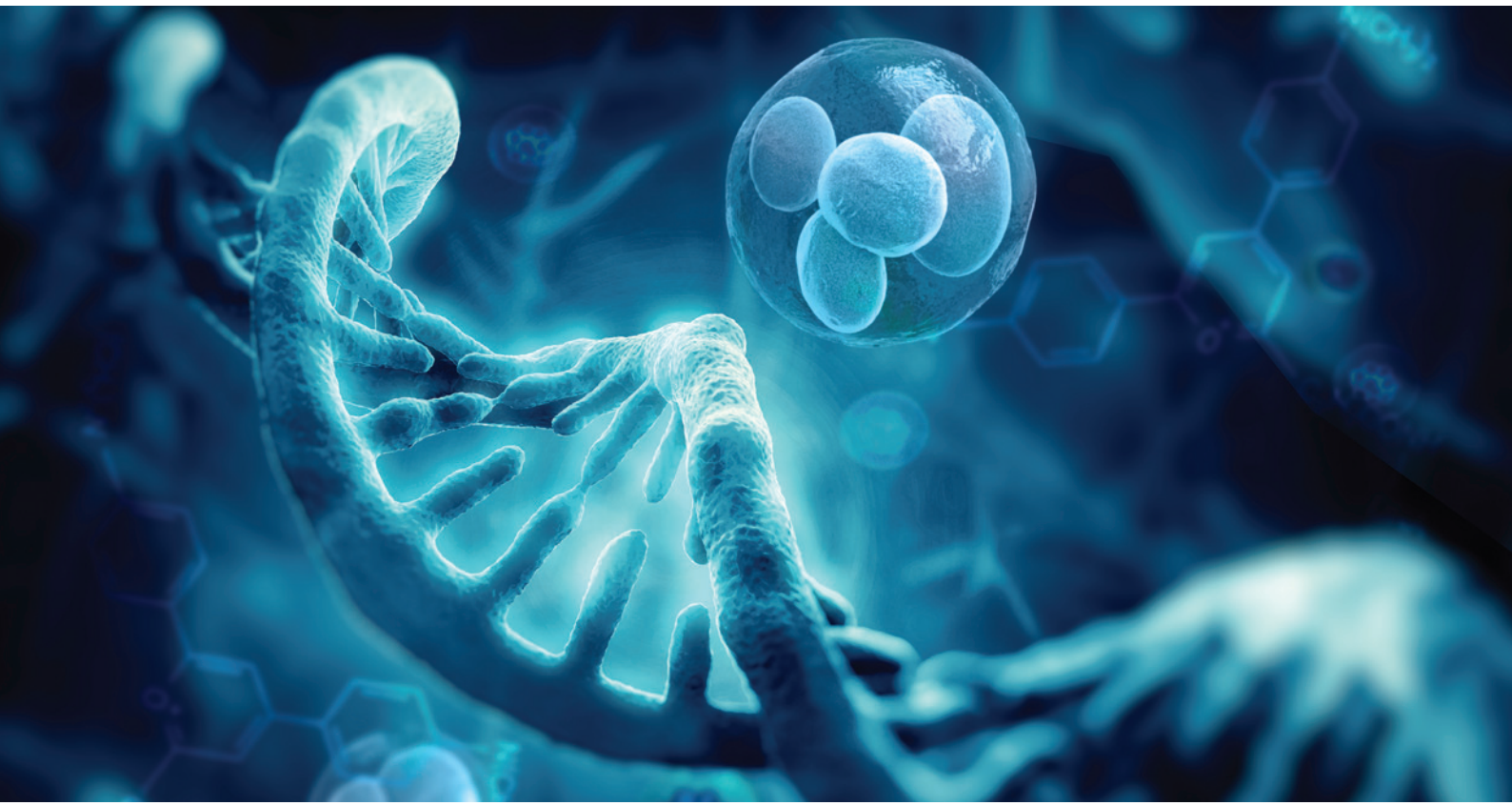

Regenerative Medicine

Opportunities For Australia

October 2018

MTPConnect
MedTech and Pharma Growth Centre

L.E.K.

Australian Government
Department of Industry, Innovation and Science

Industry Growth Centres

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1 FOREWORD

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Australia is respected around the world for its expertise and achievements in regenerative medicine (RM), a relatively new field of study that treats injuries and diseases by utilising the body's own regenerative capabilities.

Australia has contributed to a number of global RM discoveries, including conducting some of the world's first human stem cell trials. The RM field now accounts for approximately 10 per cent of our medical researchers across Australian medical research institutes and universities and there are more than 30 companies in Australia developing products with a RM focus. The field receives strong Australian Government support through the Australian Research Council and National Health and Medical Research Council and other sector-specific grants.

Australia is well-placed to capitalise on its strong research base in developmental biology, genetics, and tissue manufacturing that underpins RM and secure an even more prominent share of the global RM market which industry experts believe will be worth AU$120bn by 2035. However, given the nuances around R&D and commercialisation that set the sector apart from traditional pharmaceuticals and clinical procedures, there is a need to ensure the investment and effort is reflected in the potential health and economic returns.

In 2016, AusBiotech established a Regenerative Medicine Advisory Group to provide advice on current and emerging issues and trends facing the RM sector in Australia and overseas; improve and engage the sector; generate a clear definition of RM; and address key advocacy issues. The Advisory Group, along with MTPConnect, identified a need for a national, sector wide report to assess the current state of the Australian RM sector and make recommendations on the priorities and goals for the sector. To this end, MTPConnect has lead a sector-wide effort to develop a national RM opportunity paper.

Between June and September 2018 more than 60 key sector stakeholders participated in surveys, interviews and workshops and their insights were supplemented with published reports. This has culminated in this publication, which also presents a series of recommendations and priority actions designed to give Australia a prominent place and share in the global RM market. RM offers a curative approach to disease and injury: the science is truly innovative, its promise is tantalising, and the benefits already within our reach.

This report has been developed as part of an Industry Growth Centre Initiative. It was funded by MTPConnect and a sector-informed grant allocated by the Commonwealth Department of Industry, Innovation and Science (DIIS). We are grateful to everyone who contributed to this report, including members of the AusBiotech Regenerative Medicine Advisory Group, DIIS, L.E.K. Consulting, World Courier, CCRM Australia and other key contributors from the medical and research sector, industry and government; all have dedicated significant time and provided invaluable insights.

2 EXECUTIVE SUMMARY

Regenerative medicine (RM) holds the promise of curative healthcare. Unlike traditional medicines and devices, it harnesses cells and tissues, often in combination with gene therapy and devices, to enable the body to regenerate and, in effect, heal itself. Global investment in RM has escalated over the last five to seven years, and 37 therapies have been approved and marketed for clinical use. A wave of new therapies is expected in the next five years, particularly in immunotherapy and cell therapy.

The UK Cell and Gene Therapy Catapult estimates that the burgeoning RM market will reach AU$120bn in revenues by 2035. Australia is a well-respected competitor in the global R&D market. It ranks tenth in global publications in the RM field; second, when adjusted for population[1]. If Australia were to capture a five per cent share of the market, this would represent AU$6bn in annual revenue, and create approximately 6,000 jobs. However, many competing nations are investing heavily to build capability and capacity to put their RM sectors at the forefront of research and commercialisation of therapies. It is within this fast-moving and competitive market place that Australia must define where it can best compete and identify the priorities and actions required to make this a reality.

This report provides a roadmap for the Australian RM sector. It assesses Australia's strengths and weaknesses, and recommends priority actions to elevate the sector and enable it to compete robustly at a global level. It has been developed with the collective wisdom and input from over 60 local and international sector stakeholders. This report is not a comprehensive action plan. Instead, it should be viewed as a common vision and platform from which the sector can springboard to accelerated growth.

The vision is to create an end-to-end world leading value chain (from discovery to delivery) that grants Australian patients access to world-class RM therapies, creates jobs and enables the export of Australian therapies to the world.

Australia has a strong platform upon which to build. It is not starting from scratch. Specific strengths include: depth of talent in fundamental research and clinical trials; an ethnically diverse patient population with an interest in supporting medical innovation; financial incentives that make Australia an attractive destination to conduct health and medical research, e.g. the R&D tax incentive; a high quality and rapid clinical trial system; and targeted world-class manufacturing and cell processing technologies, e.g. Cell Therapies Pty Ltd, Royal Prince Alfred Hospital, South Australia Medical Research Institute, QIMR Berghofer.

However, there are a number of barriers that need to be addressed if Australia is to fully realise its potential in the global leader in RM field. While many of these barriers are common to health and medical research, in several cases they are more exaggerated in RM due to the immature state of the sector and the fact that RM is neither a product, device, nor medical procedure: it is often a combination of all three. The short shelf life of many RMs means that efficient and rapid supply chains to the patient are critical.

- **Capability** gaps exists in certain key areas, e.g. manufacturing of cell therapies, commercialisation know-how specific to RM, and clinicians with RM.
- **Collaboration** needs to be improved to accelerate commercialisation. This is more challenging in RM than traditional pharmaceuticals and devices given the ecosystem is not fully formed and there are few organisations with experience in taking products to market who can collaborate with and guide early research organisations.

[1] Dimension Data. Keywords used were "regenerative medicine". Number of publications divided by population in each country

- **Funding** sources outside government are only emerging in RM. There is not yet a strong and diverse pool of funders and venture capital (VC) in Australia with experience in RM due to its less mature state.
- **Regulation and policy** must evolve. For example, alignment of RM regulatory classification to leading jurisdictions is needed. The broadening of accelerated approval pathways from medicines to RM would align Australia with other markets such as Japan and the US. Further, reimbursement pathways need to be clarified.
- **Infrastructure** is of a high standard in Australia. The opportunity exists to expand manufacturing capacity and capability to support commercial scale manufacture of locally and internationally developed therapies and, in doing so, create jobs and economic benefit.
- **Australia's distance** from major markets is a barrier for traditional pharmaceutical manufacturing. However, the short supply chain for autologous products (and access to a diverse donor pool for allogeneic product) gives us a competitive base, particularly for the Asia Pacific region, that does not exist in other sectors.

These barriers are not insurmountable. In fact, many are common to the RM sectors in other countries. We can learn from what other nations have done, e.g. the UK's Cell and Gene Therapy Catapult Program, Canada's Ontario Institute of Regenerative Medicine (OIRM) and Center for Commercialization of Regenerative Medicine (CCRM). We have identified five priority action areas to overcome these barriers and achieve the sector vision, as well as suggested specific actions (as outlined in the table below). The five priority action areas are:

- **Capabilities and workforce:** Attract, build and retain world-class talent, particularly people with experience in research translation, clinical applications, commercialisation, scale manufacturing of both inputs (e.g. viral vector) and outputs (e.g. allogenic cell engineering). Australia should be encouraging capability development across the value chain (from researchers to clinicians, including private sector 'operational' support functions). Specific capabilities that could help expedite translation include clinical cell handling, transfusion/transplant capabilities, cell tracking and cell characterisation skills.
- **Collaboration:** Increase collaboration within and across the Australian RM sector to accelerate the development of world-leading therapies for export (either by Australian-based biotech and pharmaceutical companies or by multinationals). The quality and pace of research discoveries should increase through interdisciplinary cooperation.
- **Funding:** Secure long-term investment from diverse sources (public and private), that ideally have experience with RM, to help unlock the potential of the sector. Significant funds are needed to boost research translation and commercialisation.
- **Regulation and policy:** Evolve and align regulation with leading global markets and create a clear market access pathway that is aligned to leading global markets. Any changes to regulation should ensure high patient safety standards are retained.
- **Infrastructure:** Develop Australian manufacturing capability to serve both local and international companies and treat local and international patients in the Asia Pacific region.

