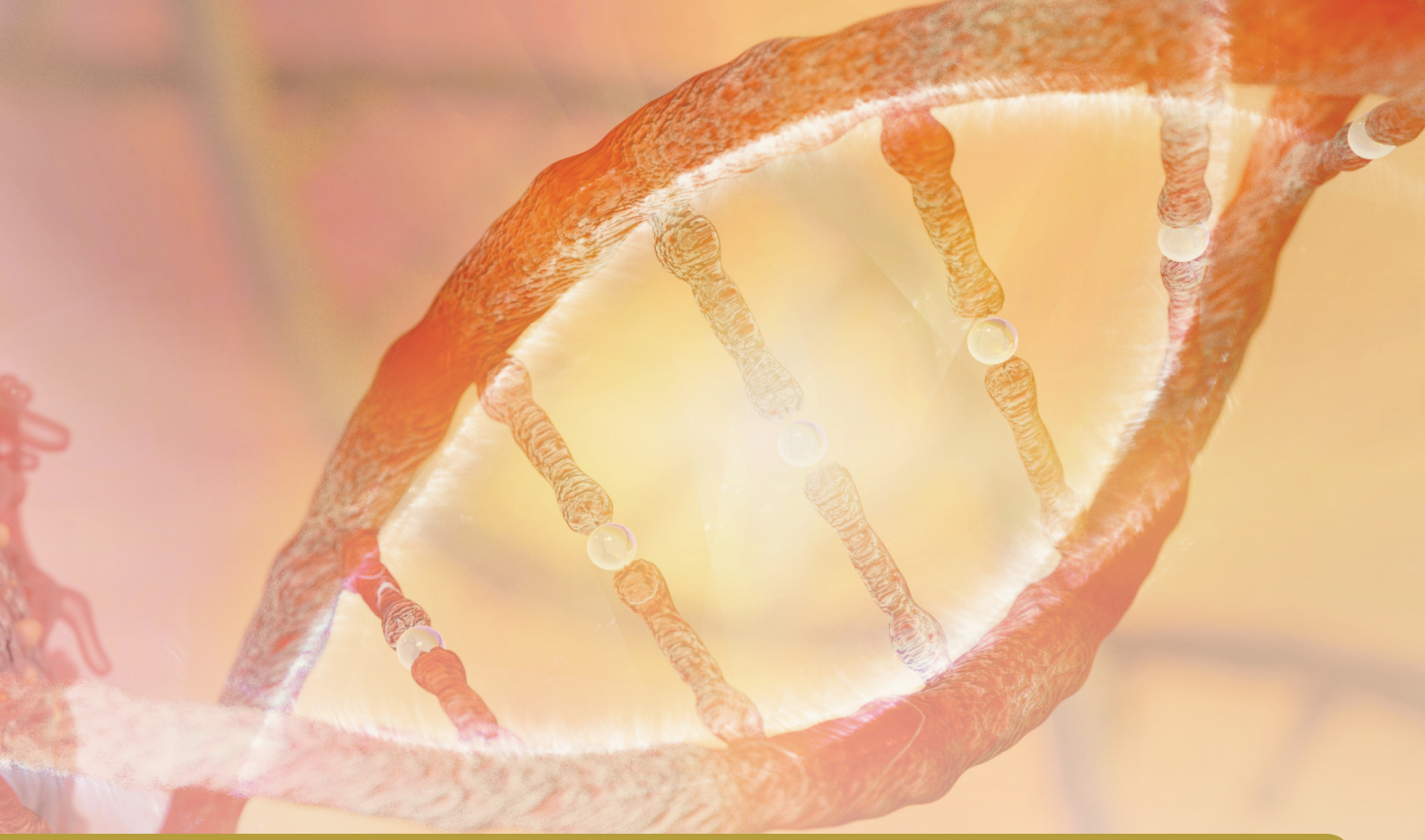


Australia's Regenerative Medicine Clinical Trials Database

Prepared by GlobalData

AusBiotech

Biointelect

cell therapies

Medicines Australia

Supported by MTPConnect MedTech and Pharma Growth Centre

NOVARTIS

RS RESEARCH STRATEGIES AUSTRALIA

Disclaimer

While the Regenerative Medicine Catalyst Project consortium has taken all due care to ensure that the information contained in this work is accurate at the time of publication, it provides no express or implied warranties or makes any representations in relation to this work or any content. The information contained in this work is provided 'as is' and without any guarantees as to its accuracy, currency, completeness or reliability. To the extent permitted by law, the Regenerative Medicine Catalyst Project consortium excludes all liability for any loss or damage occasioned by use of this work or information contained in this work. The Regenerative Medicine Catalyst Project consortium is not responsible for decisions or actions taken on the basis of the content of this work and you use the information in this work at your own discretion and risk.

Acknowledgements

This *Australia's Regenerative Medicine Clinical Trials Database* project was conducted between September 2020 and June 2021 as a key part of the Regenerative Medicine Catalyst Project. The project has been supported by a consortium of seven members that hold extensive insight and experience in the life sciences and regenerative medicines landscape in Australia: AusBiotech, Medicines Australia, Cell Therapies Pty Ltd, Novartis Pharmaceuticals Australia Pty Ltd, Biointelect Pty Ltd, Research Strategies Australia and Australia's Industry Growth Centre, MTPConnect.

The Regenerative Medicine Catalyst Project is funded through MTPConnect's Growth Centre Project Fund Program, an Australian Government initiative supported by the Department of Industry, Science, Energy and Resources. It is a competitive matched funding program that aims to invest in ideas to boost the innovation, productivity and competitiveness of Australia's MTP sector. Six consortium members are providing matched funding.

Requests and inquiries pertaining to the report, including copyright permissions, should be directed to the consortium via AusBiotech.

Regenerative Medicine Catalyst Project also thanks GlobalData for its assistance in preparing this report, www.globaldata.com, info@globaldata.com.

Contents

Table of Figures

Foreword

The Regenerative Medicine Catalyst Project has brought together seven partners in a consortium to build the foundations for a national regenerative medicines (RM) sector 'catalyst' collaboration body. The Regenerative Medicine Catalyst Project will address priority action areas including: workforce capabilities, collaboration, funding, regulation and policy infrastructure, and Australian manufacturing capability. The Catalyst Consortium and the subsequent Catalyst Body aim to support the Australian RM industry to see it thrive and drive benefits to the health of its people and Australia's economy. This *Australia's Regenerative Medicine Clinical Trials Database* report forms a key part of the Regenerative Medicine Catalyst Project.

The significance and need for the Regenerative Medicine Catalyst Project was highlighted in a national, sector-wide report that assessed the current state of the Australian RM sector and made recommendations on the priorities and goals, see *Regenerative medicine: Opportunities for Australia* (MTPConnect, LEK, 2018).

Major outcomes of the project include other reports and data that each add further to the body of evidence and understanding of the sector. The reports include:

- A researched, strategic roadmap for the RM sector's development in Australia, including sub-reports on skill and talent specific to the sector, determining a plan to attract patient venture capital investment and the role of Australian biotech companies partnering with global companies, and case studies;
- Determining a sustainable funding and model structure for an RM sector 'catalyst' collaboration body;
- A regulatory white paper;
- Establishing annual data points and information resources to: map/benchmark GMP manufacturing capability and capacity, establish a model for an annual clinical trial database (this report); and capture investments in Australian RM;
- Mapping the pathway for a typical product from early research to market, and patients receiving a therapy; and
- Mapping the global pipeline of gene and cell therapy products on the horizon.

Context

Australia has an opportunity to harness and leverage a growing and active global RM industry. If we get this right, success could be worth at least $6 billion (B) in annual revenue, 6,000 new jobs for Australia by 2035 and earlier access to ground-breaking therapies for Australian patients[1].

RM is a multidisciplinary field that seeks to develop the science and tools that can help repair, augment, replace, or regenerate damaged or diseased human cells, tissues, genes, organs, or metabolic processes, to restore normal function. It may involve the transplantation of stem cells, progenitor cells, or tissue, stimulation of the body's own repair mechanisms, or the use of cells as delivery vehicles for therapeutic agents such as genes and cytokines.

RM includes gene therapies, cell therapies, and tissue-engineered products intended to regenerate or replace injured, diseased, or defective cells, tissues, or organs to restore or establish function and structure.

[1] MTP Connect, LEK Consulting. (2018). Regenerative Medicine - Opportunities for Australia

Globally, the growing sector has more than 1,200 clinical trials in progress, and attracted about AU$26.3B (or US$19.9B) in financing in 2020[2]. With 97 ongoing RM Phase 3 clinical trials or products awaiting regulatory decisions in the coming months, therapeutics companies are turning their attention to the RM sector[3]. There are also increasing numbers of gene and cell therapies being developed in and brought to Australia for patient access.

Australia has a strong and active RM industry eco-system with basic and translational research capabilities, a clinical trials framework and clinical centres that are all internationally-recognised. More than 60 companies in Australia are developing RM products and more than 130 clinical trials in progress[4].

Executive Summary

Australia is an active and globally-popular destination for clinical trials, with more than 1,360 commencing in 2015, 1880 in 2019, showing a compound annual growth rate (CAGR) of 7% between 2015 and 2019[5]. This report, for the first time, captures the portion that are occurring in RM, and further categorises them into types.

As of January 2021, there were over 1,220 ongoing clinical trials investigating RM globally[6]. At the same time 11%, 130 clinical trials were ongoing and investigating RM in Australia and 2 clinical trials in progress and being conducted by Australian companies overseas.

For the purposes of this report, RM clinical trials were considered in various ways, such as disease areas, to give further insight, and the following therapeutic categories were analysed:

1. Gene Therapies
2. Cell Therapies
3. Gene Modified Cell Therapies
4. Tissue Engineered Products

In Australia, since March 2015, over 220 new RM clinical trials have been recorded and the number of trials has grown at a CAGR of 15.5% between 2016-2020. This growth was attributed to the increase in new trials for gene therapy and gene modified cell therapy. The highest number of new trials were recorded for gene therapies followed by cell therapies and gene modified cell therapies.

Of the 222 new clinical trials recorded for RM in Australia during the study period, oncology was the leading therapy area followed by central nervous system and infectious diseases. Genetic disorders and haematological disorders ranked 4th and 5th place.

In cell therapies, mesenchymal stem cells were the most studied in clinical trials whereas in gene therapy trials, antisense therapies were the predominantly studied technology.

The companies developing RM therapies included both small biotechs and larger biopharmaceutical firms. Overall, four of the top five sponsors for RM trials were from the industry. Among the top industry sponsors,

[2] 2020: Growth & Resilience in Regenerative Medicine, Annual Report Cell & Gene State of the Industry Briefing, Alliance for Regenerative Medicine, 2021

[3] 2020: Growth & Resilience in Regenerative Medicine, Annual Report Cell & Gene State of the Industry Briefing, Alliance for Regenerative Medicine, 2021

[4.] Regenerative Medicine Catalyst Project. (2021). Australia's Regenerative Medicine Clinical Trials Database.

[5] MTPConnect. (2021). Australia's Clinical Trials Sector. mtpconnect.org.au

[6] Alliance For Regenerative Medicine, State of the Industry Briefing 2021. alliancerm.org

Novartis AG was the leading sponsor followed by Alnylam Pharmaceuticals Inc and Ionis Pharmaceuticals Inc. Monash Health was the leading sponsor among the top non-industry sponsors.

Industry-sponsored trials (~80%) outnumbered non-industry sponsored trials in Australia. In terms of growth, the industry sponsored trials grow with a CAGR of 21% from 2016-2020, which was seven times higher than non-industry sponsored trials for the same period. Over the study period, the highest number of new trials were recorded in 2019 and 2020 both for industry and non-industry sponsors.

There were four new trials recorded for tissue engineered products. Three new trials were recorded (one trial each by Orthocell Ltd, Piramal Healthcare (Canada) Ltd, and by University of Western Australia) in Australia and one trial recorded by an Australian company overseas.

There were 17 new RM clinical trials recorded by Australian companies overseas between 1 March 2015 to 31 March 2021.

The top three Australian sponsors conducting RM trials overseas between 1 March 2015 to 31 March 2021 were Benitec Biopharma Inc, Mesoblast Ltd and Ascend Biopharmaceuticals Ltd.

Introduction

This report presents the results of the inaugural *Australia's Regenerative Medicine Clinical Trials Database*. The aim of the report is to establish annual data points and information resources to map current clinical trials and to establish a model for an annual clinical trial database. The report aims to assess the current state, progress and direction of the RM clinical development landscape. The report is intended to be a comprehensive and accurate review of the Australian clinical trials. The data in this report will provide a benchmark against which growth of Australia's RM clinical trials sector can be measured and tracked.

