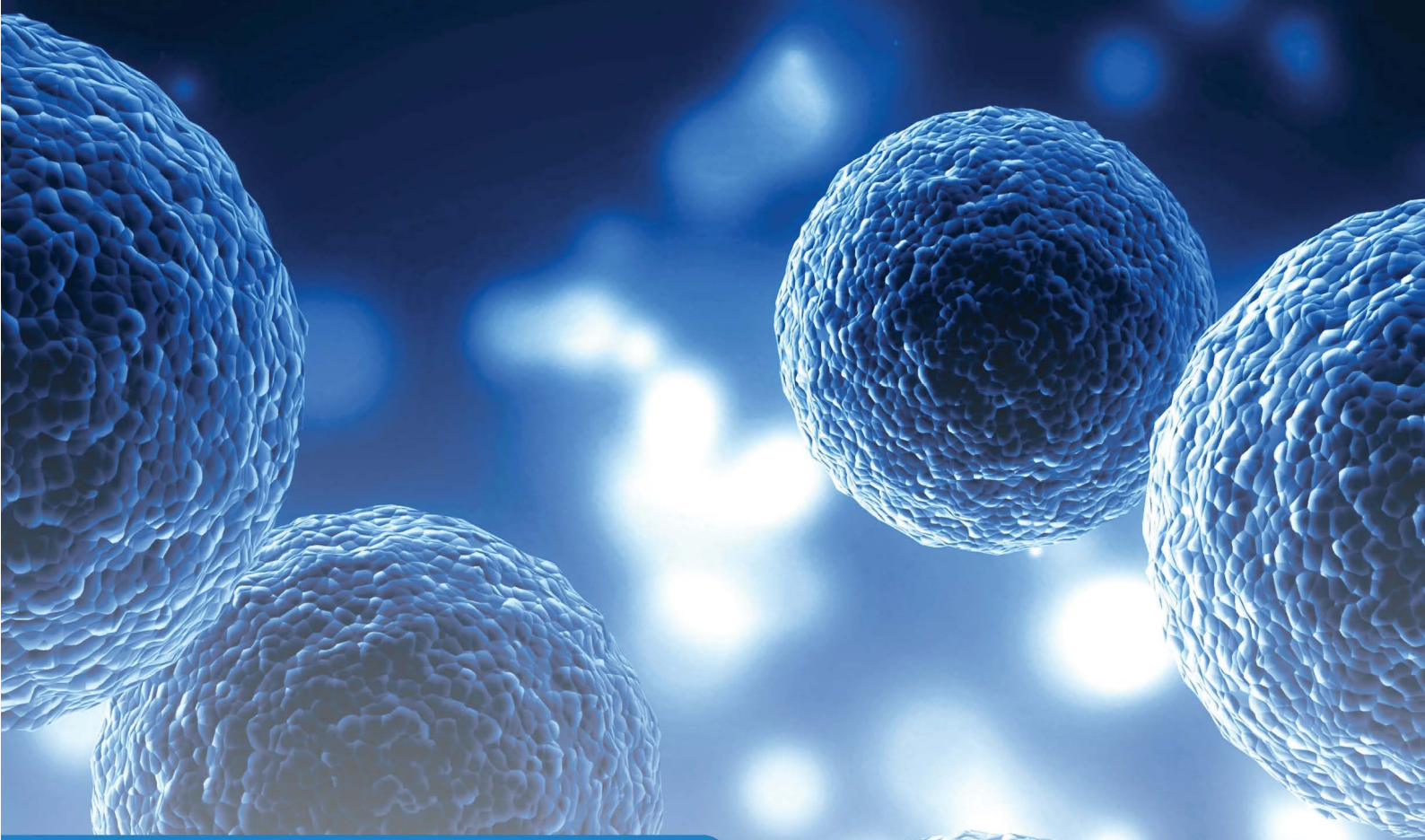

Australia's Regenerative Medicine Global Pipeline Tracker

Prepared by GlobalData

AusBiotech

Biointelect

cell therapies

Medicines Australia

Supported by MTPConnect
MedTech and Pharma Growth Centre

NOVARTIS

RESEARCH STRATEGIES AUSTRALIA

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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 Global Pipeline Tracker 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; 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 (this report).

