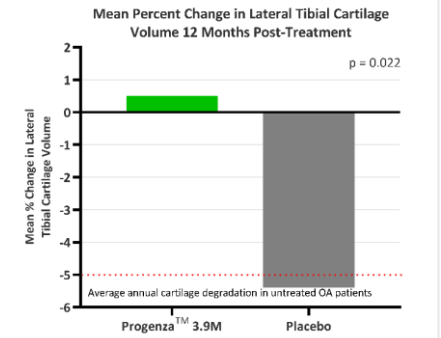
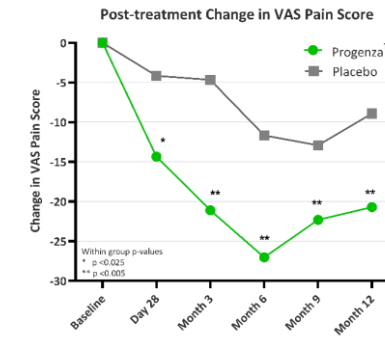


The product platforms are protected by a portfolio of 80+ patents covering multiple indications in key markets and expiring in late 2030s

# Strong nonclinical and clinical data

## Progenza Osteoarthritis Phase 1 (STEP) <sup>1</sup>

- Confirmed the Primary Endpoints of **safety** and **tolerability** at both low and high doses with a **single injection**
- Confirmed the Secondary Endpoints of efficacy:
  - Pain:** significant, rapid and sustained pain relief achieved via VAS and WOMAC Pain scores
  - Cartilage:** halting of disease progression 12-months post-treatment



## Progenza Neuropathic pain Preclinical

- Neuropathic pain is central in many disease indications (chronic lower back pain, trigeminal neuralgia, etc.) with no cure for the underlying causes
- Performed a study on Chronic Constriction Injury (CCI) model using rats and touch stimulator
- Demonstrated that a single injection of Progenza modifies disease in 14 days

## Sygenus Various indications Preclinical

Primary indication	Study Type	RoA	End Date	Subject #	Conclusions
Topical safety	Safety & tolerability	Topical	Aug 2017	33 humans	✓ <b>Safety:</b> Safe & well tolerated in acne prone patients
Topical safety	Safety – RIPT	Topical	Oct 2017	50 humans	✓ <b>Safety:</b> non-sensitizing and non-irritating
Acne	Safety & efficacy	Topical	Jan 2018	30 humans	✓ <b>Safety:</b> Safe and well tolerated ✓ <b>Efficacy:</b> Significant improvement in acne measurements
Age spots	Safety & efficacy	Topical	Mar 2018	36 humans	✓ <b>Safety:</b> Safe and well tolerated ✓ <b>Efficacy:</b> Significant reduction in age spot size and pigmentation

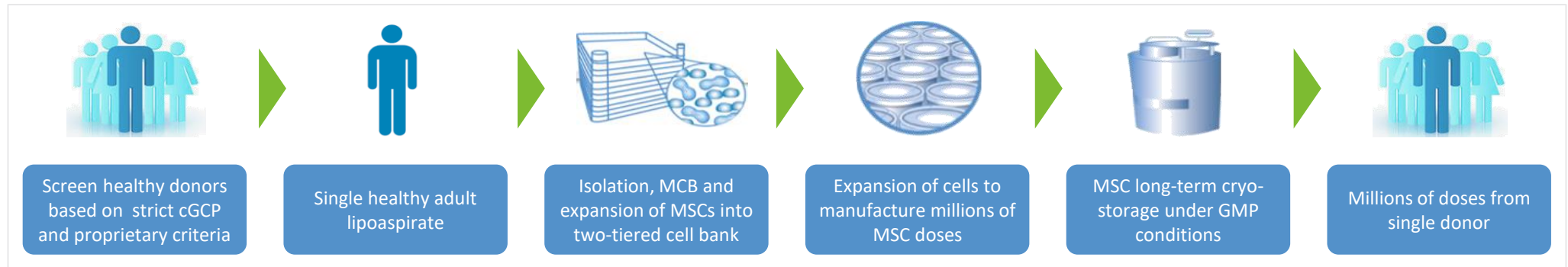
Source: (1) Kuah D, Sivell S, Longworth T, et al. Safety, tolerability and efficacy of intra-articular Progenza in knee osteoarthritis: a randomized double-blind placebo-controlled single ascending dose study. J Transl Med 2018;16:49.