The following RMs are approved in Australia[7]:

Brand Name	Regenerative Medicine Category	Indication	Company	Approval Date (Australia)
Imlygic® (talimogene laherparepvec)	Gene Therapy	Metastatic Melanoma	Amgen	21-Dec-15
Spinraza® (nusinersen)	Gene Therapy	Spinal Muscular Atrophy (SMA)	Biogen	03-Nov-17
Kymriah® (tisagenlecleucel)	Gene-Modified Cell Therapy	B-Cell Acute Lymphocytic Leukemia; Diffuse Large B-Cell Lymphoma (DLBCL)	Novartis	19-Dec-18
Yescarta® (axicabtagene ciloleucel)	Gene-Modified Cell Therapy	Diffuse Large B-Cell Lymphoma, Primary Mediastinal Large B-Cell Lymphoma, High Grade B-Cell Lymphoma, and DLBCL arising from Follicular Lymphoma	Gilead	11-Feb-20
Luxturna® (voretigene neparvovec)	Gene Therapy	Leber Congenital Amaurosis (LCA); Retinitis Pigmentosa (Retinitis)	Novartis	05-Aug-20
Zolgensma® (onasemnogene abeparvovec)	Gene Therapy	Spinal Muscular Atrophy (SMA)	Novartis	04-Mar-21

[7] ARTG website: https://www.tga.gov.au/australian-register-therapeutic-goods, sourced June 2021

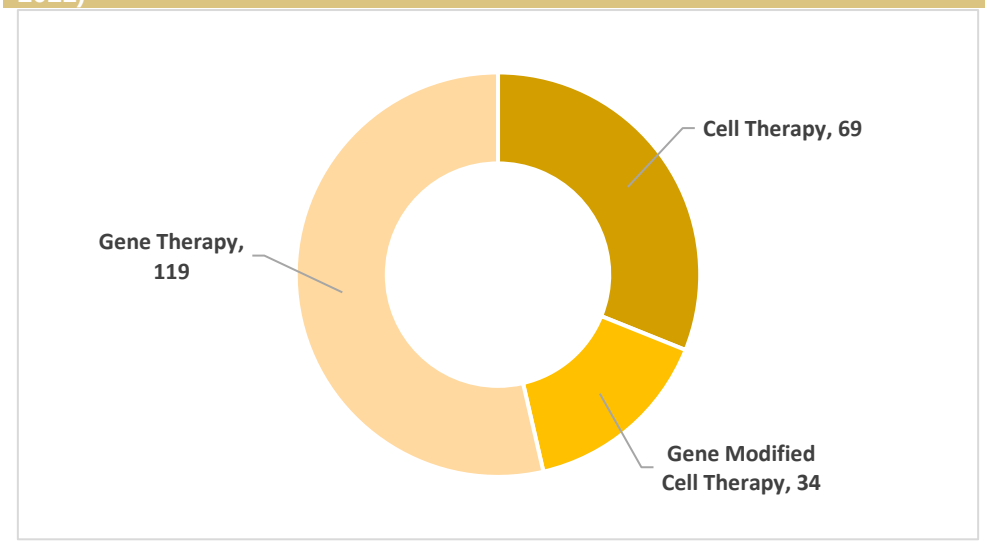
Commentary on key findings

Section 1: Analysis of New Clinical Trials Recorded in Australia

As of January 2021, there were over 1,220 ongoing clinical trials investigating RM globally[8]. At the same time 11%, 130 clinical trials were ongoing and investigating RM in Australia and 2 clinical trials in progress and being conducted by Australian companies overseas.

1.1: RM by Therapy Type

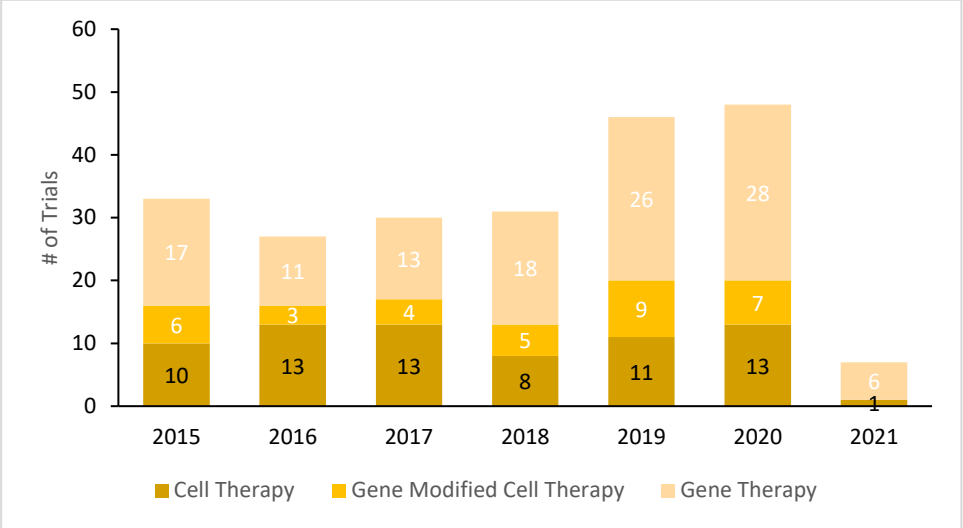
Figure 1: RM – Number of New Clinical Trials Recorded by Therapy Type (2015-2021)



Of the 222 new RM clinical trials recorded with start date from March 1, 2015 to March 31, 2021 in Australia (Figure 1), gene therapy accounted more than 50% of the trials followed by cell therapy (31%) and gene modified cell therapies (15%).

[8] Alliance For Regenerative Medicine, State of the Industry Briefing 2021. alliancerm.org

Figure 2: RM – Year-on-Year Number of New Clinical Trials Recorded by Therapy Type (2015-2021)

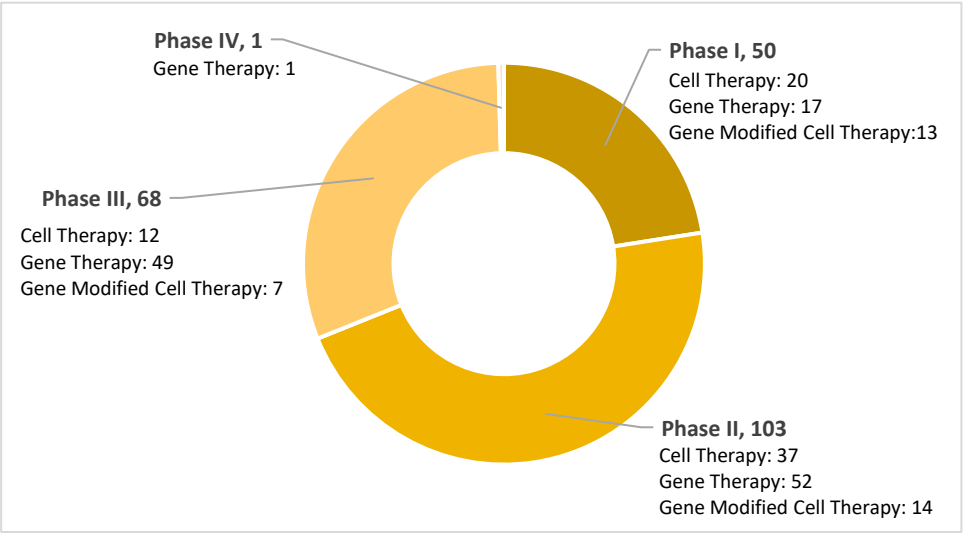


Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

There was a growth in the number of new trials recorded from 2016-2020 with an overall CAGR of 15.5% between 2016 and 2020. This growth was attributed due to increase in number of new trials for gene therapy and gene modified cell therapy. In 2019 and 2020 the highest number of new clinical trials were recorded across all therapy types in Australia.

1.2: RM by Therapy Type and Phase

Figure 3: RM – Number of New Clinical Trials Recorded by Therapy Type and Phase (2015-2021)

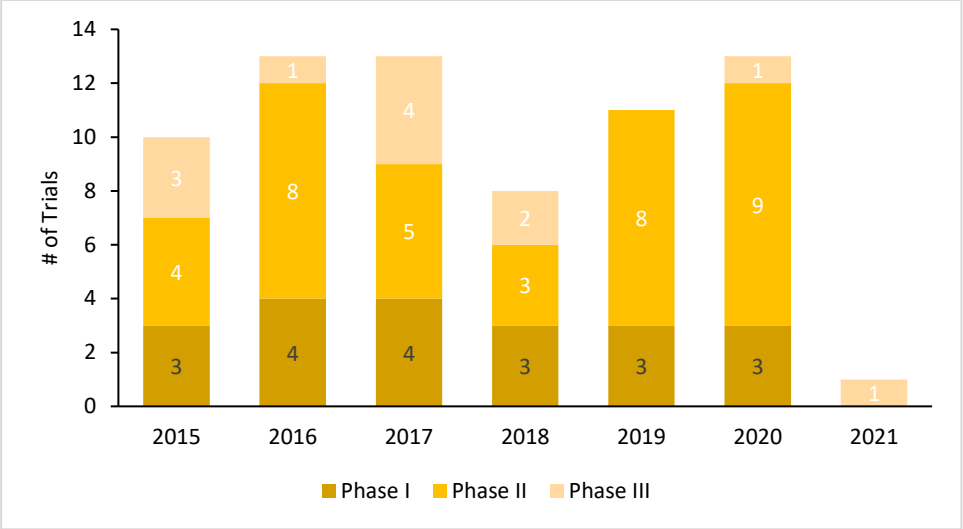


Source: GlobalData

As shown in Figure 3, in late phase (Phase II and Phase III) gene therapy recorded highest number of new trials.

1.3: Cell Therapy by Phase

Figure 4: Cell Therapy – Year-on-Year Number of New Clinical Trials Recorded by Phase (2015-2021)

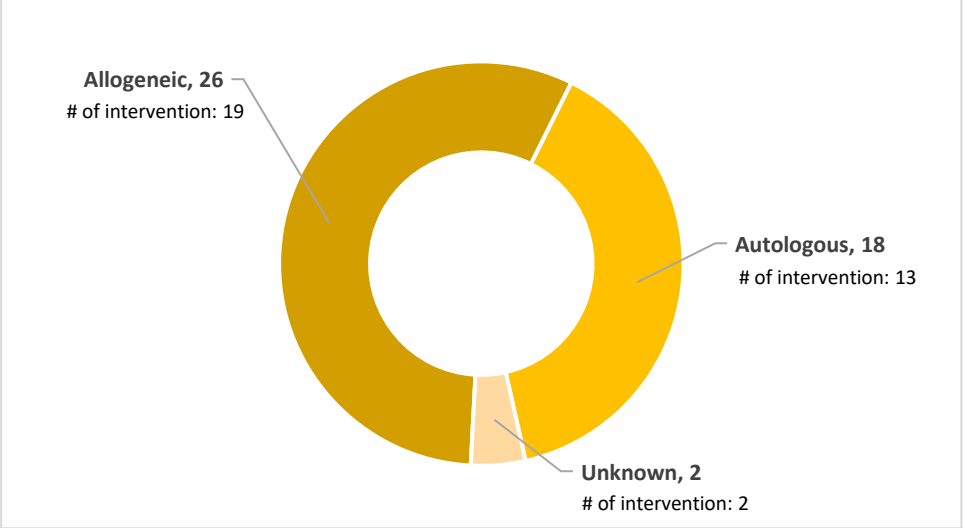


Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

Overall, no growth was observed in the number of new trials commencing each year for cell therapy from 2016-2020.

1.4: Cell Therapy by Cell Source

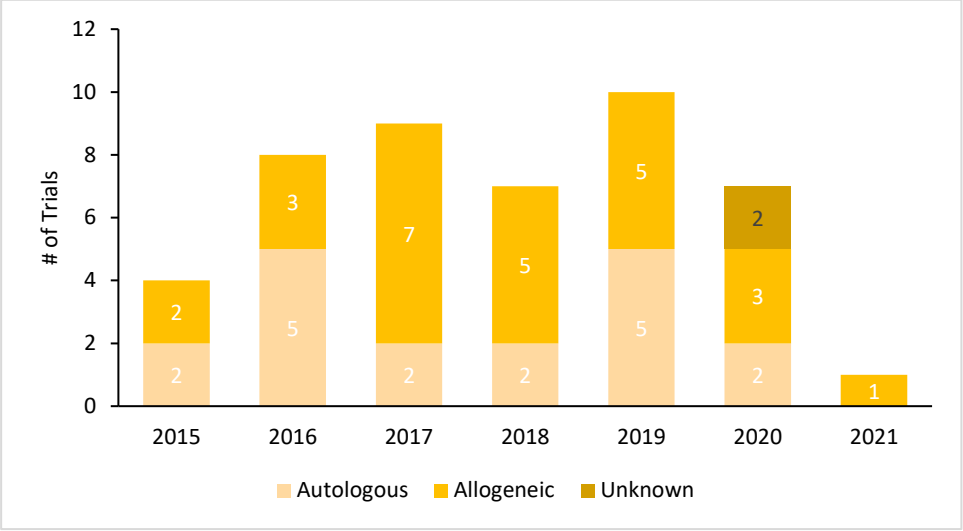
Figure 5: Cell Therapy – Number of New Clinical Trials Recorded by Cell Source (2015-2021)



Source: GlobalData

Allogeneic cell therapies were studied in the majority of clinical trials involving cell therapies. There were 19 allogeneic and 13 autologous interventions evaluated in 26 and 18 trials respectively.