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 AU$26.3B (or US$19.9B) in 2020[2]. With 97 ongoing RM Phase III 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].

[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.

Introduction

This report provides a horizon scan of the global pipeline of regenerative medicine (RM) products that may become available in Australia within the next 5 years. This global pipeline analysis includes therapies that are already registered overseas and those that are likely to come to market through global clinical development pipelines and then to the Australian market with. The reports focus is on RM products that are in phase III clinical development and beyond.

RM is an emerging multidisciplinary field of medicine intended to augment, repair, replace, or regenerate organs, tissues, cells, genes, and metabolic processes in the body. As RM research continues to explore novel treatments in cancer and rare diseases which are previously underserved by currently available treatments, RM has emerged as an attractive area of development for pharmaceutical companies. Considering the large global pipeline of RM products, several new therapies and advances are expected in this space over the next few years. Growth in RM is driven by increasing prevalence of chronic diseases, genetic disorders, and cancer along with increasing investments and collaborations for research.

For the purposes of this report, the RM pipeline was analysed through consideration of RM products already in market internationally (and not yet in Australia) and of late-stage assets, RM products at pre-registration and Phase III (also include Phase II/III and Phase I/II/III) clinical development. The in-market RM products considered were those in the United States of America (US), the European Union, and Japan as these are the jurisdictions most likely to feed the pipeline of products to the Australian market. Pre-registrations and phase III trials were chosen as the cut off, rather than earlier phases of clinical development, as pragmatically these are the products in clinical development most likely to come to market in the foreseeable horizon. The pre-registration and phase III trials analysis considered products under development globally. The four categories of RM products analysed in this report are:

1. Cell Therapies
2. Gene Therapies
3. Gene Modified Cell Therapies
4. Tissue Engineered Products
   (see Appendix 1 for category definitions)

For this analysis, cell therapies, gene therapies and gene-modified cell therapies were categorised under cell and gene therapies (CGT). Tissue engineered products have been analysed separately as the clinical development stages for these are defined differently compared to CGTs. Tissue engineered products development stage was defined as clinical, in approval process and marketed whereas for CGTs, clinical development stages are defined as Phase III, Phase II/III, Phase I/II/III, pre-registration and marketed.

Further analyses of CGT products likely to enter the Australian market in the next five years and the timelines for entry were undertaken. Likelihood to enter the Australian market was based on estimates of the likelihood of approval, companies' existing presence in Australia and clinical trials of the product conducted in Australia. Timelines for entry were based on RM approved products average timings of phase III completion, phase III to regulatory filing, filing to approval and average approval gap US vs Australia. Estimates of potential entry in Australia of tissue engineered products were calculated using estimated approval date for the product in the US and average approval gap US vs Australia.

Key Takeaways -The Global Pipeline to Australia

There are 140 late-stage assets in clinical development across CGTs targeting a variety of diseases across multiple therapeutic areas globally. Cell therapies are the dominant category of RM products in development followed by gene therapies, and gene-modified cell therapies.

In the global pipeline for CGTs, ~70% assets are in phase III of development and 11% assets are undergoing regulatory review mostly in major developed markets (US and EU). Phase II/III accounted for 16% of the pipeline.

Despite the COVID-19 pandemic, RM companies continue to advance their late-stage pipeline assets. Based on the number of early-stage clinical trials, the number of late-stage pipeline products is expected to continue to rise, resulting in a higher number of approvals in the future.

In the cell therapy space, smaller companies lead the race with four assets (one each from Enzyvant, Bluebird Bio, PTC and Rheacell) are undergoing regulatory review in the US and EU. In June 2021, Mallinckrodt received US FDA approval of StrataGraft® for treatment of adults with thermal burns.

The gene therapies pipeline is more focused on rare diseases and dominated by large companies, with Novartis leading the race followed by Biogen and Pfizer. However, many smaller companies (e.g., BioMarin, Akcea Therapeutics Inc and others) are entering into this space which will intensify future competition. In February 2021, the US FDA approved Sarepta Therapeutics' Amondys 45™ (casimersen) for the treatment of Duchenne muscular dystrophy.