# Established chemistry, manufacturing and controls (CMC) process

## Source material

- Adipose-derived: adipose contains 500-1000 times more MSCs than bone marrow
- Allogeneic: multiple patients from a single donor. Improved product safety, potency, and consistency
- Rigorous donor screening process
- No genetic reprogramming of cells

## Process overview



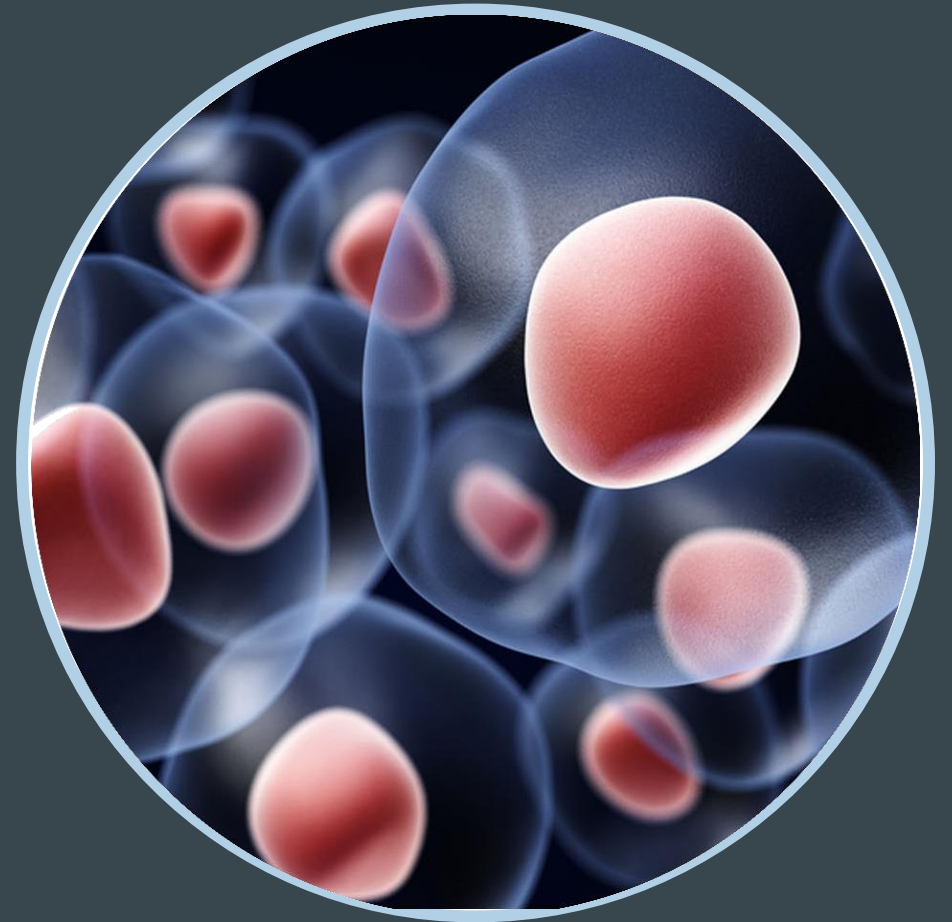
## Advantages

- Optimised, highly scalable manufacturing process of up to 300 million doses from a single donor
- No source material or process variability, resulting in a homogenous final product
- Lower cost of goods (COGS) compared to autologous therapies, pluripotent stem cell therapies, or EV therapies
- Potential for further COGS reduction by transitioning to a 3D bioreactor-based manufacturing process