Figure 6: Cell Therapy – Year-on-Year Number of New Clinical Trials Recorded by Cell Source (2015-2021)

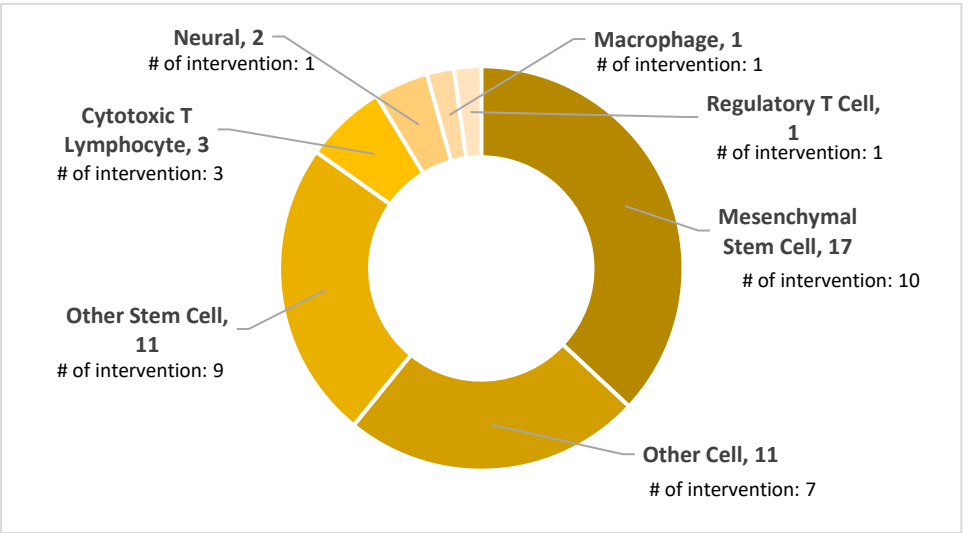


Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

The highest number of new trials using allogeneic cells were recorded in 2017, whereas the highest number of new trials using autologous cells were recorded in 2016 and 2019.

1.5: Cell Therapy by Cell Type

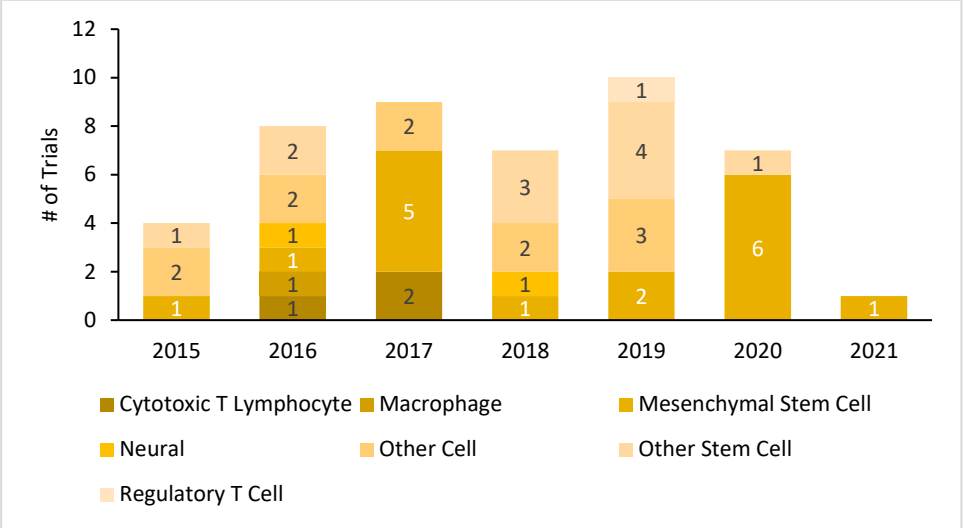
Figure 7: Cell Therapy – Number of New Clinical Trials Recorded by Cell Type (2015-2021)



Source: GlobalData

Among new cell therapy trials, the greatest number of trials involved mesenchymal stem cells in 17 trials with 10 interventions.

Figure 8: Cell Therapy – Year-on-Year Number of New Clinical Trials Recorded by Cell Type (2015-2021)

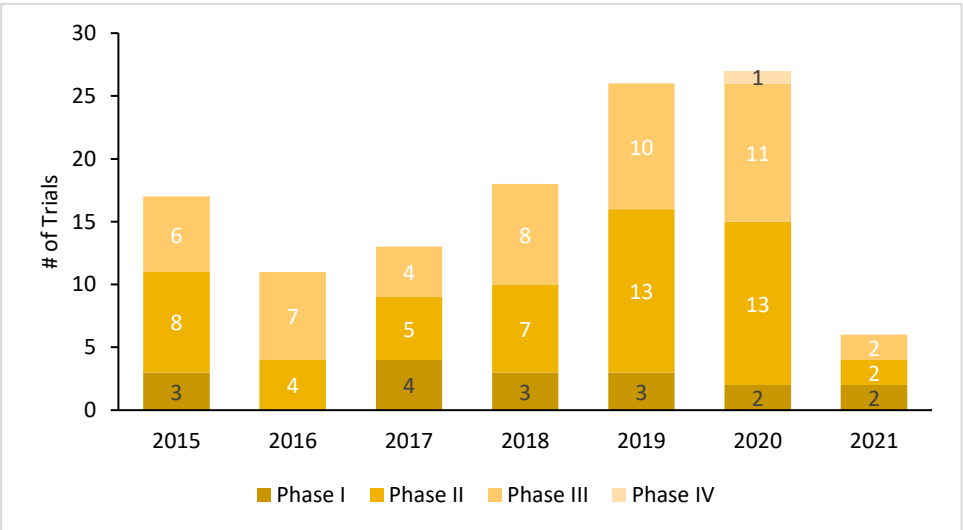


Source: GlobalData; Note: 2015 and 2021 represent 10 months (Mar-Dec) and 3 months (Jan-Mar) of data respectively

As shown in Figure 8, mesenchymal stem cells were consistently studied in RM trials from 2015-2021, though the number of trials has fluctuated. Other cell types were less consistently involved in trials.

1.6: Gene Therapy by Phase

Figure 9: Gene Therapy – Year-on-Year Number of New Clinical Trials Recorded by Phase (2015-2021)

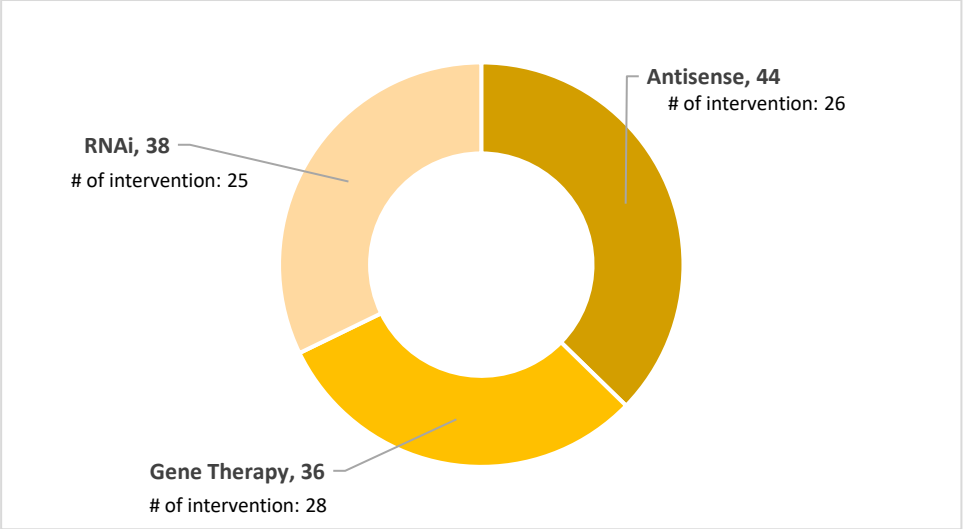


Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

The number of new trials recorded for gene therapy grew at a CAGR of 26.3% between 2016-2020. In terms of phase distribution, an increasing trend was observed both for Phase II and Phase III trials. No new Phase I trials were recorded in 2016. The highest number of new trials were recorded in 2019 and 2020 across all phases.

1.7: Gene Therapy by Type

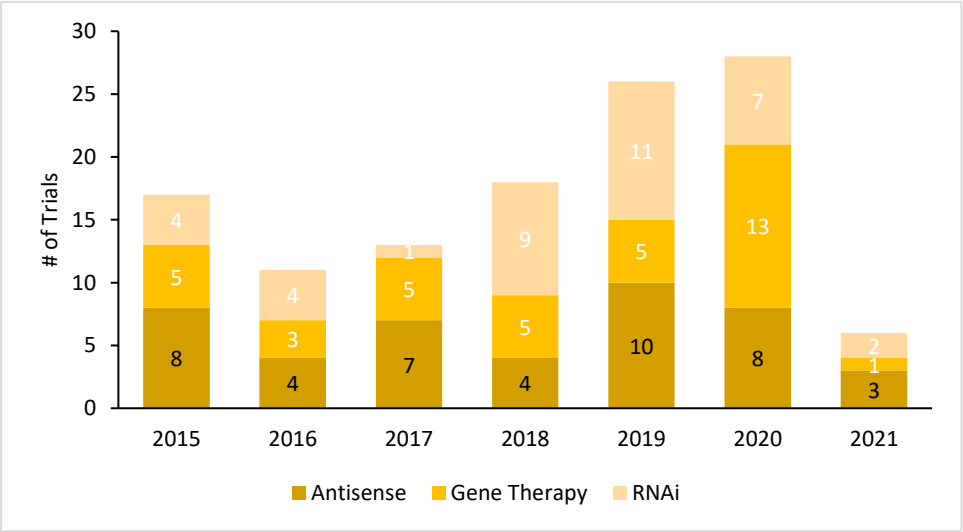
Figure 10: Gene Therapy – Number of New Clinical Trials Recorded by Gene Therapy Type (2015-2021)



Source: GlobalData

As shown in Figure 10, in gene therapy antisense therapies were the predominantly studied technology, however, no significant difference was observed in terms of number of interventions studied.

Figure 11: Gene Therapy – Year-on-Year Number of New Clinical Trials Recorded by gene Therapy Type (2015-2021)

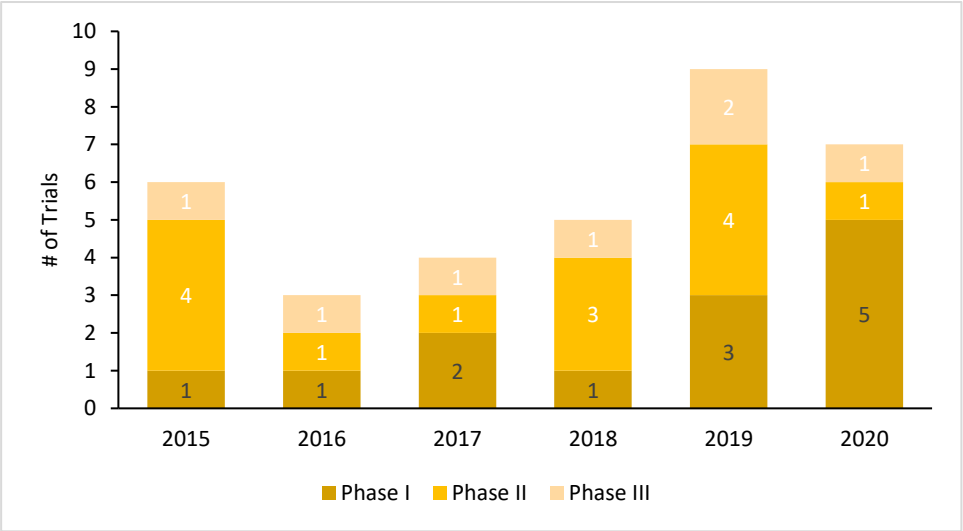


Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

Overall, an increasing trend was observed in terms of number of new trials recorded using gene therapy technologies from 2016-2020.