SUMMARY: AUSTRALIAN REGENERATIVE MEDICINE SECTOR VISION AND PRIORITY ACTION AREAS					
Vision	Create an end-to-end world-leading value chain (from discovery to delivery) that grants Australian patients access to world-class regenerative medicine therapies, creates jobs, and enables the export of Australian therapies to the world				
Action areas	Capabilities / workforce	Collaboration	Funding	Regulation and policy	Infrastructure
	Attract, build and retain world-class talent	Collaborate across the value chain	Secure long term investment in the sector	Create a clear market access pathway that is aligned to leading global markets	Build Australian manufacturing capability in stages
Example actions	• Further develop world-leading training programs. • Continue / increase financial incentives that encourage RM operations in Australia. • Increase resources to expedite translational research.	• Create or support a nationally focused RM 'catalyst' strategic body. • Support a nationally focused commercialisation hub. • Establish a disease-team based approach.	• Effectively target MRFF funding to build the RM sector. • Encourage investment through alignment of sector activities with government priorities. • Attract private investment and international VC.	• Harmonise regulation with leading global markets. • Extend pharmaceutical accelerated approval pathways to biologicals. • Provide a clear path to market access and broaden scope for reimbursement.	• Actively pursue and encourage opportunities to build and/ or attract flexible and commercially viable manufacturing capability.

Delivering on these priority actions will enhance Australia's RM ecosystem and elevate Australia to be a leading nation in what is estimated to be a c.AU$120bn global market by 2035[2]. If Australia were to capture a five per cent share of this market, this would represent AU$6bn in annual revenue, and create approximately 6,000 jobs.

This is not a mild ambition. It will require focus, persistence and the entire sector working together. This document is not a panacea, but it represents a roadmap that the sector can commit to, refine and take forward, one step at a time, towards a common goal.

[2] 'Response to the House of Lords Inquiry – Life Sciences and the Industrial Strategy'. September 2017, Catapult Cell and Gene Therapy, UK

3 INTRODUCTION

3.1 Regenerative medicine promises to advance health outcomes

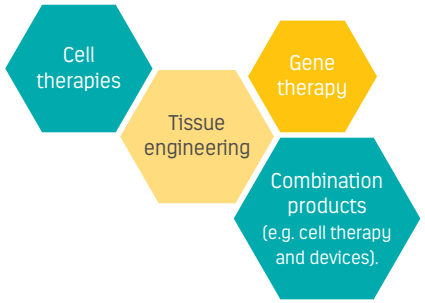
In 1984, two young brothers with burns to over 97 per cent of their bodies were admitted to Massachusetts General Hospital in Boston, USA. Skin grafts were not an option due to the severity of the burns. Instead, healthy skin cells were collected from small, unaffected areas of their lower abdomens and armpits and used to culture epidermal cell sheets that the surgeons successfully used to replace half of their skin[3]. This was the first reported clinical use of regenerated tissue, a process that falls into the category of what is now referred to as RM.

RM is defined as the use of stem cells, biomaterials, and molecules to repair, regenerate or replace damaged or diseased cells, tissues and organs for the purposes of restoring and establishing normal function (not enhancement). The early applications of RM were in haematology. This is perhaps not surprising given the ease of extraction and extensive research and history of blood transfusions, which were first attempted in the seventeenth century. The next major leap in the field dates back to the middle of the twentieth century when bone marrow transplants, which contain haematopoietic stem cells (HSCs), began to be used for treatment of patients with leukaemia and other blood cancers.

What is Regenerative Medicine?

Regenerative Medicine (RM), aims to **harness the power of stem cells, biomaterials and molecules to repair, regenerate or replace diseased cells, tissues and organs** for the purposes of restoring and establishing normal function (not enhancement).

Key therapy areas include:



This report is **focused on therapies that are regulated by the TGA.** The TGA does not regulate medical practice. Some products that would otherwise be considered biologicals and RMs are excluded from TGA regulation (through the 'Therapeutic Goods (Human Cells, Tissues and Organs) Determination 2018').

Australia's pioneering efforts came to the fore in 1987, when one of the first successful peripheral blood apheresis and stem cell transplants was developed by researchers and clinicians at the Royal Adelaide Hospital[4]. RM has expanded to encompass a broader range of cell therapies and stem cell types, such as embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). It now incorporates the creation of biomaterials to provide the 3D structures to support cell and tissue growth that may lead to the development of organs that could address organ donor shortages and support the development and testing of new medicines and therapies. Already miniaturised and simplified versions of kidneys and brains (organoids) have been grown in small dishes in the lab and are yielding new insights into biological function and disease.

This ability to re-program and coax stem cells into taking one of many specific forms opens the door to new treatments in multiple therapy areas – retinal disease, diabetes, cardiovascular disease, neurodegenerative, orthopedic and immune disorders to name but a few. RM can also include gene therapy whereby normal genes are inserted into cells with missing or defective genes, or where faulty genes are corrected through gene editing processes. Notably, 2015 saw the first successful use of gene-edited immune cells to treat leukaemia in two baby girls in London[5].

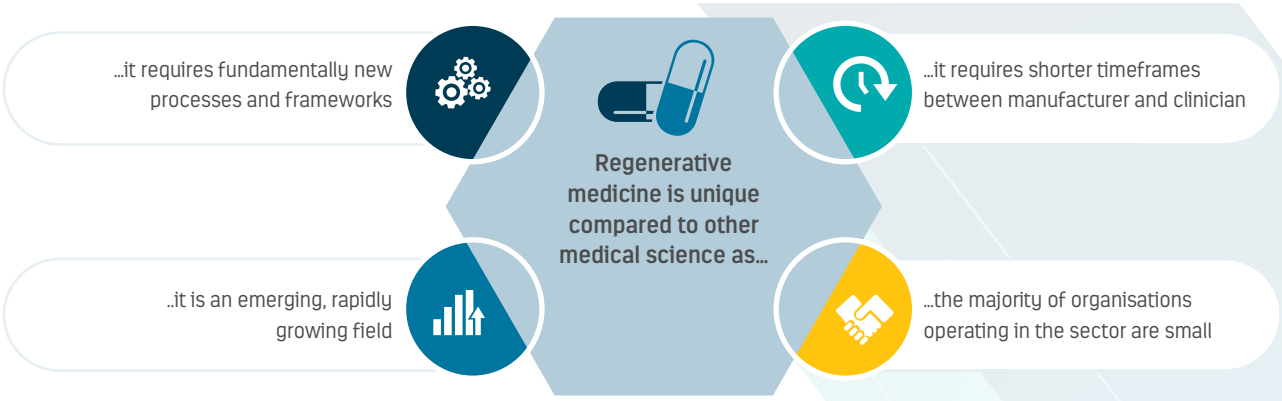
[3] Altman, L. "Test Tube' Skin Helps Save 2 Burn Victims'. August 1984, NY Times, US
[4] Körbling, M, Freireich, E J. 'Twenty-five years of peripheral blood stem cell transplantation'. 16 June 2011. Blood, USA
[5] MacDonald, F. 'Gene Editing Has Saved The Life of a Girl With "Incurable" Leukaemia'. November 2015, Science Alert

The excitement around the possible impact that RM could have on quality of life and reducing the disease burden has been offset by high cost, limited examples of successful efficacy, regulatory hurdles and ethical dilemmas. But we are now on the cusp of realising the benefits arising from decades of fundamental research into developmental biology and related fields. By 2017, 37 RM products had been approved in the US, EU or Japan[6].

With healthcare costs in Australia expected to increase to almost sixteen per cent of GDP by 2040[7], from the current level of less than ten per cent, RM offers the chance to reduce the burden of disease and associated costs as well as improve quality of life. RM also has the potential to offer a single intervention that will circumvent lifelong treatment for a disease or injury.

3.2 Regenerative medicine is distinct

While RM is a branch of medical therapy, it is distinct from most pharmaceuticals and devices and represents a new paradigm in science. Outlined below are four key differences that have implications for regulation, funding and the supply chain of regenerative medicines.



Fundamentally different approach

RM has the potential to revolutionise the treatment of injuries and disease by taking a long-term curative approach in contrast to many pharmaceuticals and surgical procedures that generally manage rather than cure disease. Although this is an exciting prospect, existing well established frameworks and processes underpinning commercialisation are not typically directly applicable. RMs are not strictly a pharmaceutical product, a device or medical service, and often combine elements of one or more of these common classifications. For example, CAR (chimeric antigen receptor) T cell treatment involves extracting and genetically engineering human T cells before re-administering them to the patient. This is both a service and a quasi-pharmaceutical and therefore the traditional regulatory frameworks for medicines, devices and services don't neatly apply. Many stakeholders across the value chain (e.g. funders, regulators and clinicians) need to develop competencies in this new field. At the same time, the policy frameworks need to evolve.

[6] FDA, Citeline, PMDA, MHLW, EMA

[7] Fitzgibbons, O. 'Roadmap paves way for healthier economy'. April 2017, CSIRO, Australia

Emerging, rapidly evolving field

The small list of FDA approved RM therapies reflects the immaturity of the field. However, growth in the sector is strong with research discoveries and translation occurring at an increasing pace as indicated by the number of companies with products in the clinical phase. The global RMs market generated $17.03bn revenue in 2016[8] and analysts expect its value to exceed $50bn within the next few years.

The handful of examples of commercially available RM therapies means that, as yet, there is neither best practice methodology nor significant numbers of experienced people to take these products through to market. This is in contrast to other areas of medical science, such as small molecule drug development, where extensive global capabilities, including finely honed R&D processes for medicinal chemistry and high throughput screening systems support product development.

Shorter timeframes between manufacturer and clinician

Since RM is based on the use of living cells and biomaterials, some therapies need to be rapidly transported between manufacturers and patients. Although some pharmaceuticals require specific storage conditions such as refrigeration, biological or living therapies have an even more limited shelf life. Whereas small molecules may lose potency over time, tissues and cells can perish and be unusable after as little as 24 hours. As a result, supply chain logistics for RM are more significant and urgent than in other areas of medical science.

Largely comprised of small organisations

Unlike traditional pharmaceuticals, the key commercial participants in the RM sector are typically small to medium sized biotechnology companies. This fragmented landscape is symptomatic of the growing grass roots sector development and its early stage of growth. Without an established end-to-end ecosystem from preclinical to clinical research to manufacturing and marketing, the collaboration opportunities are not as well developed. Collaboration is key to accelerating translation of research into the clinic. 'Big Pharma' and VC companies are not as heavily invested in this field as in other areas of medical science and, while this is expected to evolve and change, it creates a current funding gap.

3.3 Regenerative medicine has the potential to drive significant growth for Australia

Like the broader pharmaceutical sector, RM must be considered from a global perspective. A sole focus on developing RM therapies for the Australian population is not feasible due to the significant cost of R&D and commercialisation. But, an ambitious, supportive and self-sustaining local RM ecosystem can propel leading Australian research to international success and, in return, provide significant economic growth.

Australia is considered to have been a first mover in the global RM sector. The 2003 establishment of the Australian Stem Cell Centre was one of the world's first major investments in a multi-institution R&D program to develop stem cell therapies. Since then, however, RM sector activity in other jurisdictions has caught up to and, in some areas, exceeded Australia. In 2017, there were 37 RM products marketed globally, with the large majority originating from the US, EU and Japan[9]. To date, only a small number of products developed by an Australian research organisation or company have reached the market, including:

[8] 'Global Regenerative Medicines Market – Analysis and Forecast (2017-2025)'. January 2018, BIS Research, US

[9] Marketed products include those that have been withdrawn from the market. Source: FDA, Citeline, PMDA, MHLW, EMA

- Mesoblast's TEMCELL® HS Injection, a registered trademark of JCR Pharmaceuticals Co Ltd of Japan, which is licensed (and reimbursed) in Japan.
- Orthocell's Ortho-ACI® treatment, which has been approved by the TGA in Australia.
- AVITA Medical's RECELL® System, which received FDA "compassionate use" approval under the Investigational Device Exemption (IDE) program in the US.

Australia's more recent activities should be viewed in the context of other leading global jurisdictions, including:

Japan

The Japanese Government views RM development as a key priority, following the awarding of a Nobel Prize shared by Japanese scientist Shinya Yamanaka for the invention of induced Pluripotent Stem Cells (iPSCs). Government initiatives include:

- Six RM projects that sit within the Japan Agency for Medical Research and Development's (AMED) under the Japan RM program. The aim is to promote the 'development of regenerative medicine from basic research to clinical studies and creation of evaluation standards.'
- The 2012 government announcement of a commitment to spend AU$1.4bn on iPSC research over a ten-year period.[10]
- The introduction of an expedited approvals process under the Pharmaceutical and Medical Device Act (PMD) Act for RM therapies.