## Current status

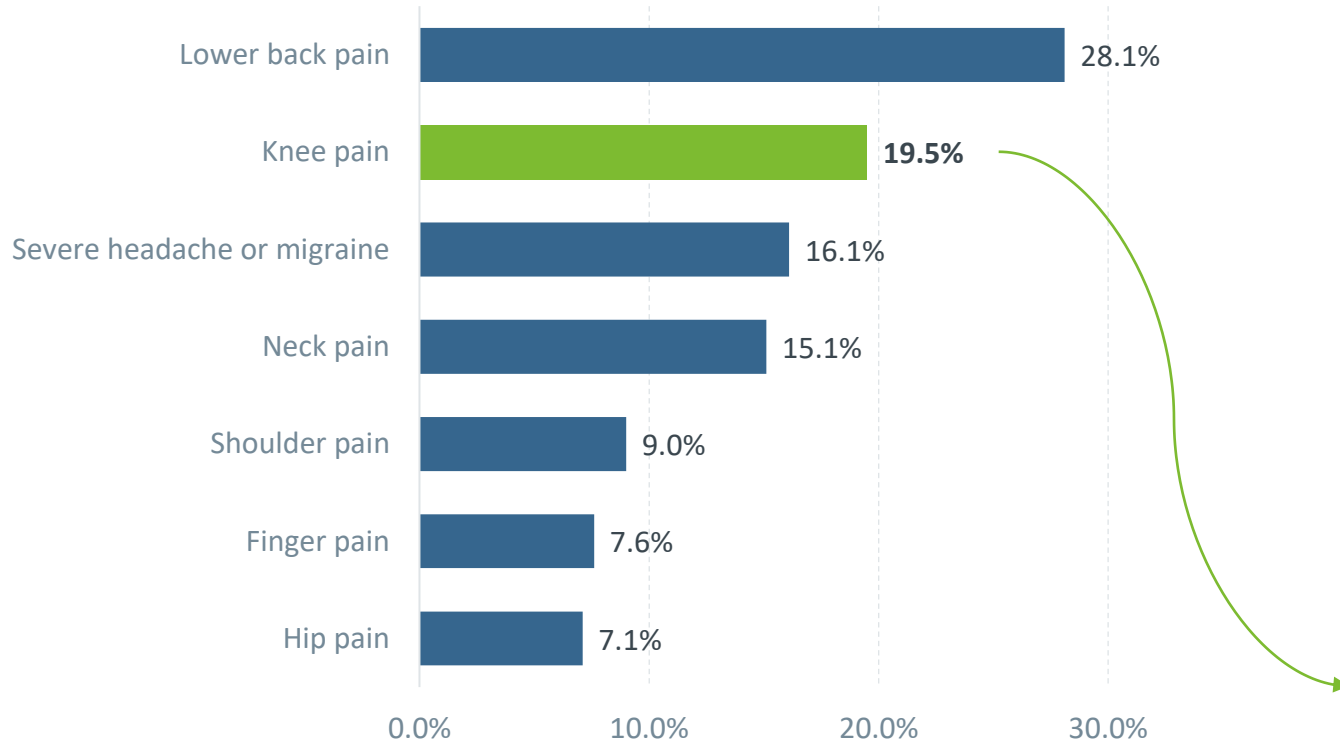
- Advanced process development work for manufacturing cGMP Master Cell Bank (MCB) with a US contract manufacturing organisation
- Final Product (FP) will be available in late 2021 for Progenza OA Phase 2 trials in the US and Australia
- Well characterised final product
- Established Quality Control (QC) and product release criteria

# Pain and osteoarthritis market opportunity



# Pain – large and growing problem

## Prevalence of chronic pain <sup>(1)</sup>



## Large addressable market

**1.5bn**  
people worldwide suffering from pain <sup>(2)</sup>

**50%**  
of patients report inadequate relief <sup>(2)</sup>

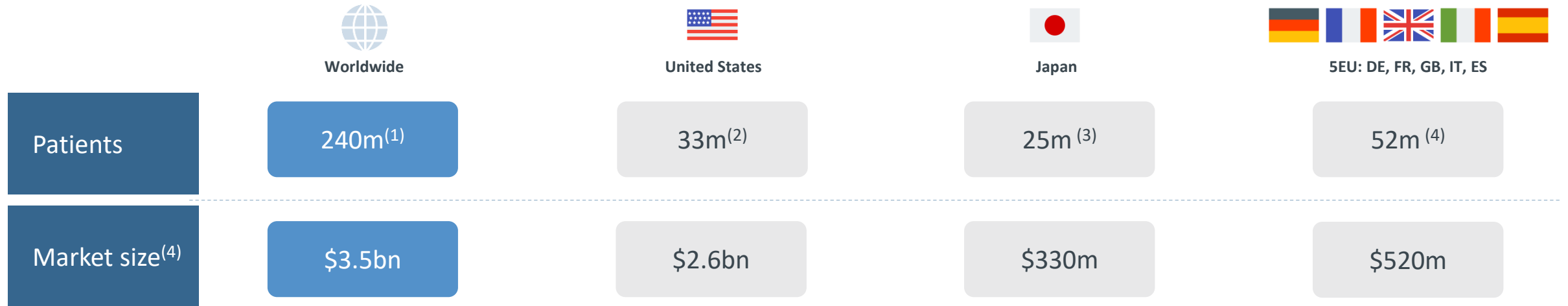
**Knee Osteoarthritis**  
is pain and inflammation around the joint  
from 'wear and tear' on the tissue