Gene-modified cell therapies (e.g. Kymriah® and Yescarta®) have changed the treatment paradigm for patients with certain hematologic malignancies. Though the gene-modified cell therapies space is dominated by large companies like Novartis, Gilead and Bristol Myers Squibb (BMS), smaller companies such as Legend Biotec and JW Cayman Therapeutics are also in the race with their assets in the late stage of development. In March 2021, BMS received US FDA approval for Abecma® (idecabtagene vicleucel), which is the first gene-modified cell therapy for adult patients with multiple myeloma.

In the global CGT pipeline, oncology is the leading therapy area followed by central nervous system diseases and cardiovascular diseases. In oncology, cell therapies account for the largest number of assets in late-stage development followed by gene-modified cell therapies and finally gene therapies.

The majority of pipeline assets for cardiovascular diseases are cell therapies based and dominated by smaller players like Helixmith Co Ltd, Mesoblast, BioCardia, Inc. and Japan Regenerative Medicine Co Ltd.

In haematological disorders, many companies including the large players like Pfizer and Sanofi are focusing on haemophilia treatment (six assets are in late-stage development for haemophilia A and haemophilia B).

In the global CGT pipeline, glioblastoma (GBM) and osteoarthritis are the leading indications followed by critical limb ischemia and heart failure. There are five late-stage cell therapy-based assets targeting COVID-19 infection and its complications, four assets targeting COVID-19 acute respiratory distress syndrome (ARDS), one asset from CellTex Therapeutics, targeting COVID-19 infection.

Companies developing CGTs include both small biotechs and larger biopharmaceutical firms. Industry-sponsored (>80%) assets vastly outnumber non-industry sponsored assets. Novartis AG sponsored the highest number of assets followed by BMS, Pfizer Inc, Biogen Inc, Akcea Therapeutics Inc and Mesoblast with equal number of assets (three each) in late stages of development. Mesoblast and Cynata Therapeutics Ltd are the two Australian sponsors involved in the CGT global pipeline. As the CGT market becomes more established, both small biotechs and larger biopharmaceutical firms are seeking to get a larger share and entering into strategic alliances or acquiring small- to mid-size players or assets.

In the global CGT pipeline, the highest number of assets are in stem cell therapy-based development followed by chimeric antigen receptor (CAR)-T cells and vaccines. CAR-T cell therapies are for the dominant treatment for a variety of blood cancers B-cell malignancies and myeloid myeloma (MM).

In the global CGT pipeline, Asia-Pacific (APAC) region is emerging as a key region supporting CGT RM product development with several local companies including Tella Inc, Cynata Therapeutics Ltd, Stempeutics Research

Pvt Ltd, Tego Science Inc and Seneca Biopharma Inc having potential products expected to enter into the market in the next three to five years.

There are 43 assets in development for tissue engineered products. Musculoskeletal disorders are the leading therapy area for these products followed by dermatology and cardiovascular diseases.

Industry-sponsored assets dominated the tissue engineered products pipeline. All top industry sponsors had equal number of assets (two each) in development.

- CorMatrix's Cor® PEDIATRIC Tricuspid ECM® Valve and Cor® TRICUSPID ECM® Valve Device, are in clinical development for heart valve disease in the US.
- Anteris' (formerly Admedus) tissue engineering process-treated (ADAPT®) technology-based assets, are undergoing regulatory review for cardiovascular and neurological diseases in emerging markets.
- Tissue Regenix's Cardiopure™ asset category, are undergoing regulatory review in EU for aortic valve disease and pulmonary valve disease.
- LeMaitre's CardioCel® asset category, is undergoing regulatory review for cardiovascular and gastrointestinal diseases in many countries such as China, Australia and Mexico and are already approved in multiple countries including major markets (US and EU). VascuCel® is undergoing regulatory review for carotid artery disease in China, Philippines, Taiwan, and Thailand, which are already approved in major markets.