United Kingdom

In 2010, the UK Government announced its AU$370m plan for technology and innovation centres[11], leading to the establishment two years later of the Cell and Gene Therapy (CGT) Catapult to support the development and commercialisation of cell therapies. In 2018, the Catapult network was awarded c.AU$1,450m[12] in additional funding to expand R&D and train hundreds of apprentices and doctoral students with the in-demand technical skills.

Canada

Canada has a vibrant RM sector, with the Canadian Government investing over AU$760m in stem cell research from 2001-15[13]. Recent development has been led in part by CCRM, an industry government academia consortium[14]. In addition, The Ontario Institute of Regenerative Medicine (OIRM) has strategically boosted RM R&D in the province of Ontario through investment and collaboration initiatives, helping to increase cell therapy trials from five in 2014 to 13 in 2018[15].

[10] Ando, K. 'Japan faces new competition in the race for 'regenerative medicine''. November 2017, Nikkei Asian Review, Japan; converted from USD using 0.71 AUD:USD exchange rate, as per 10-Oct-2018

[11] 'Technology and innovation centres – Closing the gap between concept and commercialisation'. Catapult Cell and Gene Therapy, UK ; converted from GBP using 0.54 AUD:GBP exchange rate, as per 10-Oct-2018

[12] 'UK Government Grants Catapult Network £780M in Additional Funding'. August 2018, Catapult Cell and Gene Therapy, UK; converted from CAD using 0.92 AUD:CAD exchange rate, as per 10-Oct-2018

[13] Quigley, J. 'Canada's stem cell research needs 'big investment' to move forward, experts say'. January 2016, CBC, Canada

[14] 'CCRM: Cultivating a culture of cooperation to advance the global regenerative medicine industry'. February 2017, RegMedNet

[15] 'OIRM Impacts'. Ontario Institute for Regenerative Medicine

United States of America

As in other areas of medical research and development, the USA is a key participant in the global RM sector. The California Institute of Regenerative Medicine (CIRM) has funded more than 750 projects since 2004, with over AU$4.2bn in funding[16]. Another state with significant sector activity is Massachusetts, where AU$1.4bn of state government funding in biotechnology was announced in 2008, including AU$700m for infrastructure including a stem cell bank at the University of Massachusetts[17].

Over the last 15 years, Australia has invested in building a local RM sector. Well over AU$1bn has been invested in the sector through Australian government grants and private capital raisings to progress RM research and development. However, the **investments and sector activity have not been guided by an overarching sector strategy and currently a national RM roadmap for Australia does not exist.** This reflects a gap relative to other leading nations in the field such as Canada, the UK and Japan.

This report has brought together over 60 sector stakeholders[18] to input into the creation of a national roadmap with priority actions designed to position Australia as a leading RM market. The following sections of this report provide an overview of Australia's current position, its strengths and weaknesses. Chapter 5 report outlines a vision for the sector and the priority actions that are required to achieve that vision.

[16] Maxmen, A. 'California's $3-billion bet on stem cells faces final test'. April 2017, Nature; converted from USD using 0.71 AUD:USD exchange rate, as per 10-Oct-2018

[17] 'Szep, J. 'Massachusetts to spend $1 billion on biotechnology'. June 2008, Reuters; converted from USD using 0.71 AUD:USD exchange rate, as per 10-Oct-2018

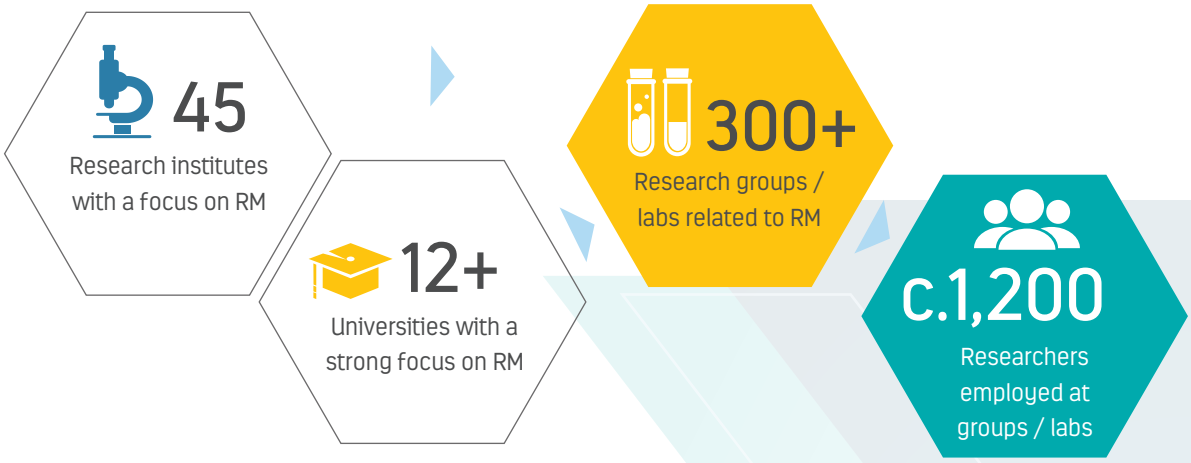
[18] Refer appendix for details of sector stakeholders.

4 THE AUSTRALIAN REGENERATIVE MEDICINE SECTOR

4.1 Snapshot of the Australian sector

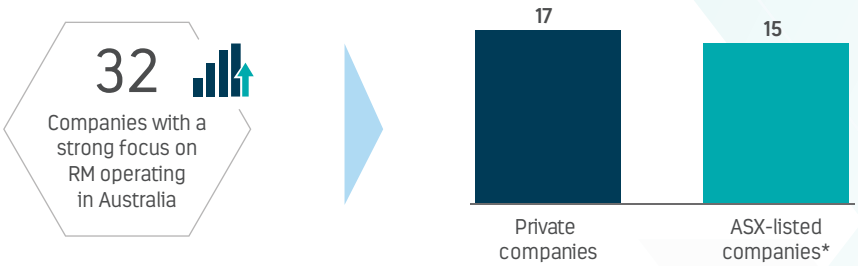
Australia has a sizeable research presence in RM, despite it being a relatively new research area. A quarter of Australia's 43 universities[19] and almost two thirds of Australia's 70 medical research institutes (MRIs)[20] have a strong focus on RM. The RM groups and labs at these universities and MRIs account for 1,200 researchers – around 10 per cent of all medical researchers in Australia[21].

Research



There are also at least 32 RM-focused companies that operate in Australia. These companies span the supply chain and include biotechs with a focus on product development, cell manufacturing and device innovation.

Private entities / companies



Excludes physician-led clinics not regulated by the TGA

Note: * Includes one NYSE listed company with operations in Australia

[19] 40 Australian universities, two international universities, and one private specialty university

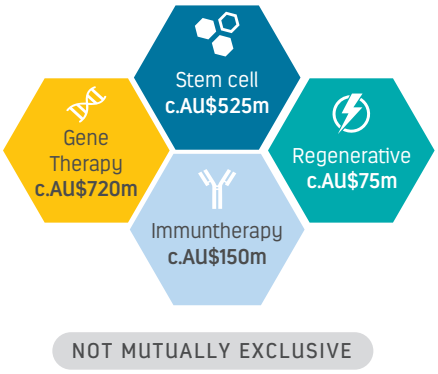
[20] 'List of independent Medical Research Institutes'. Department of Health, Australia

[21] 'Australia's health and medical research workforce – Expert people providing exceptional returns'. October 2016, Deloitte Access Economics, Australia

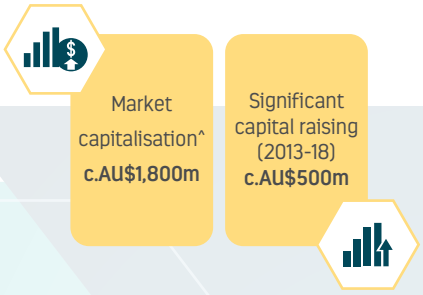
According to Dimension Data, a range of government grants (from NHMRC, ARC and other specific grants to universities and research institutes) have been distributed for RM since 2001[22]. Using RM-specific search terms, AU$720m has been allocated for 'gene therapy', over AU$500m for 'stem cell', $150 for 'immunotherapy' and AU$75m for 'regenerative' (it is important to note that these amounts may not be mutually exclusive and individual grants may span across multiple RM-related fields). Monash University is one of the largest recipients, with AU$150m of grants for stem cell research alone. Furthermore, c.AU$32m of NHMRC funding has, on average, been allocated to RM research each year since 2016.

Investment / funding

Government grants: research funding by search term* (2001-18)



Non-government investment: Twelve ASX-listed RM companies **



Note: * Major to universities and research institutes; ** Includes one NYSE listed company. Twelve include: Admedus, AmpliPhi Biosciences, Avida Medical, Benetic Biopharma, Cynata Therapeutics, Immugene, Immutep, Living Cell Technologies, Mesoblast, Orthocell, Phylogica, Regeneus; ^ As at 11 October 2018
Source: Dimensions database; ASX

In addition, there has been significant non-government investment in listed RM-focused companies with operations in Australia. As of October 2018, the market capitalisation of twelve ASX-listed RM companies totals c.AU$1.8bn[23]. The same twelve companies have raised c.AU$500m in significant capital raising over the past five years, including share issues to pharmaceutical companies, investment funds, asset managers and medical technology conglomerates – many of which are based outside of Australia.

4.2 Assessment of the Australian regenerative medicine sector

Australia is well placed to join the leading nations in the rapidly evolving global RM sector. This strong competitive position is a product of Australia's excellent research capabilities, significant investment to date (particularly in research) and the local development of targeted world class manufacturing and cell processing technologies. There are, however, multiple barriers to growth. This section outlines the strengths of the sector and highlights key barriers and opportunities that need to be addressed to unlock future progress. These strengths, barriers and opportunities were developed through a stakeholder survey, interviews with local and international sector participants, a series of workshops across Australia and a review of secondary sources (data and industry publication). They have been grouped into six key areas:

[22] Dimensions Data

[23] Includes one NYSE listed company, AmpliPhi (market capitalisation of AU$14m)