1.8: Gene Modified Cell Therapy by Phase

Figure 12: Gene Modified Cell Therapy – Year-on-Year Number of New Clinical Trials Recorded by Phase (2015-2020)

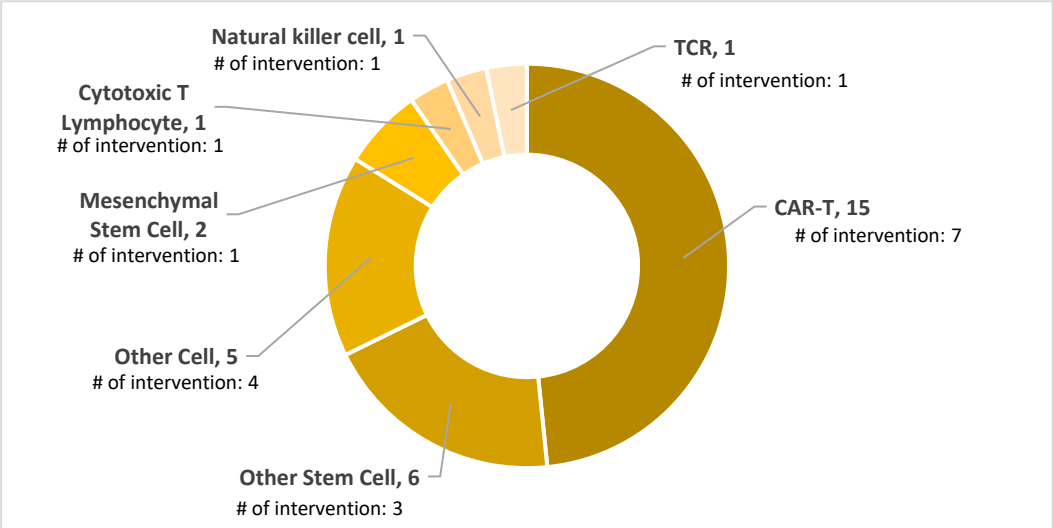


Source: GlobalData; Note: 2015 represents 10 months (Mar-Dec) data; Data for 2021 was not available

New gene modified cell therapy trials grew at a CAGR of 23.6% from 2016-2020. The highest number of new gene modified cell therapy trials (regardless of phase) were recorded in 2019.

1.9: Gene Modified Cell Therapy by Cell Type

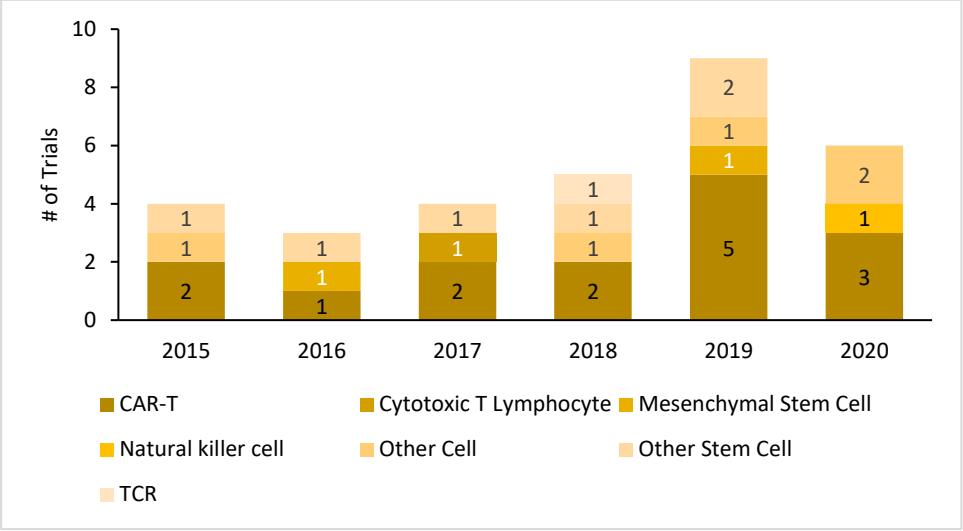
Figure 13: Gene Modified Cell Therapy – Number of New Clinical Trials Recorded by Cell Type (2015-2021)



Source: GlobalData

As shown in Figure 13, CAR-T cells were clearly the most commonly investigated gene modified cell groups in new RM trials recorded in Australia. None of the other cell types were commonly included in clinical trials.

Figure 14: Gene Modified Cell Therapy – Year-on-Year Number of New Clinical Trials Recorded by Cell Type (2015-2020)

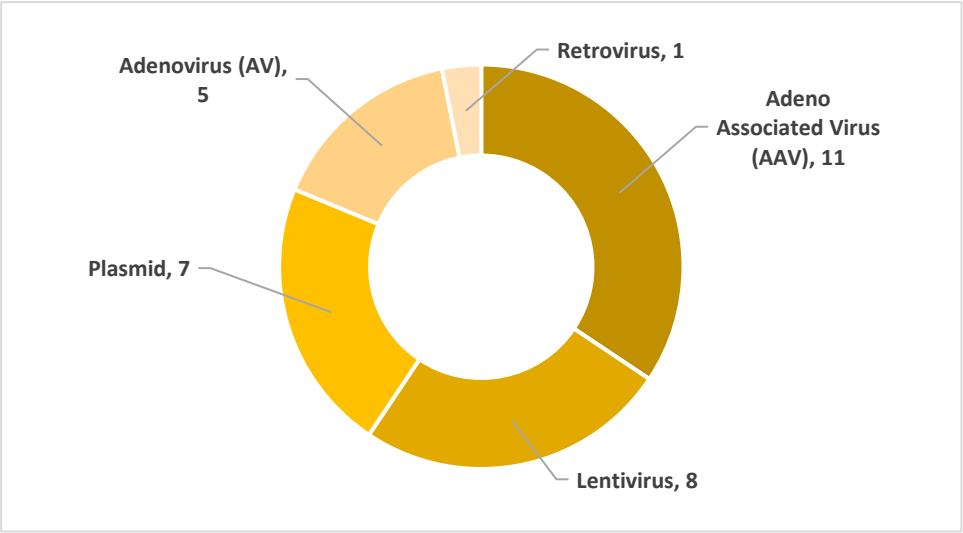


Source: GlobalData; Note: 2015 represents 10 months (Mar-Dec) data; Data for 2021 was not available

CAR-T cell therapies were the most studied in trials from 2015-2020. The highest number of new trials were recorded in 2019 across all cell types.

1.10: RM by Vector Type

Figure 15: RM – Number of New Clinical Trials Recorded by Vector Type (2015-2021)

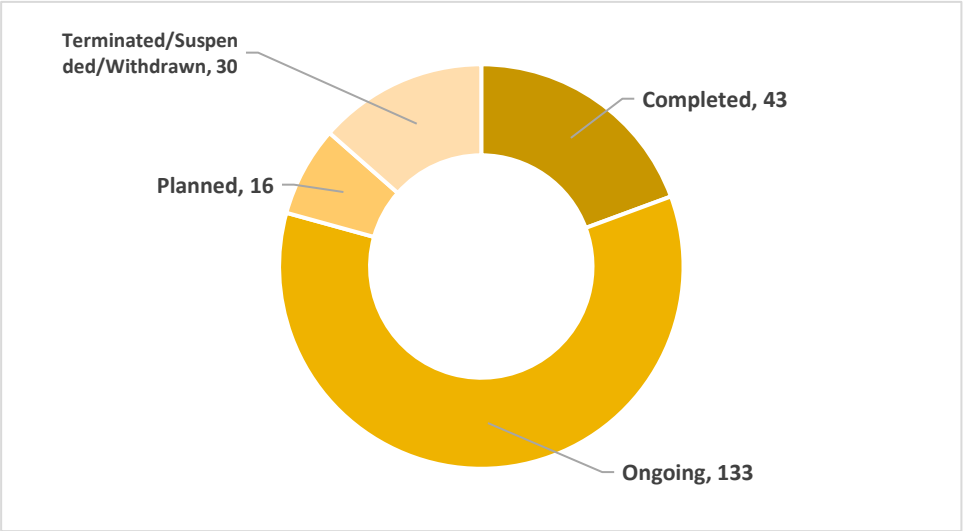


Source: GlobalData

Regardless of therapy type, viral vectors are involved in most RM trials. Among viral vectors, adeno-associated viruses (AAVs) were the most commonly used followed by lentiviruses and adenovirus. Retroviruses were also investigated as potential vector technologies. Plasmids were used as non-viral vectors.

1.11: RM by Trial Status

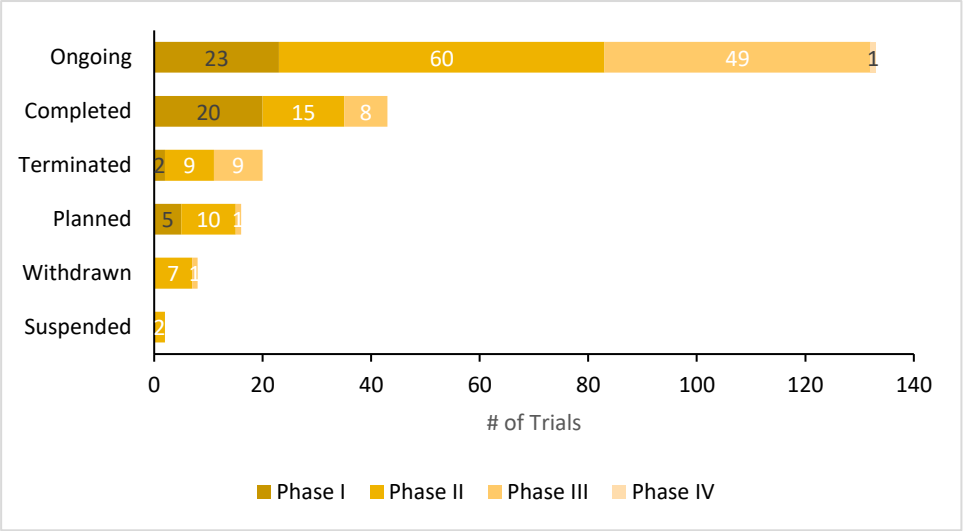
Figure 16: RM – Number of New Clinical Trials Recorded by Trial Status (2015-2021)



Source: GlobalData

As shown in Figure 16, ongoing trials made up a significant proportion of the overall recorded trials (60%), highlighting increased activity in RM research. Completed trials accounted for ~20% of the trials recorded followed by terminated/suspended/withdrawn trials (14%).

Figure 17: RM – Number of New Clinical Trials Recorded by Trial Status and Phase (2015-2021)

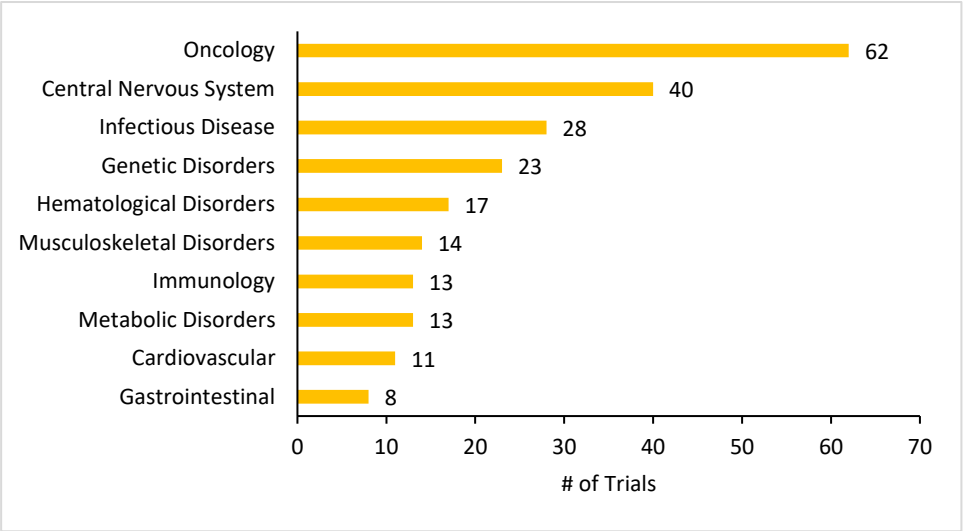


Source: GlobalData

In terms of phase distribution in ongoing trials, the highest number of trials were recorded in Phase II (45%) followed by Phase III (37%). Among completed trials, ~50% and 35% were Phase I and Phase II respectively.