Based on the likelihood and timeline estimates the following products were considered to be the most likely to enter the Australian market:

- Cell Therapy: StrataGraft® (*Mallinckrodt Plc) and RVT-802 (Enzyvant Sciences Ltd)* in 2023; Omidubicel (*Gamida Cell Ltd*) and Stapuldencel-T (Sotio AS) in 2024
- Gene Therapy: Vutrisiran (*Alnylam Pharmaceuticals Inc*) in 2023; Fitusiran (*Sanofi*) and Etranacogene dezaparvovec (*UniQure NV*) in 2025
- Gene Modified Cell Therapy: Lisocabtagene maraleucel (*Juno Therapeutics Inc*) in 2023; Ciltacabtagene autoleucel (*Legend Biotech Corp*) in 2024

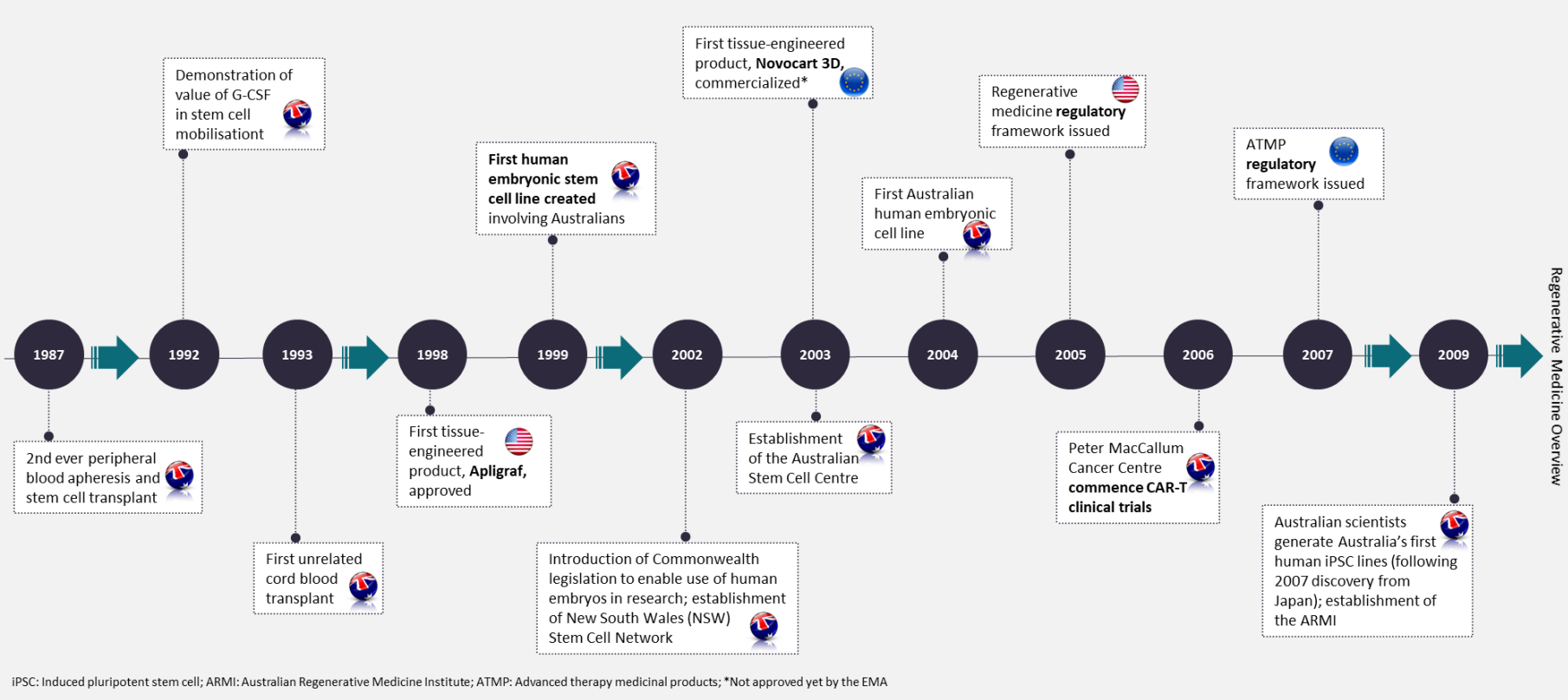
The three tissue engineered products likely to enter the market in Australia in the next 12 months are CelGro® - Tendon Regeneration (Orthocell Ltd), CGX-443 (Antibe Therapeutics Inc) and MAP Tissue Scaffold - Acute Wound (Tempo *Therapeutics Inc).*