SUMMARY: ASSESSMENT OF THE AUSTRALIAN REGENERATIVE MEDICINE SECTOR

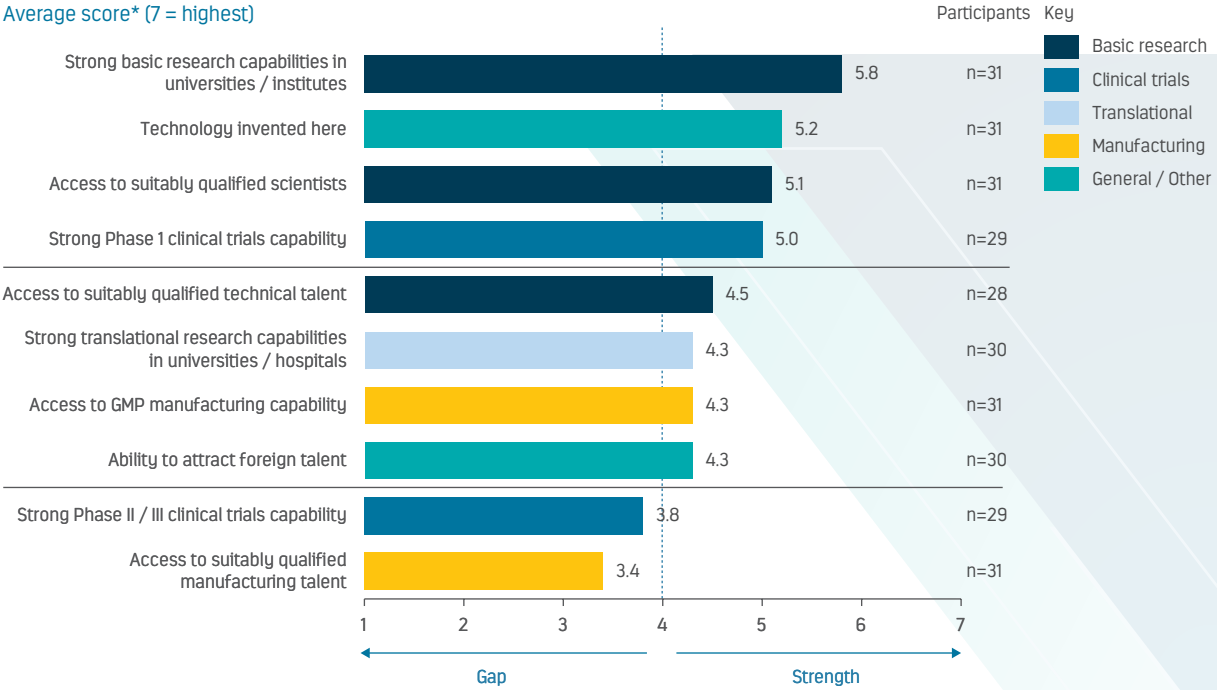
Key area	Capabilities / workforce	Collaboration	Funding	Regulation and policy	Infrastructure	Geography / demographics
Strengths	• Depth of talent in **basic research** and **clinical trials.**	• **Effective collaboration** within basic research and with international bodies.	• **Financial incentives** that support R&D activities in Australia. • Specific investment in regenerative medicine to date by government.	• Regulators and policy makers are engaged in the development of the sector. • Australian regulatory approval has global recognition.	• **World-class manufacturing** facilities for clinical trials. • **World-class health care facilities.** • **World-class research infrastructure.**	• Australia is on **the doorstep of Asia** and well positioned to be a regenerative medicine **'hub' for Asia-Pacific.**
Barriers / opportunities	• Limited capability in **clinicians** and **translation.** • Need for greater depth in commercialisation expertise. • Need to invest in developing a workforce to support a commercially successful sector, e.g. manufacturing, regulatory.	• Need for greater collaboration between research, industry, clinicians and investors to drive **outcome-based research.**	• Gaps in available funding for **therapy optimisation** and **translation** stages of the value chain.	• Need for regulatory **harmonisation** with leading international bodies. • No formally defined **accelerated approvals** pathway. • Lack of **clear pathway to reimbursement and market access.** • An anticipated **lack of resources** in key TGA functions as the sector grows.	• **Need to invest in capacity** to support the commercial scale up of regenerative medicine product manufacturing. • Potential need for **financial incentive** schemes to support global competitiveness.	• **Distance** from the large USA and European markets can create supply chain complications. • **Australia is much smaller** than other nations that are active in this sector (e.g. US, UK, Japan, Canada).

Capabilities and workforce: Australia has world-class talent in some areas of the value chain, but a shortage in others

Strengths

Australia has a rich history of health and medical research (HMR) excellence and has numerous innovation success stories, e.g. the Gardasil vaccine, Spinifex and Resmed to name a few. A survey completed by a cross section of RM sector participants and stakeholders shows that Australia's highest perceived capabilities and strengths within the sector mirror those found more broadly in the Australian HMR sector, i.e. fundamental academic-led research and clinical trials (notably phase I).

Survey responses on Australia's global competitiveness – Capability areas (2018)



Note: * Survey average excludes blank or N/A responses. Number of participants in each survey question may be lower than the total number of participants
Source: Market participant interviews and analysis

Basic research: Research institutions and universities in Australia have a reputation for attracting and retaining world-class researchers. This research excellence is particularly evident in RM where 300+ research labs, 45 research institutes and at least twelve universities have built programs with a strong focus in this field. Furthermore, Australian researchers have published 1,735 papers in the fields of cell therapy, tissue engineering and gene therapy, which places Australia tenth based on number of publications (second, when adjusted on a per capita basis)[24].

[24] Dimension Data. Keywords used were "regenerative medicine". Search from 1995 onwards.

Clinical trials: Further down the value chain, Australia holds a high level of clinical trial expertise, including within RM. Australia has a global reputation for a high-quality and efficient clinical trial capability. This has been developed through years of successful trials, with ethical review processes and protocols that are accepted in other leading jurisdictions, supported in part by the R&D tax incentive and the accelerated Phase 1 clinical trial notification (CTN) approval pathway. A thriving clinical trial sector has led to the attraction and retention of the world-class talent in this field and an annual increase in registered trials including non-drug trials[25].

Barriers / opportunities

If Australia wishes to unlock significant growth in this sector, an assessment of the potential shortage of talent in other key areas of the value chain will need to be conducted. In particular:

- Commercialisation.
- Clinical.
- Regulatory approvals (covered in regulation / policy section).
- Manufacturing (covered in infrastructure section).

Commercialisation: There is a shortage of commercialisation experience in the RM sector, which should change as the number of successful therapies brought to market increases. Commercialisation skills include identifying an unmet need, demonstrating proof of concept, creating the appropriate IP strategies, navigating regulatory requirements, clinical trial design and establishing strategic partnerships. In Australia, Mesoblast and Orthocell are two of a few successful examples. This highlights a future need to ensure Australia has individuals with the skills and capabilities required to take a therapy all the way through from clinical trials to the clinic and that there are in-country opportunities to apply these skills.

International case studies

Investment in RM skills development

In May 2018, the UK Cell and Gene Therapy (CGT) Catapult announced **c.AU$5.6m of government investment** in regenerative medicine **skills development programs,** including:

AU$2.8m for Advanced Therapies Treatment Centres

AU$2.8m for Medicines Manufacturing Industry Partnerships

The investment is designed to **"bridge the gap between regulatory approval … and their integration into front line health services"** and target the capability set required to manufacture, supply and administer regenerative medicine therapies

CATAPULT Cell and Gene Therapy

Source: UK Catapult

[25] ANZCTR

Clinical: A vital element in the success of RM is the delivery of a product or therapy to the patient by skilled and qualified clinicians. The delivery of cell (and other RM) therapies typically requires specific, highly specialised procedures: it is not as simple as prescribing a new orally administered pharmaceutical. Thus, Australia's medical professionals will need additional and significant levels of training to gain the expertise needed to meet the anticipated demand of a thriving RM sector.

In summary, to be globally competitive in the field of RM, Australia needs to demonstrate high-level capabilities and workforce strengths. It must continue to address the identified skills gaps by attracting or developing and retaining these skills at a local level.

Collaboration: Greater collaboration is required between participants and across the value chain to accelerate translation success

Strengths

Participants in all workshops expressed a strong willingness to increase collaboration across the RM sector and several examples of successful collaboration within and across the sector were uncovered. Examples that were highlighted include:

- **Collaboration in basic research -** combined research projects across universities. For example, engineering specialists from Victoria-based Deakin University and medical researchers from Western Australia-based Ear Science Institute of Australia (ESIA) have partnered to develop eardrum membrane implants[26].
- **Collaboration with international bodies –** agreements between international bodies and Australian Government research centres. The UK Cell and Gene Therapy (CGT) Catapult have a collaboration agreement with the Australian Co-operative Research Centre for Cell Therapy Manufacturing (CTM CRC) and will test, at scale, CTM CRC's patented scaffold technology for the commercial production of T-cells.[27]

Barriers / opportunities

Collaboration in the Australian pharmaceutical and medical technology sectors (across industry academia and clinicians) is reported to be relatively low compared with other jurisdictions[28]. This is no different within the RM sector where a lack of collaboration is a key barrier to sector growth. A number of factors are thought to drive this. They include:

- Research is not currently designed around a clinical or commercial outcome.
- Scarcity of funding drives competition between researchers.
- There is no overarching RM hub that represents the Australian sector.

[26] 'Grant smooths way for silk eardrum trials'. June 2017, Deakin University, Australia

[27] 'CGT Catapult & CTM CRC sign agreement to advance T-cell scaffold technology'. May 2016, Cell Therapy Manufacturing Cooperative Research Centre, Australia

[28] According to stakeholder consultations

Research not designed around a clinical outcome: Participants in the sector noted that encouraging researchers to take a more market/patient-led rather than researcher-led approach will be critical to accelerating the success rate of taking research into the clinic. Existing funding structures have contributed to this researcher-led approach. This primary focus on science and researchers can often result in R&D teams that are siloed in the basic research end of the spectrum and lack collaboration across the value chain. Collaboration across researchers, industry and clinicians is critical to success.

Competition level is high: The metrics section of this report outlined the vibrant nature of the sector, over 12 universities, and 45 research institutes have a strong focus on regenerative medicine. A byproduct of this, when coupled with limited grant funding, is competiveness between research groups. This competitiveness can result in a sub-optimal level of collaboration.

There is no overarching Australian RM hub: As of 2018, there is no clear sector hub that represents the entire regenerative medicine sector. This has multiple implications:

- Collaboration partnerships are typically circumstantial and ad-hoc, rather than strategically developed with a view of the whole sector.
- Regulators find it difficult to engage with the sector – there is a lack of obvious access points. Instead of liaising with one group that assembles and disseminates information, extensive consultation with industry and academia across a number of groups is required.

International case studies

Collaboration for clinical outcomes

In 2014, Prime Minister Shinzo Abe established the Japan Agency for Medical Research and Development (AMED). This agency was tasked with **"tackling the biggest systemic constraint on Japanese regenerative medicine: [a] lack of co-operation".**

Education* → Health** → Trade***

AMED centrally manages research funding of over ¥140bn (c.AU$1.8bn) that was previously divided between Education, Health and Trade. AMED's funding distributions are co-ordinated by a Cabinet Office (the Headquarters for Healthcare Policy) and are allocated to hospitals and institutes based on an alignment with long-term strategic goals. AMED also facilitates collaboration between researchers, regulators (PMDA^) and R&D infrastructure providers.

Japan Agency for Medical Research and Development

Networks of Centres of Excellence

Multidisciplinary collaboration throughout Canada's regenerative medicine sector has been attributed to the Networks of Centres of Excellence (NCE) program. These include:

- The Canadian Stem Cell Network (est. 2001)
- The Centre for Commercialization of Regenerative Medicine (est. 2010)
- Regenerative Medicine and Cell Therapy Network (est. 2014)

The NCE program is designed to mobilise multi-disciplinary research across Canada, engage partners across the value chain and increase collaboration within Canada and abroad.

This investment has led to a reported increase in strategic investments across research networks, organisations and infrastructure since 2004.

Note: * Ministry of Health, Labour and Welfare (MHLW); ** Ministry of Education, Culture, Sports, Science and Technology (MEXT); *** Ministry of Economy, Trade and Industry (METI); ^ Pharmaceutical and Medical Devices Agency
Source: Financial Times, Japan Health Policy Now; Council of Canadian Academie

Funding: Investment to date has placed the Australian sector in a strong position globally but investment for translation and commercialisation is scarce

Strengths

Investment in Australia's regenerative medicine sector has enabled the development of an ecosystem with a strong global position. In particular, government grants have, to date, played a significant role in the growth of the sector. The majority of this funding has come from the following sources:

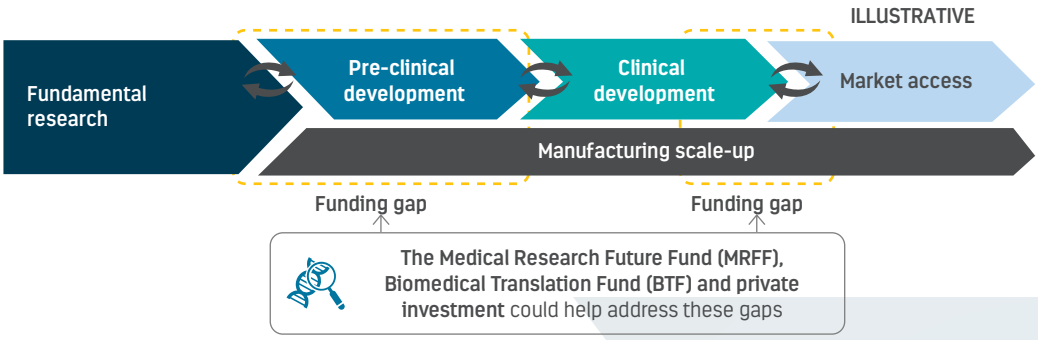
- Department of Health.
- Department of Industry, Innovation and Science.
- Department of Education and Training.
- Specific government grants schemes / incentives.