1.12: RM by Top Therapy Areas

Figure 18: RM – Number of New Clinical Trials Recorded for Top 10 Therapy Areas (2015-2021)

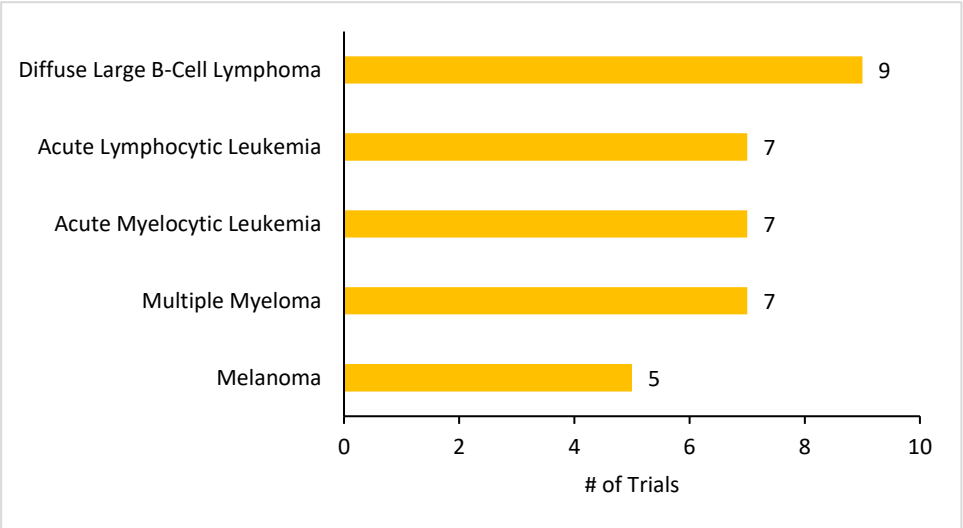


Source: GlobalData

Of the 222 new clinical trials recorded for RM in Australia, oncology was the leading therapy area followed by central nervous system and infectious diseases. Genetic disorders and haematological disorders ranked in 4th and 5th place.

1.13: RM by Top Indications for Top 3 Therapy Areas

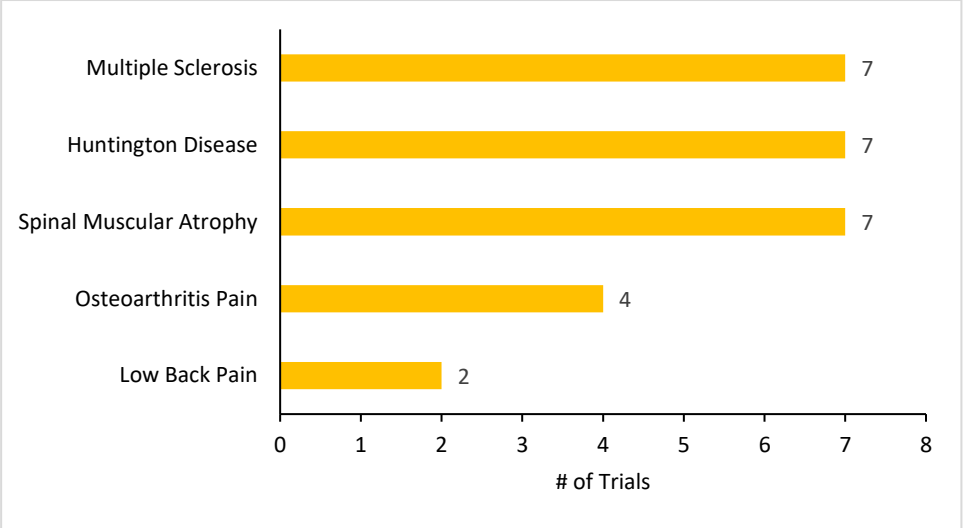
Figure 19: RM – Number of New Clinical Trials Recorded for Top 5 Indications in Oncology (2015-2021)



Source: GlobalData

The largest number of new clinical trials in oncology was seen in diffuse large B-cell lymphoma, followed by equal number of trials in acute lymphocytic leukemia, acute myelocytic leukemia and multiple myeloma.

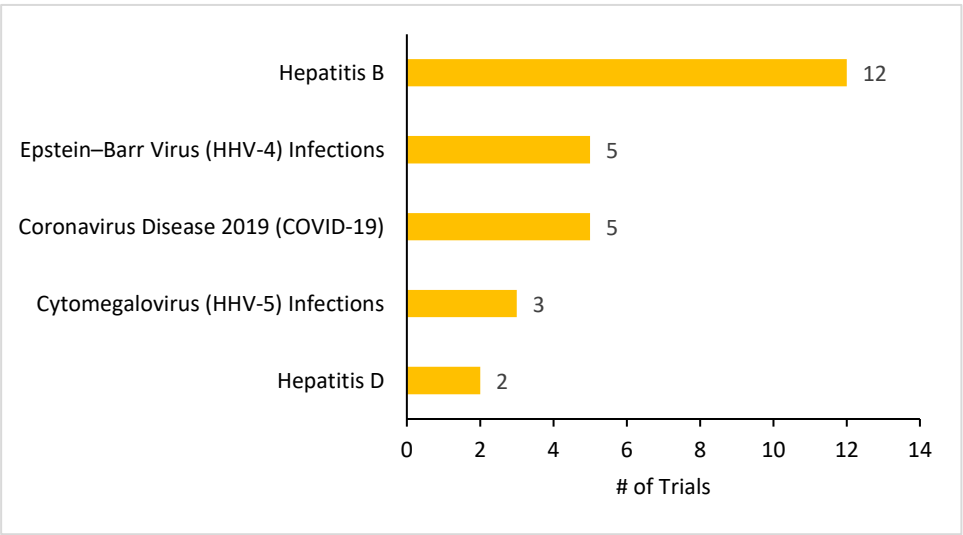
Figure 20: RM – Number of New Clinical Trials Recorded for Top 5 Indications in Central Nervous System Diseases (2015-2021)



Source: GlobalData

Among central nervous system diseases, multiple sclerosis, Huntington's disease and spinal muscular atrophy had equal number of trials (7 each) followed by osteoarthritis pain.

Figure 21: RM – Number of New Clinical Trials Recorded for Top 5 Indications in Infectious Diseases (2015-2021)

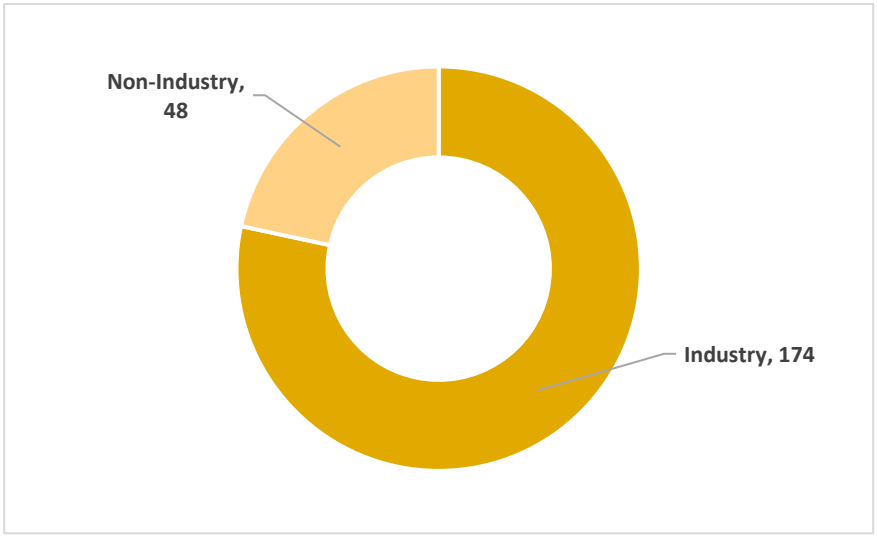


Source: GlobalData

Among infectious disease, new clinical trials for hepatitis B, outnumbered trials for Epstein-Barr virus infection and Coronavirus disease 2019.

1.14: RM by Sponsor Types

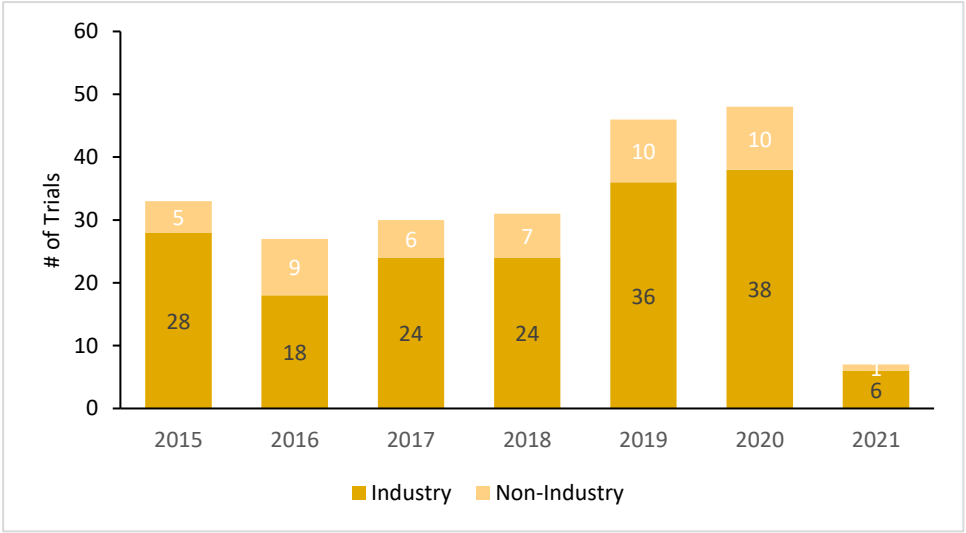
Figure 22: RM – Number of New Clinical Trials Recorded by Sponsor Types (2015-2021)



Source: GlobalData

As shown in Figure 22, industry-sponsored (~80%) trials vastly outnumbered non-industry sponsored trials in Australia.

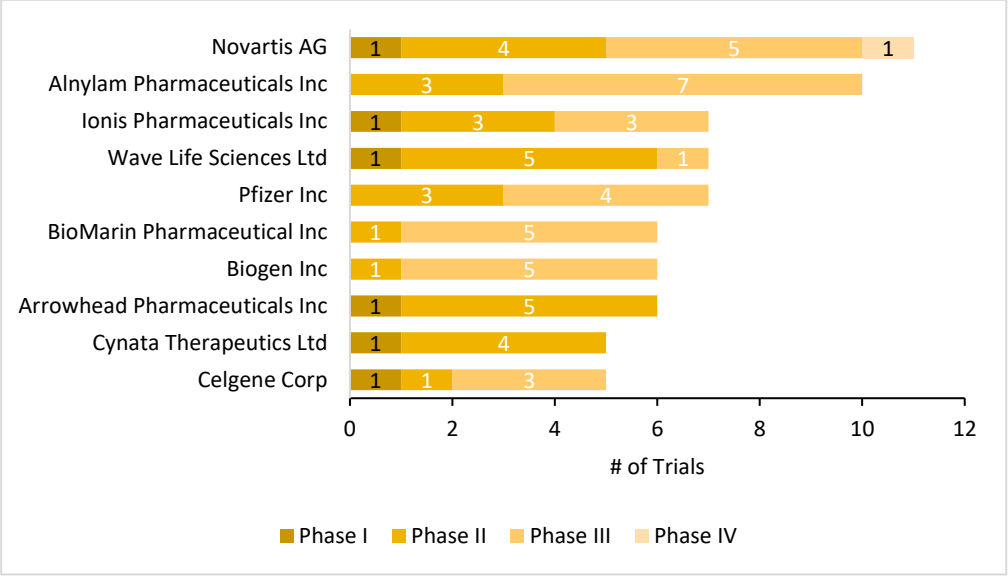
Figure 23: RM – Year-on-Year Number of New Clinical Trials Recorded by Sponsor Types (2015-2021)



Source: GlobalData; Note: 2015 and 2021 represents 10 months (Mar-Dec) and 3 months (Jan-Mar) data respectively

In terms of growth, the industry sponsored trials grew with a CAGR of 21% from 2016-2020 which was 7 times higher than non-industry sponsored trials for the same period. Over the study period, the highest numbers of new trials were recorded in 2019 and 2020, both for industry and non-industry sponsors.