Figure: Age-adjusted prevalence rates of select causes of chronic pain in US adults

Sources:  
(1) Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington DC: The National Academies Press; 2011  
(2) Chronic Pain and the Health of Populations. Boston University; 2017

# Opportunity in knee osteoarthritis

## Large addressable market



## Attractive market characteristics



### Sources:

- 1) Osteoarthritis Action Alliance, <https://oaaction.unc.edu/oa-module/oa-prevalence-and-burden/>
- 2) Centers for Disease Control and Prevention (CDC)

- 3) Knee osteoarthritis only. *Epidemiology of osteoarthritis in Japan : the ROAD study*. 2011
- 4) Estimate for 2026. *OpportunityAnalyzer: Osteoarthritis – Opportunity Analysis and Forecasts to 2026*. GlobalData

# Current osteoarthritis treatment market

Current treatments only provide pain relief – not disease modification

less severe OA

less invasive therapies

50% of diagnosed and prevalent knee OA is moderate-severe  
~5% cartilage loss per year as disease progresses

more severe OA

more invasive therapies



Lifestyle changes

Weight management, exercise and self-management

- ✗ Limited uptake
- ✗ Short-term adherence



Pain relief

Pharma: Paracetamol, non-steroidal anti-inflammatory drugs, opioids  
Injectables: Hyaluronic Acid or Corticosteroid Injections

- ✗ Target symptoms, not the cause
- ✗ Safety concerns
- ✗ Short-term relief, limited efficacy
- ✗ Risk of cartilage degradation with injectables



Disease modification

No existing therapies



Surgery & invasive procedure

Knee Replacement  
Revision Surgery  
Bone Marrow Stimulation  
Bone Realignment

- ✗ Invasive surgical intervention
- ✗ Long rehabilitation time
- ✗ Limited prosthesis lifespan
- ✗ Expensive

# Where Progenza™ fits in current osteoarthritis treatment market

Progenza addresses an unmet need in the current treatment market by providing disease modification and pain relief to address patient symptoms without having to undergo surgery and invasive procedures

less severe OA

50% of diagnosed and prevalent knee OA is moderate-severe  
~5% cartilage loss per year as disease progresses

more severe OA

## PROGENZA

Long-term pain relief, DMOAD, delayed surgery



Lifestyle changes

Weight management, exercise and self-management

- ✗ Limited uptake
- ✗ Short-term adherence



Pain relief

Pharma: Paracetamol, non-steroidal anti-inflammatory drugs, opioids  
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Disease modification

No existing therapies

- ✓ Progenza - a **safe, potent** treatment before invasive surgical intervention is required



Surgery & invasive procedure

Knee Replacement  
Revision Surgery  
Bone Marrow Stimulation  
Bone Realignment

- ✗ Invasive surgical intervention
- ✗ Long rehabilitation time
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# Competitive landscape