Source	RM value chain areas that has benefited	Example initiatives / programs within RM
Department of Health	Fundamental research Some translational research	National Health and Medical Research Council (NHMRC) grants (c.AU$28m in regenerative medicine in 2017) Biomedical Translation Fund (BTF)
Department of Industry, Innovation and Science	Fundamental research, pre-clinical development, clinical development	AU$20m grant over six years for the Cell Therapy Manufacturing Co-operative Research Centre Funding of Stem Cells Australia as a Special Research Initiative in Stem Cell Science
Department of Education and Training	Fundamental research Some translational research	Australian Research Council (ARC) grants, e.g. c.AU$24m ARC investment into Stem Cells Australia to foster excellence in stem cell research
Specific government grants / incentives	Across the value chain on an ad-hoc basis	R&D tax incentive Victorian Government c.AU$800k provisional funding for CCRM Australia NSW Government Gene and Gene Therapy grants

Barriers / opportunities

Within the Australian funding landscape there are limited available resources in the 'translation' phase of the RM value chain, that is, taking clinical trials through phase II/III into commercially available therapies. This can be seen in the illustrative view of the funding landscape below:

Funding landscape in the Australian regenerative medicine sector, to date:



Translation: There is also a funding gap when clinically validated RM products have exited the R&D phase and are ready for commercialisation. The funding required to scale manufacturing, train clinicians and market products can be significant and difficult to obtain given there are limited examples of commercial success in this emerging sector.

Participants in the sector are optimistic that the AU$20bn Medical Research Future Fund (MRFF)[29] could help to fill this gap. The aim of this fund is to unlock 'Australia's research potential and [deliver] more advanced healthcare and medical technology that will improve the health of Australians and grow our exports'. Over the coming months, as the new MRFF priorities are set, there will also be greater clarity around how RM aligns with the strategic platforms and funded initiatives.

The AU$500m Biomedical Translation Fund (BTF) is another significant H&MR investment source. It was established with 50 per cent Commonwealth capital and 50 per cent private sector/VC. This fund could help to fill this gap as it is designed to 'translate biomedical discoveries into high growth potential companies to deliver long term health benefits and national economic outcomes'[30]. However, there is a current perceived lack of clarity as to the strategic priorities of the fund (and the three separate fund managers that oversee the fund) and the proportion that might be made available to regenerative medicine. Other recently announced funding initiatives focused on medical research translation also include the MTPConnect-managed BioMedTech Horizons Program (2018), the Biomedical Translation Bridge (2019-22) and the Targeted Translation Research Accelerator (2020-28).

Funding for commercialisation through VC and other private companies (e.g. technology companies and Big Pharma) is much more common outside of Australia (particularly in North America). However, as yet there are no known significant Australian-based VC investments in RM therapies in Australia. ASX-listed biotechnology and RM-focused companies, however, have had success in attracting a range of private investors. Attracting experienced international VC firms (and other private sources) to invest in the Australian RM sector could provide a valuable source of funds as well as knowledge transfer.

[29] 'About the MRFF'. Department of Health, Australia

[30] 'Biomedical Translation Fund (BTF)'. Department of Industry, Innovation and Science, Australia

International case studies

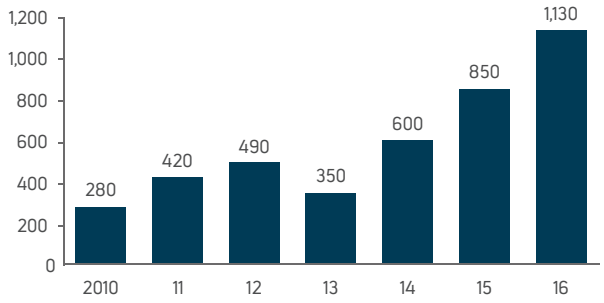
Venture capital "betting big" on regenerative medicine

Private investors in the US and Canada have become increasingly interested in regenerative medicine. Investment levels quadrupled over the period 2010-16.

Example: Toronto-based BlueRock Therapeutics **raised over AU$300m in Series A capital from Bayer and Versant Capital** in 2016. BlueRock's mission is to "cure diseases characterized by significant cell loss and diminished ability to self-repair"

VC investment in regenerative medicine – North America (2010-16)
Millions of Australian dollars

CAGR% (2010-16) **26**



	2010	11	12	13	14	15	16
Number of deals	31	30	35	34	36	40	34

Note: * Converted from USD using 0.71 AUD:USD exchange rate, as per 10-Oct-2018
Source: Goldman Sachs; Crunchbase; BlueRock Therapeutics

Regulation and policy: The regulatory environment encourages some research but evolution could foster further activity

Strengths

The current Australian regulatory and policy environment encourages the development and trial of safe therapies for use in the local market and export to the world. Within the RM sector, regulatory strengths were identified as:

- The Australian regulatory approval has global recognition.
- Regulators are engaged in the development of the sector.

Global recognition: Australia has a global reputation for being a safe jurisdiction with high quality assurance when it comes to clinical trials and approvals. Workshop participants highlighted agreements between Australia's regulators and international counterparts as a key benefit. For example, the recent FDA-TGA Memorandum of Understanding regarding the Exchange of Information on GMP Inspections[31] could help save time and resources for both agencies and industry participants. This type of arrangement was only possible due to Australia's high levels of quality assurance.

Regulators are engaged: In 2011, the Therapeutic Goods Administration (TGA) implemented a specific biologicals framework for approvals. This new framework was designed to provide a legislative basis for the regulation of human tissue and cell-based products. More recently, the TGA has been working with a number of individual companies planning to take RM therapies to market and they have been actively involved in the development of this report.

[31] 'FDA-Australia Cooperative Agreement regarding Exchange of Information on GMP Inspections of Human Pharmaceutical Facilities'. February 2018, US Food & Drug Administration

Barriers / opportunities

Evolution in regulation and policy for RM in Australia could help encourage further development of innovative, safe therapies. From a **regulatory** perspective, identified opportunities include:

- Harmonisation with leading international bodies.
- Formally defined accelerated approvals pathway.
- Addressing the anticipated lack of resources in key TGA functions as the sector grows.

From a **policy** perspective, one key need was identified:

- The introduction of a clear path to reimbursement for regenerative medicine therapies.

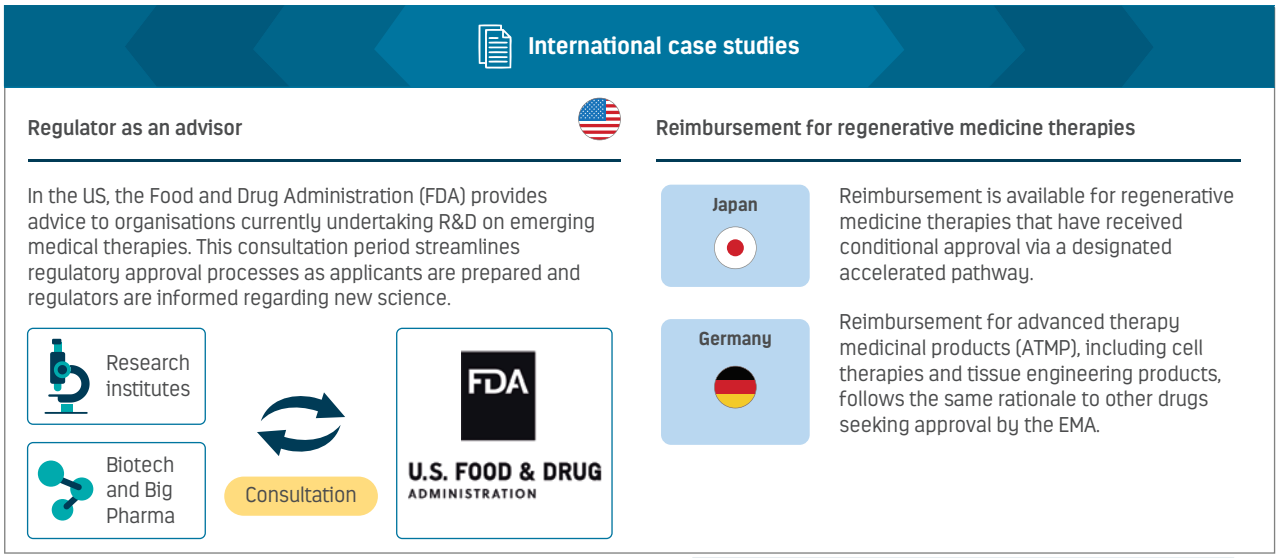
Regulation – Harmonisation: Alignment with international regulators is essential because RM is a global market. The current biologicals framework, however, does not easily align with other major jurisdictions where RM is specifically highlighted in the framework (c.f. FDA, Japan). Consistency of regulation and language (where relevant and appropriate) between jurisdictions can help minimise complexity for international organisations and Australian companies with an international presence.

Regulation - No formally defined accelerated approvals pathway: A formalised, regularly used process for expedited approvals is currently available through the TGA for pharmaceuticals (e.g. the priority review pathway), but this type of arrangement is not yet available for RM. Under the current biologicals framework, accelerated approvals may be informally considered for RM but these approvals are determined on a case-by-case basis. A formal and consistent process would be valued.

Regulation - Lack of resources: Compared to global counterparts in the US, Japan and the UK, the TGA is a small regulator in terms of headcount and resource. This is particularly relevant for the RM sector for two reasons:

- Currently, cell therapies that are the result of significant modifications are required to be evaluated by the TGA under the clinical trial exemption (CTX) scheme. There are presently c.2-3 CTX applications per annum, but with the expected increase in the number of cell therapies (and other RM therapies) progressing to clinical trials, there are likely to be processing delays if additional resources and investment aren't allocated.
- Consultation between the TGA and industry in RM is currently limited due in part to the current cost-recovery model of the TGA. The TGA does not currently offer consultation services similar to the US FDA throughout the R&D process. As a result, approval time frames are commonly extended or resubmissions required.

Policy – no clear path to reimbursement: It is currently unclear for many participants how reimbursements will work for RM therapies. A lack of formalised process or precedent has resulted in a lack of clarity across the sector, particularly for investors looking to understand potential future revenue streams.



Source: BioPharma-Reporter; Schoenermark Kielhorn Collegen; CellPress

Infrastructure: Australia's manufacturing capabilities are first-rate but may not be sufficient to support the expansion and rapid growth of regenerative medicine

Strengths

As noted in the skills section, almost a quarter of universities and two thirds of medical research institutes in Australia have research programs with a RM focus. This has created a level of competency and technical know-how that has been applied to the establishment of Australian facilities designed to support the creation of cell and gene therapy products. This provides the following strengths:

- World-class manufacturing facilities.
- A suitable market fit given Australia's advanced manufacturing focus.

World-class manufacturing facilities

In Victoria, Cell Therapies Pty Ltd (majority owned by the Peter MacCallum Cancer Centre), has been providing contract manufacturing and deployment services for cell and gene therapy products for over fifteen years. Its clean room facility is comparable in size to the Canadian Centre for Commercialization of Regenerative Medicine (CCRM) Ontario, Canada and the Centre for Advanced Therapeutic Cell Technologies (CATCT), which is supported by GE Healthcare and the Federal Economic Development Agency for Southern Ontario.

More recently, CSIRO established the M2 precinct with Monash Health Translation Partners and Monash University that can support the development of RM products. Other places with significant facilities include the Queensland Institute of Medical Research and some hospitals such as the Royal Perth Hospital. In addition, the Cell Therapy Manufacturing Co-operative Research Centre (CTM CRC) has a newly established pilot-scale translational facility in South Australia.