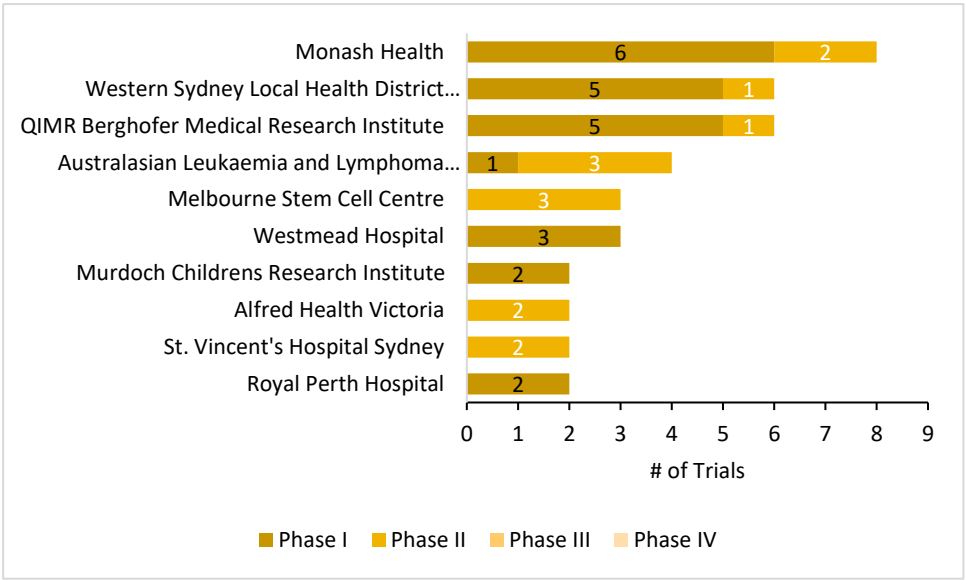
Figure 24: RM – Number of New Clinical Trials Recorded by Phase for Top 10 Industry Sponsors (2015-2021)



Source: GlobalData

Overall, four of the top five sponsors for RM trials were from the industry. The companies developing RM therapies included both small biotechs and larger biopharmaceutical firms. Among the top industry sponsors, Novartis AG and Alnylam Pharmaceuticals Inc sponsored the highest number of new RM trials, 11 and 10 trials respectively. The highest number of new trials were recorded in Phase III (33) followed by Phase II (30) and Phase I (6). One trial was recorded in Phase IV by Novartis.

Figure 25: RM – Number of New Clinical Trials Recorded by Phase for Top 10 Non-Industry Sponsors (2015-2021)



Source: GlobalData

As shown in Figure 25, Monash Health was the leading non-industry sponsor followed by QIMR Berghofer Medical Research Institute and Western Sydney Local Health District (Australia). The highest number of new

trials were recorded in Phase I (24) followed by Phase II (14). No new trials were recorded in Phase III and Phase IV.

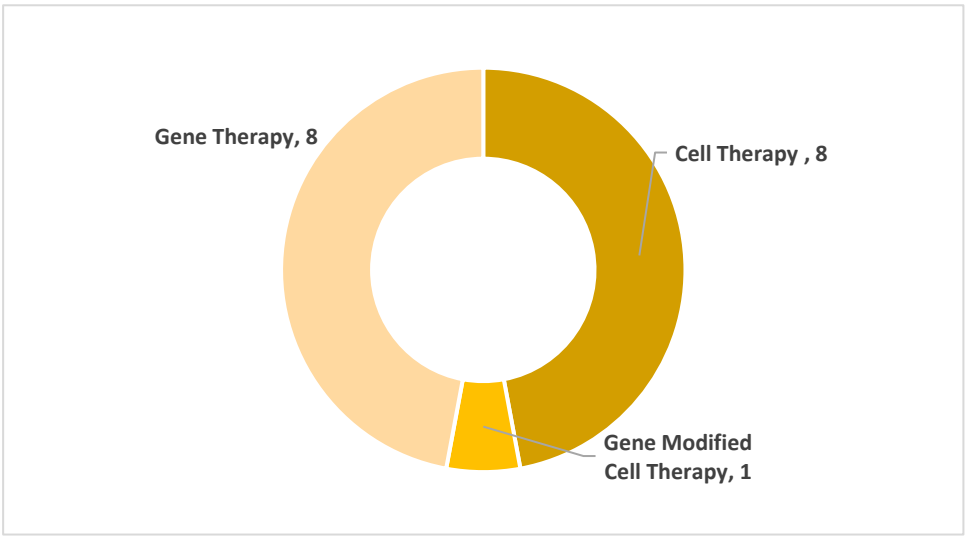
1.15: Medical Device Trials

Three new trials were recorded under medical devices (one trial each by Orthocell Ltd, Piramal Healthcare [Canada] Ltd, and by University of Western Australia) where tissue scaffolds were studied.

Section 2: Analysis of New Clinical Trials Recorded Overseas by Australian Companies

2.1: RM by Therapy Type

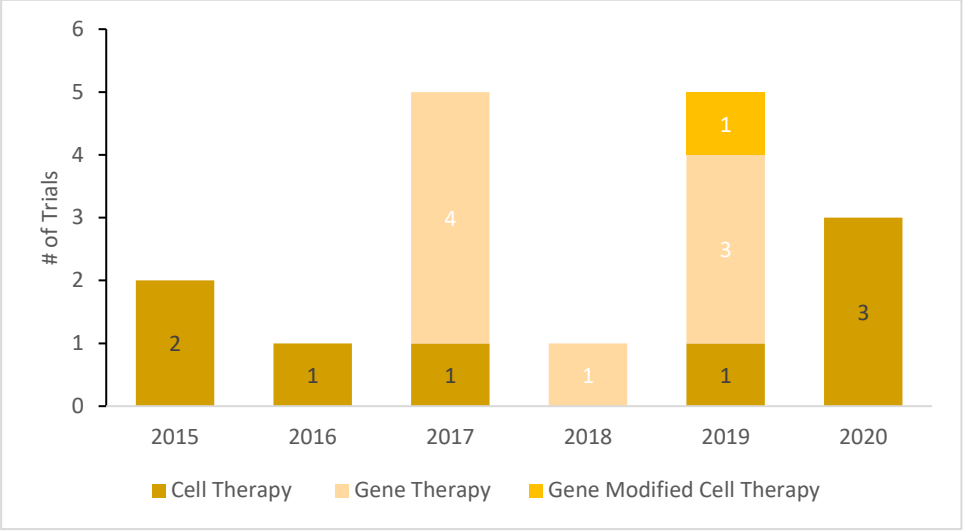
Figure 26: RM – Number of New Clinical Trials Recorded by Therapy Type (2015-2021)



Source: GlobalData

Of the 17 new RM clinical trials recorded by Australian companies overseas between March 1, 2015 to March 31, 2021, Australian companies conducted an equal number of new trials (8 trials each) for cell therapy and gene therapy.

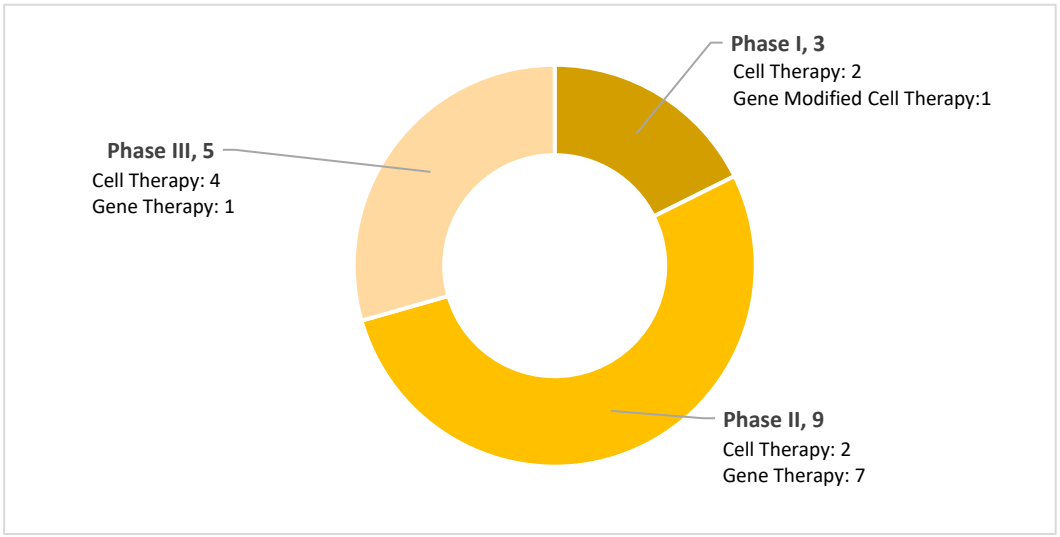
Figure 27: RM – Year-on-Year Number of New Clinical Trials Recorded by Therapy Type (2015-2020)



Source: GlobalData; Note: 2015 represents 10 months (Mar-Dec) data; Data for 2021 was not available

Over the study period, the highest numbers of new trials by Australian companies overseas were recorded in 2017 and 2019.

Figure 28: RM – Number of New Clinical Trials Recorded by Therapy Type and Phase (2015-2021)

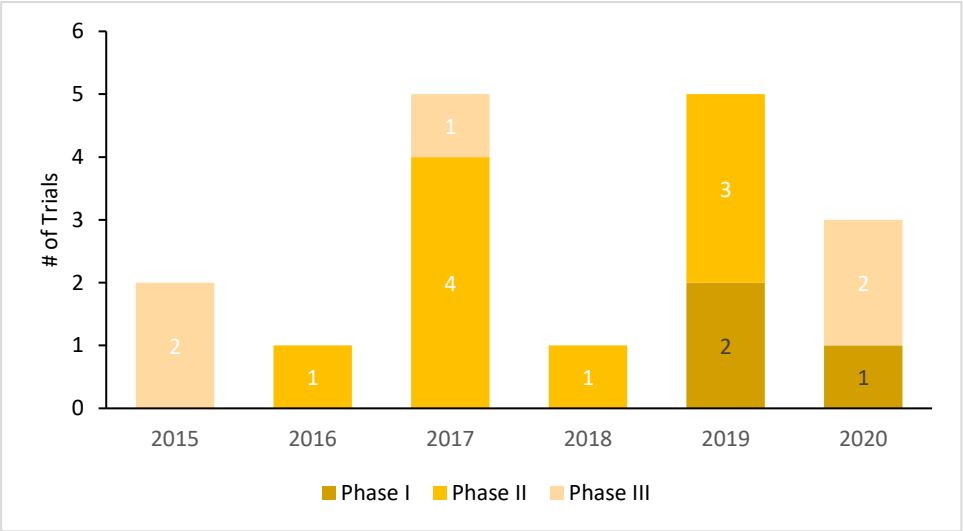


Source: GlobalData

As shown in Figure 28, gene therapy trials accounted for the highest number of late phase trials (Phase II and Phase III)

2.2: RM by Phase

Figure 29: RM – Year-on-Year Number of New Clinical Trials Recorded by Phase (2015-2020)

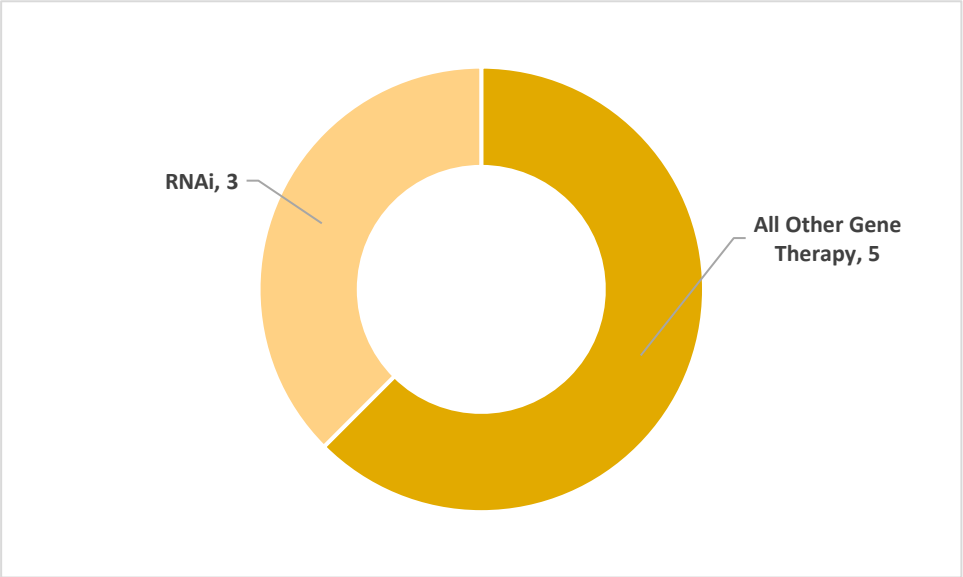


Source: GlobalData; Note: 2015 represents 10 months (Mar-Dec) data; Data for 2021 was not available

Across all phases, the highest number of new trials by Australian companies conducting trials overseas were recorded in 2017 and 2019.