Background

History of RM Development in the US, EU, Japan, and Australia

The global pipeline of products that may enter the Australian market is influenced by research advances, funding choices and regulatory decisions that have been made globally. The advances in the US, EU and Japan in the RM sector have had the greatest impact on the global pipeline to Australia. Figure 1 provides an overview of the key RM developments that have impacted the global pipeline of RM products to Australia.

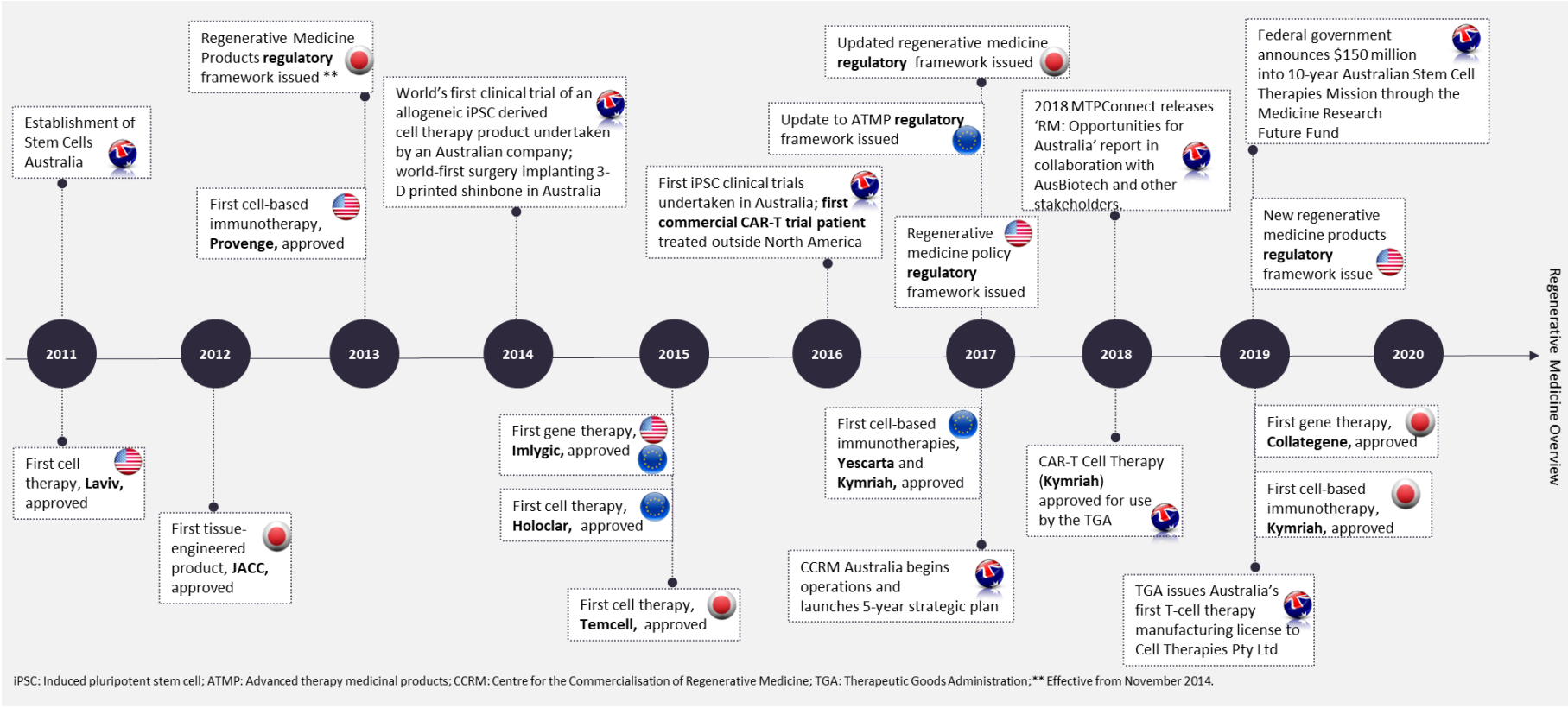
Figure 1: RM – History of RM Development in the US, EU, Japan, and Australia



iPSC: Induced pluripotent stem cell; ARMI: Australian Regenerative Medicine Institute; ATMP: Advanced therapy medicinal products; *Not approved yet by the EMA