Market suitability and fit

Cell and tissue manufacturing requires highly skilled individuals and high levels of quality assurance, which Australia provides. This includes tests for quality control to ensure therapeutic products are free from microbial contamination: another area in which we have significant capabilities.

Australia's general manufacturing strengths and point of difference within the region is deemed to be for low volume, highly technical, and high value products, which makes RM well suited to the Australian market. Australia's international reputation relating to high quality – particularly early stage – clinical trials will also support growth in this area.

Barriers / opportunities

Australia is currently limited in its ability to expand RM product manufacturing, which is needed to grow the volume of RM clinical trials and will be necessary to develop an export market. This is due, in part, to the lack of financial support schemes that would enable Australia to be internationally competitive.

Capability

Australia has high quality cell manufacturing and tissue engineering facilities and capabilities. However, these are currently only designed to meet the needs of the clinical trial market. Expanding capabilities and capacities to meet commercial market quantities will involve substantial investment in equipment and clean rooms. While infrastructure and equipment can be readily expanded (within 12 months), the more significant constraint is scaling human capital, as it has a longer lead-time.

There are specific international biopharmaceutical manufacturing training programmes available overseas, but limited examples exist in Australia. However, in April 2019, The University of Technology Sydney will open a 420m^2 GMP-Lite facility based on GE Healthcare's Flex Factory platform. This single use biomanufacturing system can be used to train the next generation of RM product operators.

Another option that may help address the skills shortage is to evaluate and assess skills, such as engineering and 3D printing, that have been developed in other sectors including agriculture and mechanical engineering. Some will likely be transferable and applicable to RM.

Financial incentives

Dedicated funding and attractive partnering programs have led to the establishment of a number of GMP facilities in Canada (see case study below on CCRM and the Centre for Cell and Vector Production (CCVP)). While UTS' GMP facility received considerable NSW State Government investment, other countries such as Singapore have built specific precincts dedicated to RM.

Singapore's well-developed and supported medical manufacturing infrastructure and proximity to Asian markets has attracted many global healthcare companies to its shores. Australian company Mesoblast and Swiss company Lonza selected Singapore's Tuas Biomedical Park as the location of their large-scale cell culture manufacturing facility. Mesoblast announced that it would receive financial incentives from the Singapore Economic Development Board (EDB) for activities in Singapore related to manufacturing, product development and commercialisation.

International case studies

World's first commercial iPS cell plant for manufacturing cell therapies

In March 2018, the Sumitomo Dainippon Manufacturing Plant for Regenerative Medicine and Cell Therapy opened in Osaka, Japan. Company reports suggest that the facility could **produce cells to treat hundreds of patients p.a.**

The facility has more than **30,000 sq. ft.** of floor space and is divided into three zones, each dedicated to different types of cells. Construction of the facility cost **c.AU$500m**

Sumitomo Dainippon Pharma

Investment in manufacturing capability and skills development

CCRM Canada and the University Health Network's new Centre for Cell and Vector Production (CCVP) is planned to be operational in late 2018. This GMP facility is designed to help solve RM manufacturing challenges through the provision of cell therapy inputs, creation of jobs and the establishment of a base for the expansion of advanced manufacturing capability in Canada.

"Services offered in CCVP include **full manufacturing** and release of cell and viral vector materials, QC testing, **access to clean rooms,** cell bank creation, **training services,** supplier management and audit support services"

CCRM

Source: The Scientist; Sumitomo Dainippon Pharma; CCRM

Geography: Although isolated, Australia has a geographical opportunity to be the Asia-Pac regenerative medicine hub

Strengths

Australia's proximity to Asia, coupled with talent, skills, infrastructure and a reputation for quality could be advantageous to the country becoming a RM centre for Asia Pacific.

Doorstep of Asia

Australia has an opportunity to focus on mechanisms that would allow it to extend into major Asian markets to provide a rapid supply of quality RM components or finished products. There are seven major international airports in Australia and more than a dozen restricted use international airports that could serve as transport bases. In addition, Australia is well placed to act as a trusted supplier in the region, given our high levels of quality (as discussed in the 'capabilities' section on page 14 of the report). This could provide Australia with a competitive advantage as a supplier to South East Asia over other countries in the region that are investing in RM (e.g. China), particularly in the next 5 to 10 years.

Hub location

The broader manufacturing sector has already acknowledged the need for Australian manufacturing to focus on high value and specialised products and that these can be component-focused in order to access global supply chains. Similarly, RM presents supply chain options. This may include an input-based or end-stage approach: the former through focussing on cell banks or 3D printed organ scaffolds, and the latter by 'packaging', testing and certifying cell, tissue and gene therapy products.

Barriers / opportunities

There are two possible opportunities that arise from Australia's location and population. The first is that, depending on the nature of the disease or injury, the RM treatment procedure may need to be conducted in a stepwise manner that would negate geographical disadvantages relating to supply logistics. The second is due to approximately half of Australia's population of 25m people being either first or second-generation migrants: this ethnic diversity makes the evaluation of therapies more applicable to real world scenarios.

Distance and time zone

The quality assurance of RM treatments is time-bound as the products are perishable by nature. Thus the urgency relating to delivery time frames needs to be considered in the context of where the opportunities lie for Australia in RM. Airline terminal and logistics operators will also need training around special handling procedures for RMs. In addition, the practicalities of running operations in Australia may be challenging for small or medium-sized biotech companies based in the US or Europe.

Small population

From a business case perspective, the size of the Australian population is said to make it a less attractive market for therapy launches. While Australia does not score highly on the Global Innovation Index[32], its high quality healthcare system (ranked number 1 in the world for health outcomes[33]) and national reimbursement system mean that innovative therapies are often available to patients in Australia. Australia's small population and geography should not prevent Australian research and therapies being developed locally. These Australian therapies could service the Asia Pacific region, with a middle class that is 80 times that of Australia's and is expected to represent 90% of global middle class population growth from 2015 to 2022[34]. As a result, the high quality health and medical ecosystem and shortened supply and logistics chain for RMs may be an advantage with a concomitant attractive return on investment within the Asia-Pacific region.

[32] 'Global Innovation Index 2018 – Energizing the World with Innovation'. Cornell University – INSEAD – World Intellectual Property Organisation

[33] 'Mirror, Mirror 2017: International Comparison Reflects Flaws and Opportunities for Better U.S. Health Care'. July 2017, The Commonwealth Fund, US

[34] Karas, H. 'The Unprecedented Expansion of the Global Middle Class'. February 2017, Brookings Institution, US; Euromonitor

5 PRIORITY ACTION AREAS FOR THE AUSTRALIAN REGENERATIVE MEDICINE SECTOR

5.1 Sector vision

The 60+ sector participants consulted in the development of this report have defined a nationwide RM sector vision. The vision will provide an important 'north star' that the sector as a whole can collectively navigate towards. The overarching vision is to:

Create an end-to-end world-leading value chain (from discovery to delivery) that grants Australian patients access to world-class regenerative medicine therapies, creates jobs and enables the export of Australian therapies to the world

Implicit in this vision is that Australia will need to create a sustainable local industry that is successful at commercialising local research and creating leading therapies for the global market and patients. Australia will need to have strengths at each of the key stages of the value chain including:

- Early stage research to feed the innovation pipeline.
- Pre-clinical development.
- Clinical trials (for locally developed therapies as well as international R&D).
- Manufacturing capability to support clinical trials and potential commercial manufacture.
- Therapy delivery via healthcare professionals.

Australian research and therapies could be taken to the global market by Australian companies or through partnerships with multi-national pharmaceutical and medtech companies that can provide resources, global market access and commercial know-how. Given the significant funding and commercial capability required to support a presence in multiple countries, partnering is likely be the most common pathway.

Australia's competitive advantage

Australia already has a strong research base to build upon. Few other countries have a comparable level of capability. Australia is ranked fifth in the world in terms of biotechnology innovation of which RM is a subset[35].

As discussed earlier, RM is at the leading edge of science and medicine and is more complex relative to other pharmaceuticals and health interventions in terms of research, pathways to market, therapy production and insertion into a supply chain, and administration of the therapy. Many areas of RM require a skilled workforce, which Australia has, and a high proportion of human intervention, e.g. CAR-T cell therapy in oncology, stem cells in neurology and ophthalmology. The future workforce created through further development of a thriving sector will position Australia at the forefront of the next wave of medtech and pharmaceutical innovation within and beyond RM.

[35] 'The 2016 Scientific American Worldview Overall Scores'. Scientific American Worldview

As the global sector grows, a significant increase in manufacturing activity of raw materials will be required. This includes viruses for gene therapies and an array of stem cells. There is a strong case for Australia to become an advanced manufacturing 'centre of excellence' to serve the RM needs of the Asia Pacific region.

Australia's competitive advantage stretches beyond RM research and a highly skilled workforce into areas that benefit the wider medical technology and pharmaceutical sector. These include:

- The R&D Tax Incentive which provides companies with crucial financial incentives.
- Internationally recognised, high quality-assurance in medical technology and pharmaceutical approvals.
- A global reputation as an attractive market to conduct clinical trials.
- A specific government focus on investing in medical innovation.

The value of achieving this vision in monetary terms is significant. The global RM market is estimated to reach AU$120bn by 2035. If Australia were to attract a five per cent market share, this would represent AU$6bn in annual revenue, predominantly in exports, and create 6,000 jobs.

5.2 Sector priority actions

To realise the sector vision and maximise the chance of success in a dynamic global market, a coordinated response is required between government, the private sector and non-profit organisations. This response should be centred around five key priority action areas, as illustrated in the table below:

SUMMARY: AUSTRALIAN REGENERATIVE MEDICINE SECTOR VISION AND PRIORITY ACTION AREAS					
Vision	Create an end-to-end world-leading value chain (from discovery to delivery) that grants Australian patients access to world-class regenerative medicine therapies, creates jobs, and enables the export of Australian therapies to the world				
Action areas	Capabilities / workforce	Collaboration	Funding	Regulation and policy	Infrastructure
	Attract, build and retain world-class talent	Collaborate across the value chain	Secure long term investment in the sector	Create a clear market access pathway that is aligned to leading global markets	Build Australian manufacturing capability in stages

ATTRACT, BUILD AND RETAIN WORLD-CLASS TALENT

Capabilities / workforce

To achieve the sector vision, Australia should prioritise skills development. RM is an emerging, highly specialised field based on cutting-edge technology. Therefore, there is a need for the workforce across the entire value chain to be highly skilled. This talent pool will need to cover a diverse capability set due to the significant range of therapies within the RM sector. Deep expertise will be required in specific areas. Specific examples include:

- Researchers with world-leading knowledge in the sector.
- Service providers with the skillset to appropriately interact with delicate materials with a short shelf-life.
- Clinicians need to be trained in the delivery of innovative therapies.

Note: investment in manufacturing skills and capability as a key priority is explored in more detail in the 'infrastructure' section (5.2.5).

Example actions that could help progress this action area include:

Further develop world-leading training programs

Bolster existing training programs and actively develop additional ones through Australian universities, hospitals and training organisations. These programs could fall into two broad categories:

- Baseline skills common to other medical technology and pharmaceuticals (e.g. commercialisation skills such as identifying a clinical need, clinical trial design, developing a business case, and strategic partnering).
- Highly-specialised RM-specific skills (e.g. cell manufacturing, tissue engineering).

Continue and increase financial incentives that encourage operation in Australia

Use financial (and other) incentives to attract and retain world-leading capabilities in Australia. This includes:

- Attracting companies and their workforce to Australia
  - Grants and other funding such as the R&D Tax Incentive can be used to incentivise RM organisations to set up their operations in the local market.
  - Other countries use the provision of funding to attract overseas companies. For example, the Japan External Trade Organization (JETRO) has a AU$12m fund for foreign investors[36] and the Singaporean government provides financial assistance, as demonstrated by their ability to attract Mesoblast to manufacture its products in Singapore.
- Initiatives to attract world-class clinicians to Australia
  - Provide funding for additional clinicians to be involved in RM clinical trials and other activities (similar to the UK Catapult investment into training at three Advanced Therapies Treatment Centres).
  - Offer financial incentives to high-performing medical students to specialise in RM therapies.