2.3: Gene Therapy by Type

Figure 30: Gene Therapy – Number of New Clinical Trials Recorded by Gene Therapy Type (2015-2021)

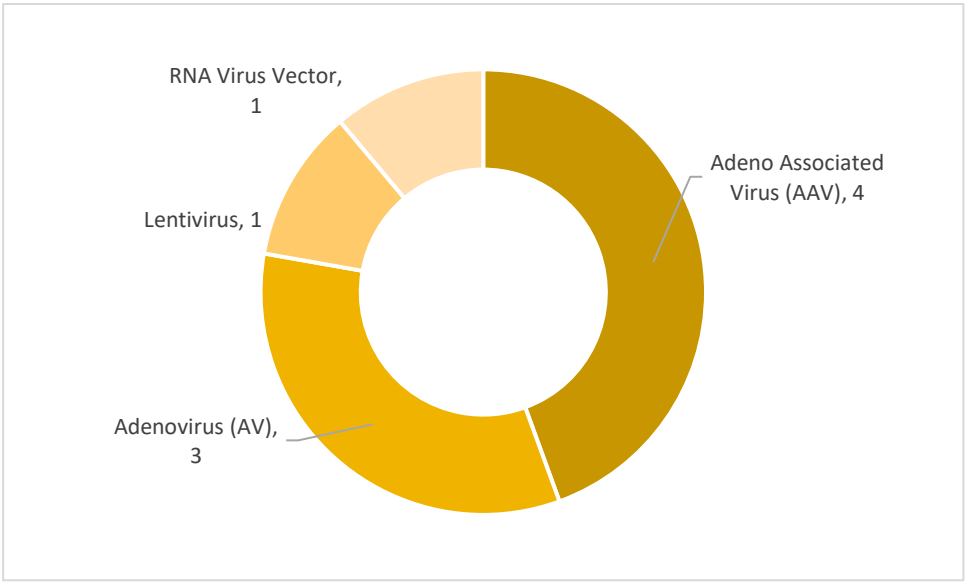


Source: GlobalData

As shown in Figure 30, there were a total of eight gene therapy new gene therapy trials recorded by Australian companies overseas, three of these were RNAi, five were across all other gene therapy types (see Appendix 2 for RM therapy categories).

2.4: RM by Vector Type

Figure 31: RM – Number of New Clinical Trials Recorded by Vector Type (2015-2021)

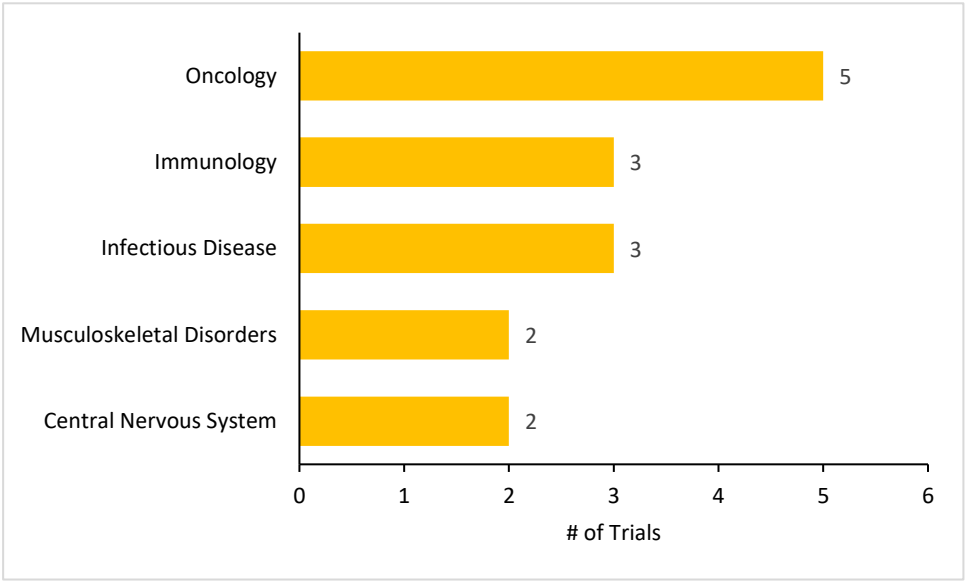


Source: GlobalData

Including both gene therapy and gene modified cell therapy trials adeno-associated viruses (AAVs) were the most studied followed by adenovirus in new clinical trials recorded by Australian companies overseas.

2.5: RM by Top Therapy Areas and Indications

Figure 32: RM – Number of New Clinical Trials Recorded for Top Therapy Areas and Indications (2015-2021)

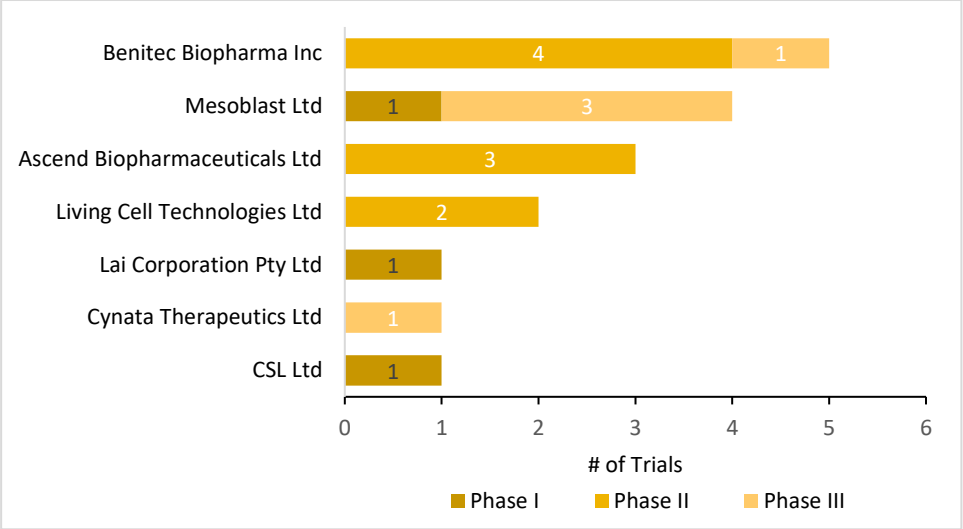


Source: GlobalData

Of the 17 new clinical trials recorded for RM by Australian companies overseas, oncology was the leading therapy area followed by immunology and infectious diseases. Head and neck squamous cell carcinoma was the top indication in oncology.

2.6: RM by Sponsors

Figure 33: RM – Number of New Clinical Trials Recorded by Sponsors and Phase (2015-2021)

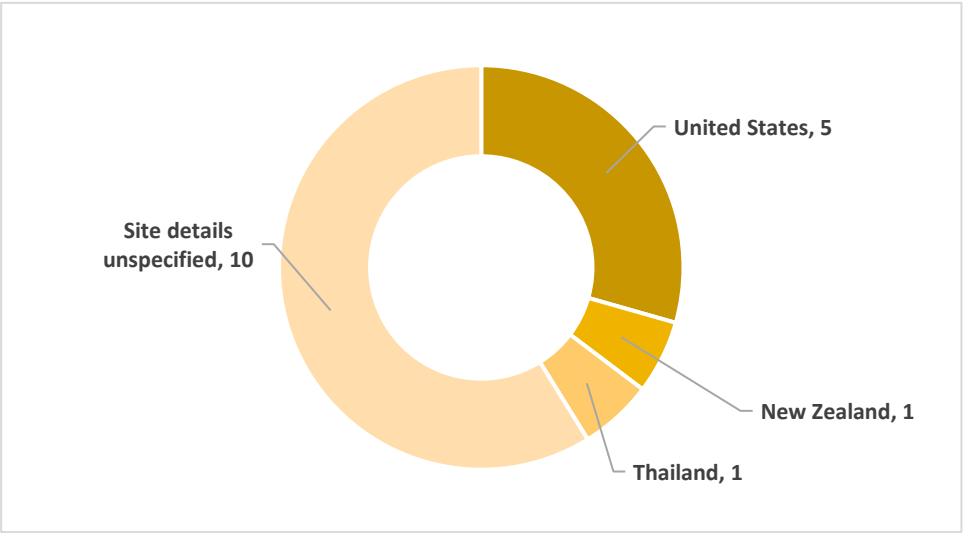


Source: GlobalData

Benitec Biopharma Inc, Mesoblast Ltd and Ascend Biopharmaceuticals Ltd were the top three Australian sponsors conducting RM trials overseas between March 1, 2015 to March 31, 2021. Mesoblast Ltd sponsored the highest number of new Phase III trials (3 trials) followed by Benitec Biopharma Inc and Cynata Therapeutics Ltd (1 trial each).

2.7: RM Trials by Country

Figure 34: RM – Number of New Clinical Trials Recorded by Country (2015-2021)



Source: GlobalData

As shown in Figure 34, many of the trials recorded by Australian companies were in the United States. For the majority of the trials, site details were unspecified.

Methodology

RM clinical trials data were extracted from GlobalData's (GD) proprietary *Pharma Intelligence Center and Medical Intelligence Center*: *Clinical Trials Database* on April 21, 2021 with the following scope:

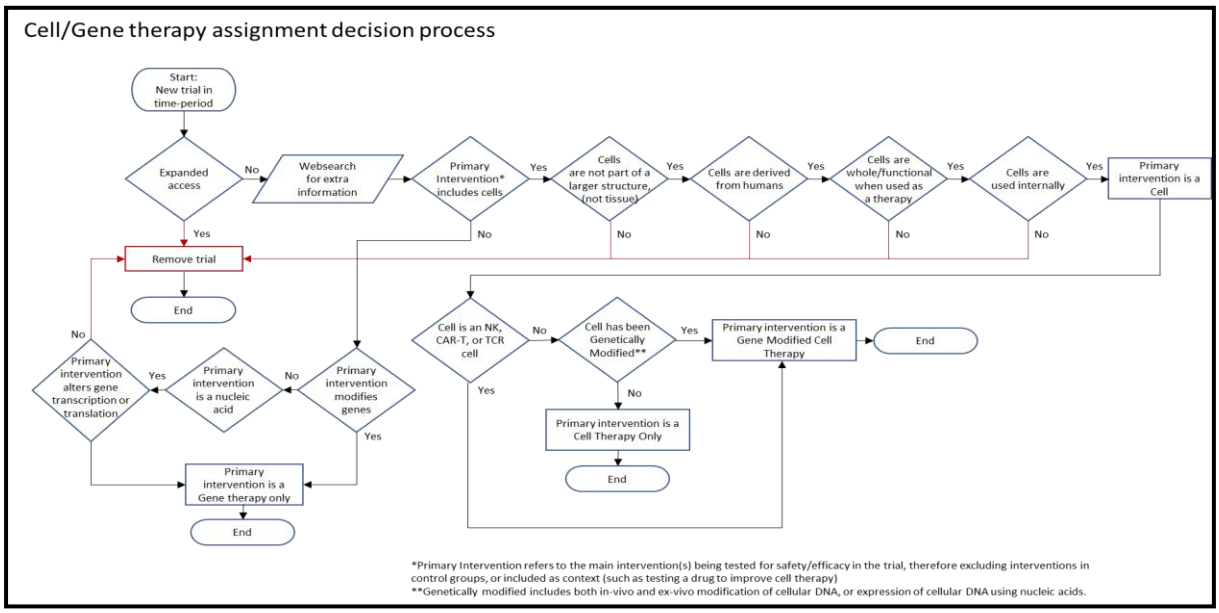
- **Trial Type & Study Period**: New clinical trials recorded from 2015 (March 1st, 2015) to Q1 2021 (March 31st, 2021)
- Trial Phases: Phases I - IV
- **Trial Status**: All trial status (planned, ongoing, completed, terminated/suspended/withdrawn)
- **Molecule Type**: Cell Therapy; Gene Therapy; Gene Modified Cell Therapy; Oligonucleotide
- Therapy Area: All
- **Location:** New clinical trials recorded in Australia, and clinical trials recorded overseas by Australian companies
- **Exclusion:** Medical Devices (other than tissue scaffolds) and service providers

This report is divided into two sections:

- **Section 1:** Analysis of New Clinical Trials Recorded in Australia:
  Include analysis of 222 unique Pharma clinical trials and 3 unique Medical trials
- **Section 2**: Analysis of New Clinical Trials Recorded Overseas by Australian Companies:
  Include analysis of 17 unique Pharma clinical trials and 1 Medical trial

RM Therapy Type Categorisation:

GD has followed the Alliance for Regenerative Medicine's (ARM) definitions to categorise RM into four different therapy types (gene therapies, cell therapies, gene modified cell therapies and tissue engineered products) as per the flowchart below.



Cell type, type of viral vector used and source (autologous/allogeneic, scaffolds) have been included in the analysis as available and reported in the registries.