Source: GlobalData Thematic Research: Regenerative Medicine in Pharma, November 2020; AusBiotech: Cellular Therapies and Regenerative Medicine in Australia, October 2019.

Continued: Figure1: RM – History of RM Development in the US, EU, Japan and Australia



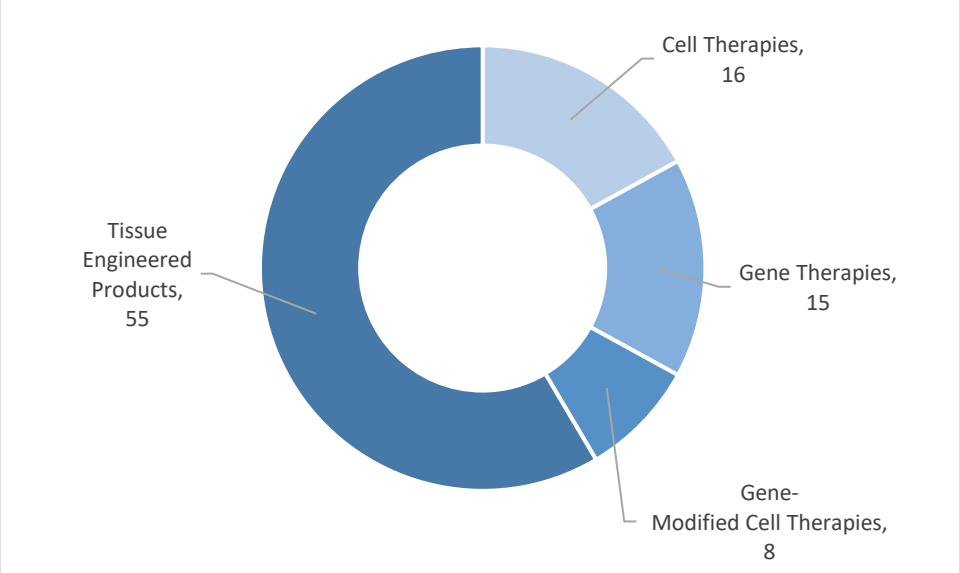
iPSC: Induced pluripotent stem cell; ATMP: Advanced therapy medicinal products; CCRM: Centre for the Commercialisation of Regenerative Medicine; TGA: Therapeutic Goods Administration;** Effective from November 2014.

Source: GlobalData Thematic Research: Regenerative Medicine in Pharma, November 2020; AusBiotech: Cellular Therapies and Regenerative Medicine in Australia, October 2019.

Section 1: RM Global Marketed Products

1.A: RM Marketed Products by Therapy Types in the US, EU, and Japan

Figure 2: RM – Number of Marketed Products by Therapy Types in the US, EU, and Japan



Source: GlobalData; Pharma Intelligence Center Drug Database [Accessed on 24/03/2021]; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