Provide resources to expedite translational research

Hospitals currently have limited resources for translational research and commercialisation. Existing funding structures are designed around the delivery of healthcare (i.e. hospital BAU) and research (e.g. NHMRC grants). However, there are some funds available that are designed to assist with non-scientific commercial elements of the process (e.g. governance and product development). Allocating specific resources to activities that support commercialisation will help to further expedite translational research and ensure faster delivery of RM therapies.

[36] 'The Quest for Advanced Regenerative Medicine'. 2016, Government of Japan; converted from JPY using 80.51 AUD:JPY exchange rate, as per 10-Oct-2018.

COLLABORATE ACROSS THE VALUE CHAIN

Collaboration

Increasing collaboration within and across the Australian regenerative medicine sector will help to accelerate the development of world-leading therapies for export (either by Australian-based biotech and pharmaceutical companies or by multinationals). The quality and pace of research discoveries should increase through interdisciplinary cooperation. Moreover, early collaboration between regulators and industry can help reduce approval delays and misallocation of resources and ensure appropriate clinical trial design and preparation.

Example actions that could help progress this action area include:

Create or support a nationally focused RM 'catalyst' strategic hub

Back a single, national strategic organisation tasked with driving collaboration (both within Australia and internationally) and industry growth. This hub does not necessarily need to be created as a new entity - there are several bodies already in the Australian market that could adopt this role. This 'catalyst' hub should encourage and facilitate collaboration across the entire value chain, from researchers through to clinicians and patient advocacy groups. It is important to include patient advocacy groups as a part of a broader public awareness campaign around the potential/benefits of proven therapies (regulated by the TGA) as well as the risks associated with those unregulated therapies available in small clinics and internationally.

This type of organisation is seen in other leading jurisdictions (e.g. AMED in Japan, CGT Catapult in the UK). These groups are an effective means by which to lead sector wide initiatives, drive collaboration and facilitate knowledge transfer to advance the development and adoption of global best practice, but they require appropriate resourcing.

Support a nationally focused commercialisation body

Continue to support a centralised body focused on the commercialisation of RM. This does not necessarily need to be separate to the 'catalyst' strategic hub. However, it is important that both commercialisation and collaboration initiatives are focused on. This organisation will help Australia with the second strategic goal of creating leading therapies for global export. Activities should be centred on addressing translational research barriers that prevent therapies moving from the lab to the clinic.

An important consideration will be how best to foster market-led initiatives such as cases where the demand for therapies has been identified through collaboration and consultation with clinicians and patient advocacy groups. An early and consistent focus on the patient will improve the likelihood of commercial success of RM therapies.

One example of a market-led initiative is the disease-team approach, which is used by both the CIRM and the Ontario Institute of Regenerative Medicine (OIRM). This approach aligns grant teams from multiple institutions that are all focused on finding a therapy for a specific disease, rather than aligning grants with an individual institution.

SECURE LONG TERM INVESTMENT IN THE SECTOR

Funding

Crucial to growth of the Australian RM sector is attracting investors who are experienced in RM, and deploying these funds towards high quality opportunities. Compared with other leading jurisdictions, investment in the Australian RM sector is relatively scarce, biased towards basic research, and significantly weighted towards government grants and investments. Securing long-term investment from diverse sources that ideally have experience with RM will help unlock the potential of the sector.

Example actions that could help progress this action area include:

Effectively target MRFF funding to build the regenerative medicine sector

As part of the 2014-15 Federal Budget, the Australian Government announced the establishment of The Medical Research Future Fund (MRFF), an ongoing source of funding for medical research over the medium to long-term[37]. The original $1bn investment is reportedly on track to grow to $20bn by 2020-21, with the net earnings of the fund to serve as a permanent revenue stream for HMR. The RM sector expects that that this fund will increasingly fill an important gap in the commercialisation of medical research.

As a result, the MRFF could be a valuable source of funding for the RM sector, but there are two areas of uncertainty surrounding this:

- Firstly, the quantum of disbursements from the MRFF may not reach the intended $1bn per annum. Capitalisation into the fund is on track to date, however, future contributions are not guaranteed and are subject to political and fiscal risks. Disbursements are also generated via investment income and, as a result, are subject to market risk.
- Secondly, RM is aligned with only one of the large MRFF programs that have been announced to date, the Frontier program. The specifics of this program are still under development and funding allocations will likely be through a competitive process. As a result, disbursements for RM are not guaranteed from this fund

It is therefore important to have ongoing dialogue with the MRFF board members to ensure emerging RM discoveries are aligned with new initiatives under the fund's six strategic platforms. It should be noted that there are initiatives underway to provide additional clarity around future MRFF disbursements. At the time of writing, consultation for the second round of Australian Medical Research and Innovation Priorities (Priorities) for 2018-20 had recently concluded. These Priorities underpin the MRFF initiatives and their relative funding disbursements. They are due to be submitted to Parliament in November, 2018.

Encourage investment through alignment of sector activities with government priorities

RM is well placed to align with broader government priorities that could unlock government funding opportunities. For example, manufacturing related to regenerative medicine (e.g. cell manufacturing) could align well with the Australian Government's priority to accelerate the growth of the advanced manufacturing sector. This building of capability in manufacturing is also explored further in the upcoming 'infrastructure' section (5.2.5).

Attract private investment based on mutual benefit

There is a notable lack of VC funding in regenerative medicine in Australia in comparison to other competing markets, such as the US and Canada. While the Australian Government has established the BTF, which is administered through licensed VC fund managers, the investment opportunities are currently focused at a later stage of translation and they do not align well with the funding need for most RM (i.e. pre clinical or earlier).

Aligning RM R&D around an end-product, with a clear line of sight to the clinic (as outlined in the collaboration section on page 16), could help articulate the potential financial upside of investment more clearly and make opportunities more clearly 'investible'. Additionally, attracting international VC firms that have experience in RM to Australia would assist in stimulating the sector.

[37] 'About the MRFF'. Department of Health, Australia

CREATE A CLEAR MARKET ACCESS PATHWAY THAT IS ALIGNED TO LEADING GLOBAL MARKETS

Regulation and policy

Regulators in Australia are engaged in supporting the successful introduction of safe and effective RM therapies to local patients. One example is the development of the biologicals framework in 2011. Alignment of this framework with regulatory bodies in leading markets (e.g. the FDA and EMA) will help to simplify operations across jurisdictions in this global market. In addition, It is important to consider that patient safety is a priority for therapies that are regulated by the TGA (and the focus of this report) as well as those that not regulated by the TGA. All regulators will need to be resourced accordingly in order to ensure patient safety is managed appropriately.

On the policy and reimbursement side, the RM sector in Australia would benefit from a clearly defined reimbursement pathway. Clarity around future revenue streams in the Australian market is a crucial consideration for biotech companies, investors and multinational pharmaceutical companies looking to introduce world-leading therapies into the market.

Example actions that could help progress this action area include:

Harmonisation with leading international markets

Alignment with international regulation will help to reduce complexity in seeking approvals for RM therapies across multiple markets. This harmonisation will likely need to be dynamic as Australian and international regulators are still evolving their regulatory frameworks for RM and 'best practice' is yet to be determined. TGA is actively examining opportunities for alignment with leading markets.

Provide a clear path to reimbursement

Develop and communicate a clear pathway for reimbursement of RM therapies that don't fit neatly into the existing reimbursement pathways, including PBAC and MSAC.

A formalised pathway to reimbursement that is widely understood by sector participants and potential investors, such as multi-national pharmaceutical companies or VC, could increase the attractiveness of investing in the RM sector.

BUILD A COMMERCIALLY VIABLE AUSTRALIAN MANUFACTURING SECTOR TO SERVE THE INTERNATIONAL MARKET

Infrastructure

In order to support an increasing number of clinical trials and, eventually, production of world-leading RM therapies at scale, increased Australian manufacturing capability and capacity is required.

While investment in manufacturing capacity, including clean rooms, will be required, the scale-up of infrastructure and equipment can be readily delivered and will often be backed by the companies commercialising the therapy. However, the skills and capabilities required to support increased manufacturing are much harder to assemble in a short time frame. As a result, ensuring a sustainable skilled workforce should be a priority action area particularly if Australia is positioning itself to be the RM 'centre of excellence' for Asia-Pacific.

Following a recent cell therapy conference, the CIRM noted that the scale up and quality control of stem cell manufacturing is critical in the development of stem cell treatments, and that this is a potential barrier to growth as more treatments enter the market. As quality control is vital to the success of all types of RM, fostering this expertise in Australia could become a key selling point for Australia. Furthermore, increased capability to support the RM supply chain in Australia is essential to realise the export growth opportunities and secure access of world-leading therapies to people in Australia.

An example action that could help progress this action area includes:

Actively pursue and encourage opportunities to attract flexible and commercially viable manufacturing capability

Actively seek manufacturing opportunities for emerging RM therapies that are about to enter the market (e.g. CAR T-cell therapies). Attracting first movers in the global sector could help position Australia as a trusted destination for the manufacturing of RMs. Offering financial benefits and promoting Australia's compatibility with highly skilled manufacture (strong quality assurance, and a highly-skilled work force) could be used to incentivise global companies. The pursuit of opportunities to build a commercially viable manufacturing sector should be coupled with efforts to boost supply chain capabilities.

SUMMARY: AUSTRALIAN REGENERATIVE MEDICINE SECTOR VISION AND PRIORITY ACTION AREAS					
Vision	Create an end-to-end world-leading value chain (from discovery to delivery) that grants Australian patients access to world-class regenerative medicine therapies, creates jobs and enables the export of Australian therapies to the world				
Action areas	Capabilities / workforce	Collaboration	Funding	Regulation and policy	Infrastructure
	Attract, build and retain world-class talent	Collaborate across the value chain	Secure long term investment in the sector	Create a clear market access pathway that is aligned to leading global markets	Build Australian manufacturing capability in stages
Example actions	• Further develop world-leading training programs. • Continue / increase financial incentives encouraging RM operations in Australia. • Increase resources to expedite translational research.	• Create or support a nationally focused RM 'catalyst' strategic body. • Support a nationally focused commercialisation hub. • Establish a disease-team based approach.	• Effectively target MRFF funding to build the regenerative medicine sector. • Encourage investment through alignment of sector activities with government priorities. • Attract private investment and international VC.	• Harmonise regulation with leading global markets. • Extend pharmaceutical accelerated approval pathways to biologicals. • Provide a clear path to market access and broaden scope for reimbursement.	• Actively pursue and encourage opportunities to build and/ or attract flexible and commercially viable manufacturing capability.

6 SUGGESTED NEXT STEPS

This report demonstrates the collective willingness of the RM sector to work together and with external partners to elevate the sector to be more globally competitive. There is much work to be done and it will require focus and persistence. In the immediate term, there is a need for a central group to represent the sector and take the lead on facilitating, coordinating and connecting stakeholders to progress the priority areas, in particular the 'collaboration' priority area. MTPConnect, in collaboration with the AusBiotech Regenerative Medicine Advisory Group will work to continue the dialogue and address the immediate needs of:

- Identifying and establishing the national RM sector 'catalyst' collaboration body.
- Assisting to secure appropriate resourcing for the 'catalyst' body.

Once established, the 'catalyst' will facilitate further sector collaboration and advance the completion of actions within the priority action areas. This includes:

- Finalising the specific priority actions for the sector (from within the 'example priority actions' or new ideas);
- Identifying interdependencies and the logical sequencing of agreed priority actions;
- Facilitating necessary collaborations across the value chain in order to enable effective completion of the agreed priority actions; and
- Monitoring progress of agreed priority actions and helping the sector overcome important barriers and bottlenecks.