Data Points/Column Headings Included in the CT Database and its Definitions:

- Trial ID: Refers to GD's internal trial ID to track trials information
- Name of sponsor: Refers to clinical trial sponsor name
  - Where trial sponsor is both industry and non-industry, GD has considered those trials under industry sponsored trials
- Title of trial: GD has captured Official or Scientific title of the clinical trial
- Clinical database numbers: These are the Primary IDs and Secondary IDs of the clinical trial
- Trial site(s): Refers to name and address of institution/hospital as reported in the registries. For multisite trials, each trial site address has been captured in different rows.
  - Where trials site details are unspecified, GD marked those trials as "site details unspecified"
- Trial status: GD has included all trial status options (planned, ongoing, completed, terminated, withdrawn, and suspended).
- Trial phase: GD has standardised trial phases as below:
  - Phase I/II to Phase II
  - Phase II/III to Phase III
  - Phase III/IV to Phase IV
- Year Trial Started: GD has considered all recorded trials with a start date is from 2015 (March 1st, 2015) to Q1 2021 (March 31st, 2021).
  - Year-on-year data presented in the analysis include data from March 1, 2015 to March 31, 2021
  - For CAGR/growth rate, the period from January 1, 2016 to December 31, 2020 has been considered
- Recruitment target: Planned number of subjects has been captured
- Therapy Type: GD inserted this column to track trials for RM therapy types (cell therapy, gene therapy and gene modified cell therapy)
- Cell Type (if applicable): Provided information as available and reported in the registries.
- Gene modification/gene therapy (if applicable): Provided information as per the flowchart above
- Type of viral vector used (as available): Provided information as available and reported in the registries
- Autologous/Allogeneic (as reported): Provided information as available and reported in the registries
- Disease (therapy) area: Trials with multiple therapy areas have been counted for each therapy area
  - For example, if a trial has both oncology and haematology therapy areas then it has been counted as:
    Oncology: 1 trial
    Haematology: 1 trial
- Indication: Trials with multiple indications have been counted for each indication
  - For example, if a trial has three indications such as breast cancer; lung cancer; melanoma, then the trial has been counted as
    Breast cancer: 1 trial
    Lung cancer: 1 trial
    Melanoma: 1 trial
- GDC IDs: These are GlobalData's trial IDs where the clinical trials are not registered in any of the registries, and trial information has been captured from company press releases, annual presentations, conferences etc.

NOTE: The term intervention used in the analysis indicates the diagnostic or therapeutic device, biologic, and/or drug under investigation in a clinical trial that is considered to have an effect on outcomes of interest in a study.

Appendices

Appendix 1: Clinical Trials Database References

GlobalData's Clinical Trials Database identifies trials from various sources, which include clinical trial registries worldwide, scientific meetings, published reports, company press releases and presentations. Key sources for the Clinical Trials Database include:

1. Pharma Intelligence Center and Medical Intelligence Center: Clinical Trials Database
2. International Conference on Harmonisation - Good Clinical Practice (ICH-GCP) Search Portal
3. WHO, International Clinical Trials Registry Platform (ICTRP) Search Portal
4. Australian New Zealand Clinical Trials Registry (ANZCTR)
5. U.S. National Institutes of Health Clinical Trials Registry (ClinicalTrials.gov)
6. National Institute of Health Clinical Trials Portal
7. European Union Clinical Trials Registry (EUDRACT)
8. *UMIN* Clinical Trials Registry (*UMIN*-CTR)
9. Japic Clinical Trials Information/JapicCTI
10. Chinese Clinical Trial Registry (ChiCTR)

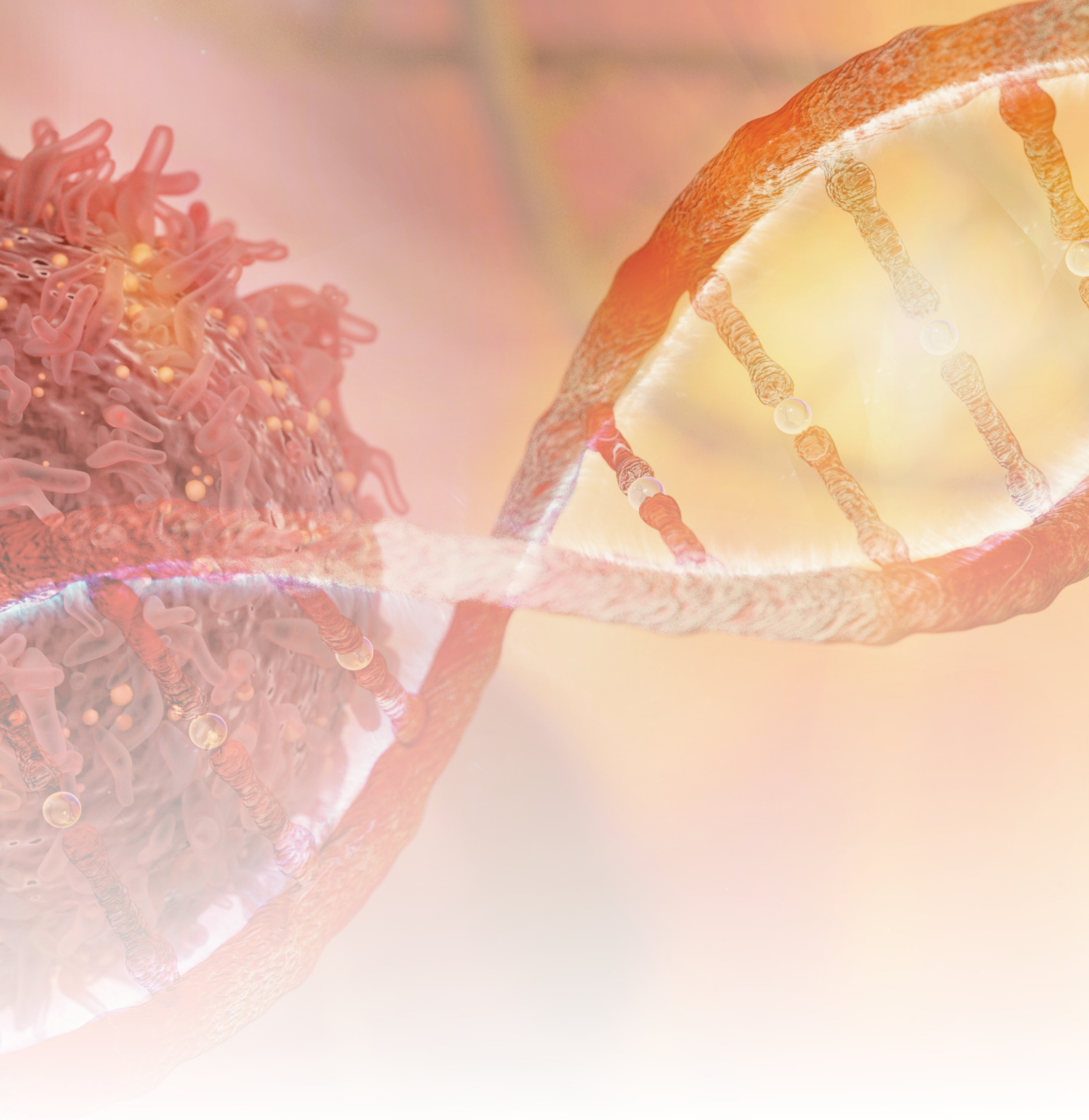
Appendix 2: Categories used in Clinical Trials Database

Categories of Regenerative Medicine*	Definitions	Examples
Cell Therapy	Cell therapy is the administration of viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue for the treatment of a disease. A variety of different types of cells can be used in cell therapy, including hematopoietic (blood-forming) stem cells, skeletal muscle stem cells, neural stem cells, mesenchymal stem cells (adult stem cells that differentiate into structures as connective tissues, blood, lymphatics, bone, and cartilage), lymphocytes, dendritic cells, and pancreatic islet cells. Cell therapies may be autologous, meaning that the patient receives cells from their own body, or they may be allogenic, meaning the patient receives cells from a donor. Allogeneic cell therapies are often referred to as "off-the-shelf" therapies, as they are derived from a donor who is not the patient, enabling advance preparation and available to the patient immediately at the time of need. Many cell-based therapies currently being developed utilise induced pluripotent stem cells (iPSCs). Unlike embryonically-derived pluripotent stem cells, these are adult cells that have been genetically	- Hematopoietic (blood-forming) stem cells - Skeletal muscle stem cells - Neural stem cells - Mesenchymal stem cells (adult stem cells that differentiate into structures as connective tissues, blood, lymphatics, bone, and cartilage) - Lymphocytes - Dendritic cells - Pancreatic islet cells - Cytotoxic T Lymphocyte - Embryonic - Natural killer cell - Pluripotent stem cell - Regulatory T Cell - TCR

	reprogrammed back into a pluripotent state, capable of becoming one of many types of cells inside a patient's body. This technology may enable the development of an unlimited type of a specific type of human cells needed for therapeutic purposes.	- Tumor Infiltrating Lymphocyte - Vaccine; δT cell - Other Stem Cell; Other Cell
Gene Therapy	Gene therapy seeks to modify or introduce genes into a patient's body with the goal of durably treating, preventing or potentially even curing disease, including several types of cancer, viral diseases, and inherited disorders. Gene therapy approaches include replacing a mutated gene that causes disease with a functional copy; or introducing a new, correct copy of a gene into the body in order to fight disease. Gene therapy may be performed in vivo, in which a gene is transferred to cells inside the patient's body, or ex vivo, in which a gene is delivered to cells outside of the body, which are then transferred back into the body. Typically, gene therapy developers introduce new or corrected genes into patient cells using vectors, which are often deactivated viruses. Deactivated viruses are unable to make patients sick, but rather serve as the vehicle to transfer the new genetic material into the cell. Viruses that have been used for human gene therapy include retroviruses, adenoviruses, herpes simplex, vaccinia, and adeno-associated virus (AAV). Other ways of introducing new genetic material into cells include non-viral vectors, such as nanoparticles and nanospheres. Genome editing is a technique by which DNA is inserted, replaced, removed, or modified at particular locations in the human genome for therapeutic benefit in order to treat cancer, rare inherited disorders, HIV, or other diseases. Several approaches rely on the use of "molecular scissors," often an engineered nuclease, to make precise cuts in the patient's DNA at a specific location in the genome. The breaks are then repaired to create the desired edit and result in a corrected gene. Genome editing nucleases that are currently used in genome editing include: meganucleases, zinc finger nucleases (ZFNs), transcription activator-like	- RNAi - Antisense - Viral vector: Retroviruses, adenoviruses, herpes simplex, vaccinia, and adeno-associated virus (AAV) - Non-viral vectors, such as nanoparticles and nanospheres - Meganucleases - Zinc finger nucleases (ZFNs) - Transcription activator-like effector-based nucleases (TALEN) - Nucleases such as Cas9 and Cas 12a that derive from the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas)

	effector-based nucleases (TALEN), and nucleases such as Cas9 and Cas 12a that derive from the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas). Alternatively, genome editing can also be performed by homologous recombination of adeno-associated virus (AAV)-derived sequences into the patient's DNA.	- Homologous recombination of adeno-associated virus (AAV)-derived sequences
Gene Modified Cell Therapy	Gene therapy techniques can also be used to genetically modify patient cells ex vivo, which are then re-introduced into the patient's body in order to fight disease, an approach known as gene-modified cell therapy. This approach includes a number of cell-based immunotherapy techniques, such as chimeric antigen receptors (CAR) T cell therapies, T cell receptor (TCR) therapies, natural killer (NK) cell therapies, tumor infiltrating lymphocytes (TILs), marrow derived lymphocytes (MILs), gammadelta T cells, and dendritic vaccines.	- Chimeric antigen receptors (CAR) T cell therapies
		- T cell receptor (TCR) therapies
		- Natural killer (NK) cell therapies
		- Tumor infiltrating lymphocytes (TILs)
		- Marrow derived lymphocytes (MILs)
		- Gammadelta T cells, and dendritic vaccines
		- Cytotoxic T Lymphocyte
		- Mesenchymal Stem Cell
		- Pluripotent stem cell
		- Regulatory T Cell
		- Other Stem Cell; Other Cell
Tissue Engineering	Tissue engineering seeks to restore, maintain, improve, or replace damaged tissues and organs through the combination of scaffolds, cells, and/or biologically active molecules. Tissue engineering often begins with a scaffold, which may utilise any of a number of potential materials, from naturally occurring proteins to biocompatible synthetic polymers. Certain tissue engineering therapies may utilise an existing scaffold by removing the cells from a donor organ, a process called decellularization, until only the pre-existing protein-based scaffold or extracellular matrix (ECM) remains. Cells—and in some cases, additional growth factors to encourage the cells to take root—are added, allowing a tissue or organ to develop and grow ex-vivo. Biomaterials include any substance engineered to interact with a patient's living biological system for a medical purpose. These biomaterials often provide support as a physical structure for engineered tissues.	- Scaffolds, cells, and/or biologically active molecules
		- Decellularization; Biomaterials
		- 3D bioprinting

*As used in this report.



Level 3, 15 Queen Street
Melbourne, VIC, 3000
www.ausbiotech.org

AusBiotech
AUSTRALIA'S BIOTECHNOLOGY ORGANISATION