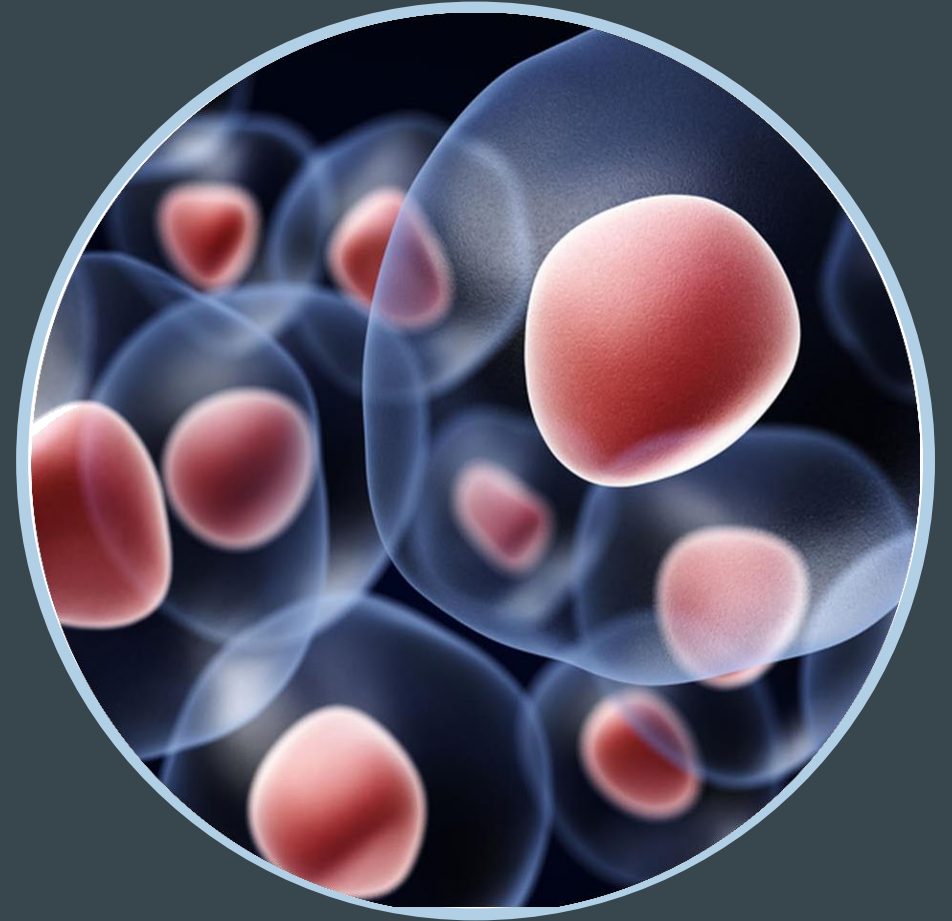
Progenza is well positioned to become the first in class disease modifying therapy in knee osteoarthritis



Product	Progenza	Tanezumab	Fasinumab	AlloJoin	Cymerus	PPS	Invossa
Stage	P2	BLA	P3	P2	P3	P3	P3 (tbc)
Treats symptoms (pain)	✓	✓	✓	✓	unknown	✓/✗	✓
Potentially disease modifying	✓	✗	✗	unknown	unknown	✗	✓
Safety profile	✓	✗	✗	✓	unknown	✓	✗
Cost of manufacturing	✓	✓	✓	✓	✓/✗	✓	✗

Source: GlobalData, internal company analysis

# Value creation plan



# Value drivers for Regeneus

Multiple levers to create shareholder value

## Licensing and partnerships

- Launch Progenza OA in partnership with Kyocera in Japan
- **Explore licensing opportunities for Progenza OA worldwide, ex-Japan**
- Progenza licensing opportunities in other indications (e.g. neuropathic pain)
- Licensing of Sygenus

## Independent development

- **Prepare for Progenza OA Phase 2 trial in the US**
- Prepare for Progenza OA Phase 2 trial in Australia
- Grant opportunities in the US and Australia
- Sygenus co-development with medical dermatology, cosmetics companies, and Government agencies
- Research partnerships with Monash University, University of Adelaide, UTS, and A\*STAR Singapore

## Strategic M&A

- **Consider strategic exit to a large pharma or a large cap biotech company**
- Assess synergistic bolt-on acquisitions

# Development pipeline



# Collaboration and licensing agreement with Kyocera for osteoarthritis in Japan



## Expedited path to market in Japan



### Background

- Japan headquartered global diversified conglomerate
- Revenue \$15.5bn, market capitalisation \$23.6bn
- Life & Environment division manufactures medical products, including orthopaedic joint implants
- With no. 4 position in prosthetic knee market, Kyocera has an established network of orthopaedic physicians to distribute Progenza™ knee OA cell therapy
- Entering into the agreement with Regeneus demonstrates Kyocera's belief in the Progenza™ technology

### Deal

- The Collaboration and License Agreement was signed in August 2020
- Includes upfront and milestones payments of US\$19m, and single to double-digit royalties on product sale
- Kyocera responsible for product development, manufacturing, regulatory, and commercialisation processes in Japan
- Exclusivity for knee osteoarthritis in Japan
- **Regeneus retains the right to negotiate licenses with parties within Japan for indications other than knee OA and outside of Japan for all indications**