7 GLOSSARY

Term	Definition
Allogeneic cells	Cells that are sourced from a donor, modified and then transplanted into several other patients
AMED	Japanese Agency for Medical Research and Development (significant funding source for regen med in Japan)
ARMI	Australian Regenerative Medicine Institution (based at Monash University)
ASC	Adult stem cells
ASCC	The Australian Stem Cells Centre. Founded in 2003. It was the precursor to Stem Cells Australia
Autologous cells	Cells harvested from a patient and reintroduced back into the same patient
BTF	The Biomedical Translation Fund (BTF) established by the Australian Government. It is made up of $250 millions of Commonwealth capital and $251.25 million private sector capital
CAR-T	An emerging cancer treatment that is described as "giving patients a living drug" - T cells (the workhorses of the immune system because of their critical role in orchestrating the immune response and killing infected cells). The therapy requires drawing blood from patients and separating out the T cells. Next, using a disarmed virus, the T cells are genetically engineered to produce receptors on their surface called chimeric antigen receptors, or CARs. The final step is the infusion of the CAR T cells into the patient - If all goes as planned, the engineered cells will recognize and kill cancer cells
CCRM	Centre for Commercialisation of Regenerative Medicine. First branch was established in Canada in 2011. Since then, they have also opened a branch in Australia
Cell therapy	Treating a disease or degenerative condition with cells that have been manipulated in vitro and subsequently introduced into the body
CTTWA	Cell and Tissue Therapies WA located in Royal Perth Hospital
Differentiated cells	Cells that perform a specific function and do not have the potential to become other cell types
DIIS	Department of Industry, Innovation and Science (Federal)
DoH	The Department of Health (Federal)
ESC	Embryonic stem cells
Good Manufacturing Practice (GMP)	Quality assurance guidelines to ensure products are consistently produced to start-of-the-art quality standards appropriate to their intended use
Haematopoietic stem cell	A stem cell that is isolated from the blood or bone marrow and can differentiate into a variety of haematological cells
HREC	The Human Research Ethics Committee (HREC) reviews clinical trials to ensure they are ethically acceptable and in accordance with standards and guidelines in Australia. There are over 200 HRECs across Australia
ICPMR	Institute for Clinical Pathology and Medical Research located at Westmead and the University of Sydney
In vivo	Experiment or procedure done in the body of a living organism
In vitro	Experiment or procedure that does not use a living organism as the host of a test
Immunogenicity	Response of a body's immune system to a foreign protein or transplant
iPS / iPSCs	Induced pluripotent stem cells are pluripotent cells that can be generated directly from adult (differentiated) cells
Mesenchymal stem cell	Mesenchymal stem cells (MSCs) are multipotent stem cells found in bone marrow that are important for making and repairing skeletal tissues, such as cartilage, bone and fat. MSCs make up a very small fraction of all the cells in human bone marrow

Term	Definition
MRFF	Medical Research Future Fund. a $20 billion fund targeted at the health of Australians, the economy and the sustainability of the health system
Multipotent	Cells that can become any of the differentiated cells within a specific lineage, but not all types (i.e. adult stem cells)
NHMRC	National Health and Medical Research Council
OIRM	Ontario Institute of Regenerative Medicine, established in 2014. The vision of OIRM is to transform the treatment of incurable diseases, making Ontario a global leader in the development and dissemination of stem cell-based products and therapies
Pluripotent	Cells that can give rise to any of >200 cells in the body (i.e. embryonic stem cells, iPS)
SCA	Stem Cells Australia
Stem cells	An undifferentiated cell capable of giving rise to a cell type with a specialised function
Regenerative medicine	The branch of research dealing with the replacing, regenerating and restoring of human cells and organs to normal functioning, commonly involving stem cells, in vitro / in vivo growth and cell and gene therapy
TGA	The Therapeutic Goods Administration, a division under the Department of Health is the regulatory body of therapeutic goods in Australia
Totipotent	Having the ability to form a complete human organism (i.e. fertilised zygotes)
Undifferentiated cells	Cells that have not yet developed into a specialised cell type (i.e. stem cells)

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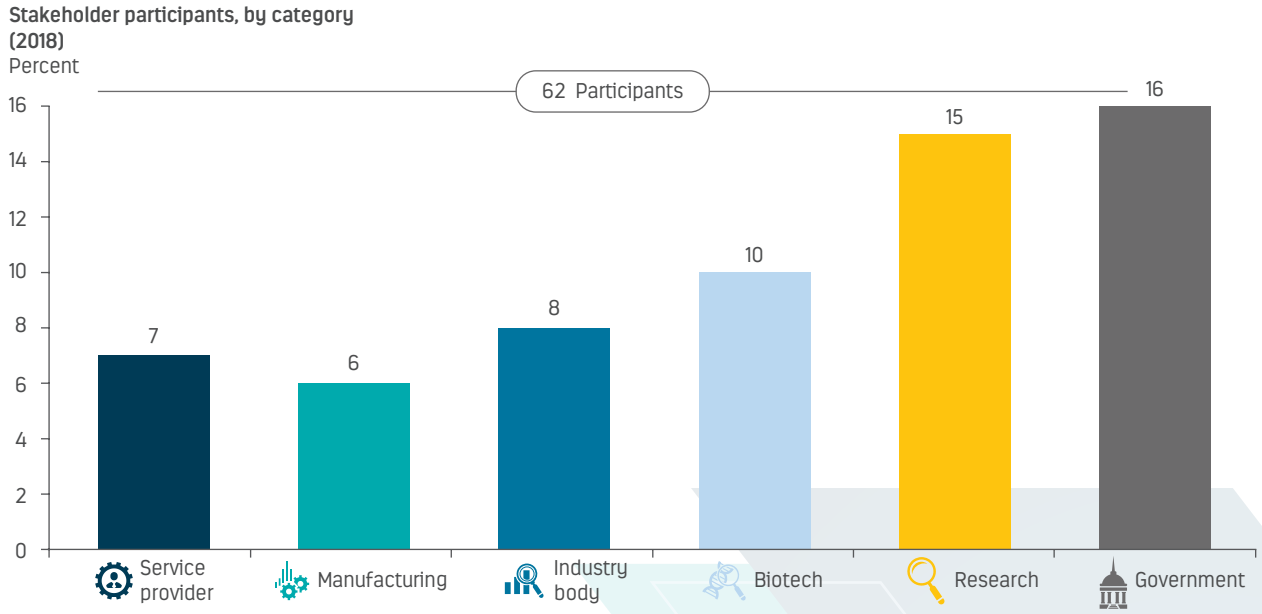
9 APPENDIX

Overview of stakeholders engaged through the development of this review



RM-focused companies in operation in Australia

Company	Ownership (Listed / private)	Description
Anatomics Pty Ltd	Private	Anatomics is an Australian company that manufactures patient-specific implants for global distribution
Admedus Ltd	Listed	Admedus is a medical technologies company. Its proprietary ADAPT engineering process produces implantable tissue bio-scaffolds for a range of cardiovascular and vascular applications
AmpliPhi Biosciences	Listed	AmpliPhi Biosciences is a clinical-stage biotechnology company focused on the development of bacteriophage-based therapies for the treatment of antibiotic-resistant bacterial infections
Avita Medical Ltd	Listed	Avita Medical is a clinical and commercial company developing and marketing a range of respiratory and regenerative products including ReCell spray-on skin for the treatment of burns
Benitec Biopharma Ltd	Listed	Benitec is a biotechnology company developing a proprietary therapeutic technology platform that combines RNA interference with gene therapy for the goal of providing sustained, long-lasting silencing of disease-causing genes from a single administration
Calimmune	Listed	Recently acquired by CSL, Calimmune has developed a portfolio of recombinant and plasma-derived products for treating bleeding disorders, immune deficiencies and chronic inflammatory demyelinating polyneuropathy

Company	Ownership (Listed / private)	Description
Cancure	Private	Cancure is a biopharmaceutical company developing a suite of oncology therapies which enhance the body's anti-cancer immune response, or kill cancer cells by exploiting novel targets within them
Cartherics	Private	Cartherics is an early-stage biotechnology company developing off-the-shelf cellular immunotherapy for cancer
Cell Therapies	Private	Cell Therapies is a leading cGMP manufacturer and distributor of cellular therapies with cell processing facilities in Melbourne
Cellcare	Private	Cell Care is Australia's largest cord blood and tissue bank
Cell Mogrify	Private	Cell Mogrify is a private biotechnology company based in the UK (with a subsidiary in Australia) developing a new approach to cell reprogramming in regenerative medicine
Cryosite Ltd	Listed	Cryosite is a biologistics company that develops and commercialises cryopreservation and offers the following services: bio-repository, clinical trials logistics, commercial drug distribution and cellular therapies manufacturing
CSL Ltd	Listed	CSL is a global biotechnology company involved in research, development, manufacture, and distribution of medical products
Cynata Therapeutics Ltd	Listed	Cynata Therapeutics is an Australian regenerative medicine company that is developing a therapeutic stem cell platform technology
Eppendorf	Private	Eppendorf is a Hamburg-based life sciences company that develops and sells instruments, consumables, and services for liquid, sample, and cell handling
Exopharm Pty Ltd	Private	Exopharm is an early-stage biotechnology company developing a clinical application of exosomes in human therapeutics
Imugene Ltd	Listed	Imugene is an Australian biopharmaceutical company developing HER-2+ gastric and breast cancer immunotherapies
Immutep Ltd	Listed	Immutep Ltd (formerly Prima Biomed) is a biotechnology company working primarily in the field of cancer immunotherapy
Invetech	Private	Invetech Pty Ltd a Australian engineering company involved in instrument development, custom automation and contract manufacturing
In Vitro Technologies	Private	In Vitro Technologies is a medical distribution company specialising in the sale and support of scientific, clinical diagnostic, medical and related products
Living Cell Technologies Ltd	Listed	Living Cell Technologies Limited is an Australian biotechnology company involved in cell encapsulation and implantation for human therapeutics
Magellan Stem Cells Pty Ltd	Private	Magellan Stem Cells are an Australian based biotechnology company dedicated to the development of cellular therapies in collaboration with Monash Immunology and Stem Cell Laboratories (MISCL)
Mesoblast Ltd	Listed	Mesoblast Limited is an Australian-based regenerative medicine company developing treatments for inflammatory ailments, cardiovascular disease and back pain
Miltenyi	Private	Miltenyi is a German biotechnology company focusing on the design, development, manufacture, and integration of products that enable cell and gene therapy
Orthocell	Listed	Orthocell is an Australian regenerative medicine company developing treatments for tendon, cartilage and soft tissue injuries

Company	Ownership (Listed / private)	Description
Phylogica	Listed	Phylogica is a Perth-based biotechnology company focused on intracellular biological therapeutics through peptide drug development
Polynovo Ltd	Listed	Polynovo Limited is an Australian medical device company that designs, develops and manufactures dermal regeneration solutions
Q-Gen Cell Therapies	Private	Q-Gen is a fully integrated facility for translational research within QIMR Berghofer, providing GMP manufacturing facilities for translating QIMR Berghofer's clinical research
Regeneus Ltd	Listed	Regeneus Ltd is an Australian clinical-stage regenerative medicine company developing a portfolio of cellular therapies that include osteoarthritis (OA) and other musculoskeletal disorders, oncology, dermatology and chronic pain
ReNerve	Private	ReNerve Pty Ltd is an Australian medical devices company specialising in the development of products involved in the repair and replacement of damaged nerves
Scinogy	Private	Scinogy is a biotechnology company that offers cell therapy manufacturing solutions for R&D, clinical trials and commercial production
Vivazome	Private	VivaZome Therapeutics Australian biotech company formed to develop and commercialise exosome-based therapies

Significant capital raising for RM-focused companies (2013-18)

Company	Market capitalisation, AU$m (as at 11/10/18)	Total significant capital raising 2013-18, AU$m
Admedus Ltd	48	48
AmpliPhi Biosciences	14	92
Avita Medical Ltd	158	48
Benitec Biopharma Ltd	42	58
Cynata Therapeutics Ltd	126	14
Immugene Ltd	79	24
Imutep Ltd	139	42
Living Cell Technologies Ltd	18	4
Mesoblast Ltd	1,028	111
Orthocell	28	4
Phylogica	69	16
Regeneus Ltd	37	6
Total	**c.1,800**	**c.500**

Source: ASX

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INFORMATION

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