### Accelerated timeline to Conditional Approval



# Progenza™ osteoarthritis opportunity in United States

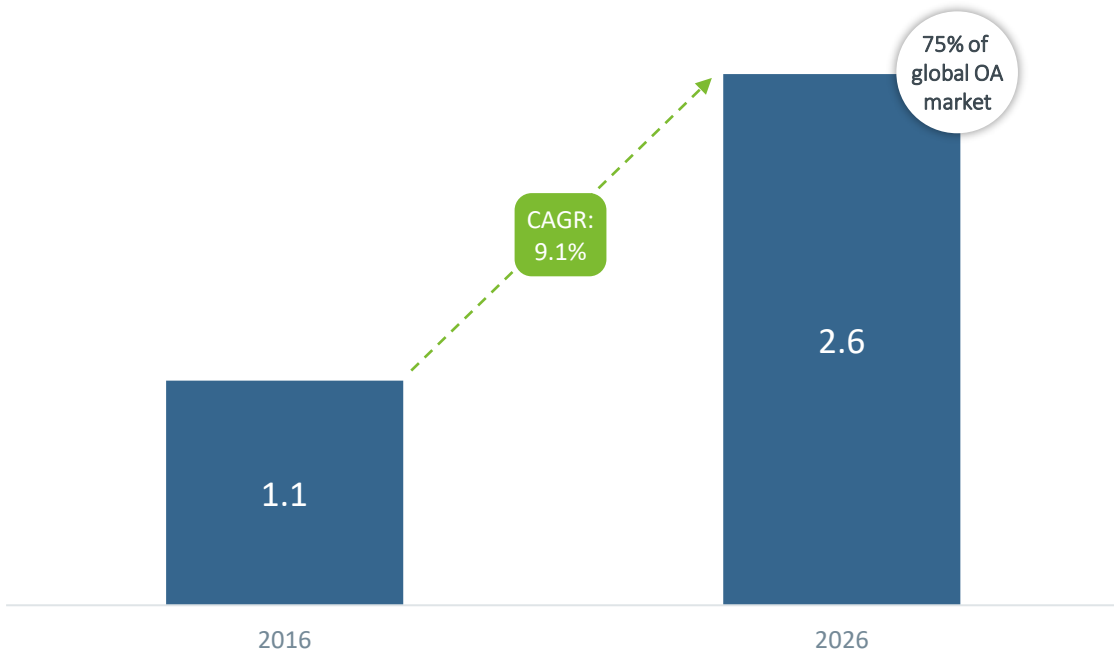


Regeneus plans to initiate a Phase 2 trial in the US in 2022

## Market opportunity

US osteoarthritis therapeutics market (USD bn)

US osteoarthritis patients



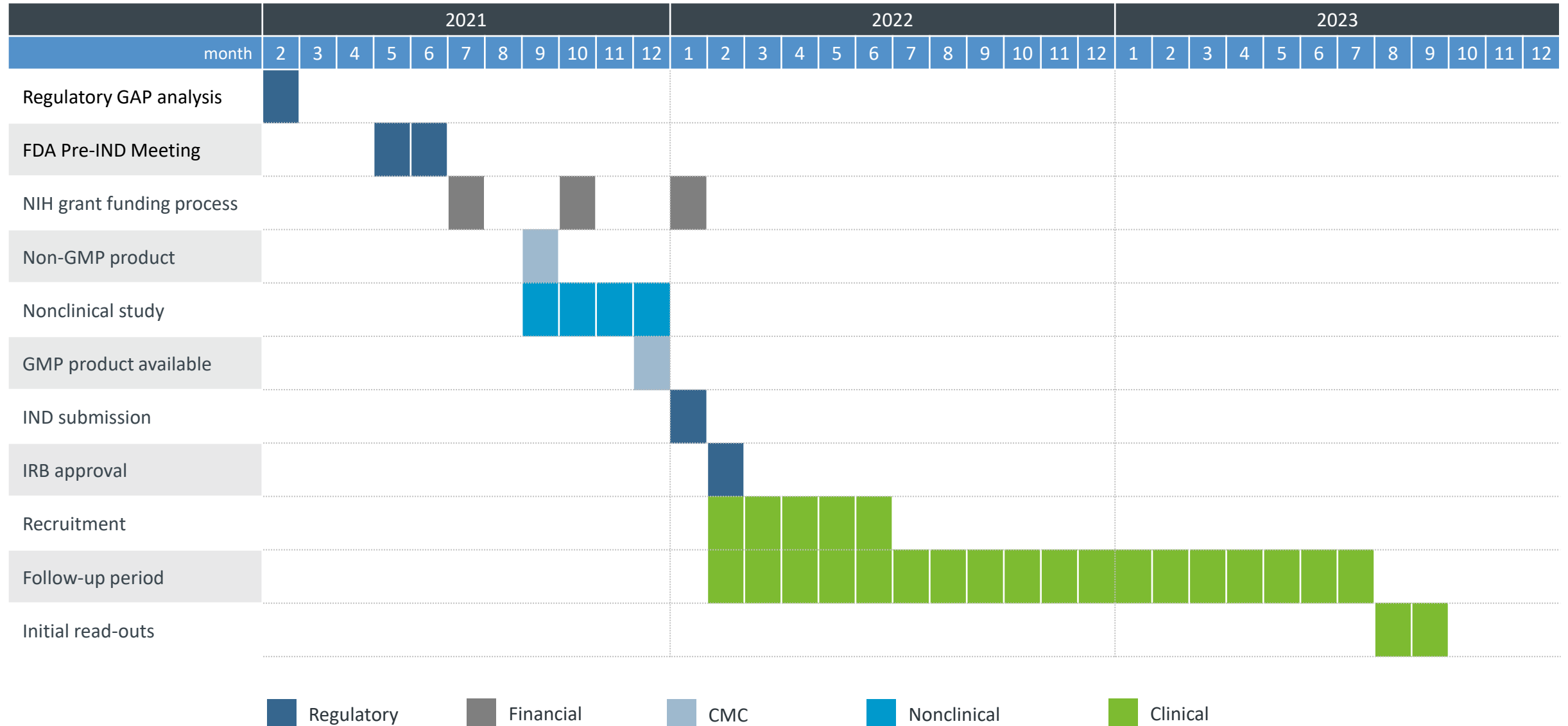
33 million

1 in 7 adults

Source: GlobalData

Source: Osteoarthritis Action Alliance

# Expected Progenza™ osteoarthritis US Phase 2 trial timeline



# Other near term value accreting opportunities



Product	Geography	Stage	Indication	Status	Timing
Progenza	Australia	Phase 2	Knee osteoarthritis	<ul style="list-style-type: none"> <li>• Similar clinical trial design to the Progenza OA Phase 2 trial in the US</li> <li>• Ability to use the same Progenza cGMP product as in the US</li> <li>• A grant application to fund the trial is being reviewed by the NHMRC</li> </ul>	Q2 2021
Sygenus	Australia	Phase 1	Pain	<ul style="list-style-type: none"> <li>• Phase 1 trial with human subjects in a pain indication</li> </ul>	Q2 2021

# Regeneus investment highlights



Leading, differentiated technology platform

- A unique combination of stem cells and their bioactive secretome exerts superior therapeutic effect
- Applicable in a broad range of pain and inflammation indications
- A scalable and cost effective manufacturing process
- IP has been developed and is fully owned by Regeneus



Attractive market potential

- Global pain management market is a growing and significant multi billion-dollar opportunity
- Large unmet market need for disease-modifying therapeutics in osteoarthritis
- Secular tailwinds in the osteoarthritis market – ageing population and increasing prevalence of obesity



Progenza™ OA Phase 2 ready asset

- Progenza OA is a Phase 2 ready asset with strong nonclinical and Phase 1 data
  - validated by Kyocera during the extensive technology due diligence process
- Active pipeline of potential licensing opportunities in key geographies



Near term value accreting opportunities

- Kyocera partnership to deliver additional US\$13m in milestone payments in the next 3-4 years
- Opportunities beyond osteoarthritis in Japan:
  - Progenza OA Phase 2 trial in the United States (2022)
  - Progenza OA Phase 2 trial in Australia (2022)
  - Sygenus Pain Phase 1 trial in Australia (2021)

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