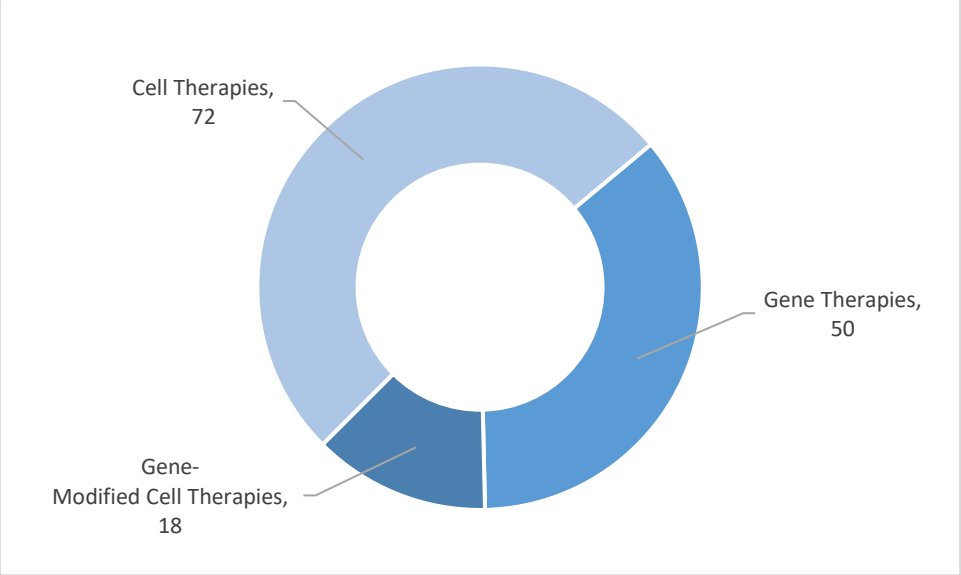
Note: Since a single product may be marketed for multiple indications/geographies, the count of total products could be higher than the actual number of marketed products.

There were 94 RM products marketed in the US, EU and Japan (see Appendix 3 for list of the marketed RM products). Tissue Engineered products lead the category with ~60% marketed products, followed by cell therapies (17%) and gene therapies (16%). The majority of products are available in the US (45%), followed by the EU (41%) and Japan (15%). Among Tissue Engineered products, the highest number of products were approved for musculoskeletal disorders followed by dermatology and metabolic disorders. In gene therapies, the highest number of products were approved for genetic disorders and metabolic disorders. The majority of gene-modified cell therapies were approved for cancer indications.

Section 2: CGT Global Late-stage Pipeline

2.A: CGT Late-stage Pipeline by Therapy Types and Phases

Figure 3: CGT – Number of Late-stage Active Pipeline Assets by Therapy Types



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites
Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography)

There are 140 late-stage assets (products at pre-registration and Phase III (also include Phase II/III and Phase I/II/III)) in clinical development globally across CGT categories targeting a variety of diseases across therapeutic areas in the global pipeline to Australia. Cell therapies comprised the most investigated category of CGT and accounted for approximately 50% of the pipeline assets followed by gene therapies (36%) and gene-modified cell therapies (13%).

Despite the COVID-19 pandemic, companies continued to advance their late-stage pipeline asset development. In the cell therapy space, smaller companies led the race with four assets (Enzyvant's RVT-802 for DiGeorge syndrome in the US; Bluebird Bio's elivaldogene autotemcel for adrenoleukodystrophy in EU; and PTC's eladocagene exuparvovec for aromatic L-amino acid decarboxylase in EU; Rheacell's Amesanar for venous leg ulcers in Germany) undergoing regulatory review in the US and EU. In September 2020, Mesoblast's remestemcel-L filing is rejected/withdrawn in the US, which is being reviewed for the treatment of paediatric steroid-refractory acute graft versus host disease (SR-aGVHD). The US FDA recommended to conduct at least one additional randomised controlled trial in adults and/or children to generate more evidence of the drug's effectiveness. In June 2021, Mallinckrodt received the US FDA approval of StrataGraft® (allogeneic cultured keratinocytes and dermal fibroblasts in marine collagen), a cell therapy product for treatment of adults with thermal burns.

The gene therapies pipeline continued to focus on rare diseases but there are several assets in development for non-rare conditions as well. The gene therapy space is dominated by large companies, Novartis lead the race followed by Biogen and Pfizer. It was rapidly expanding with many small companies (e.g. BioMarin, Akcea Therapeutics Inc, FKD Therapies Oy, GenSight Biologics and others) entering into this space, which will intensify future competition. There are four assets from small companies (GenSight's lenadogene nolparvovec for leber optic atrophy in EU; ERC's ERC-1671 for recurrent GBM multiforme in EU; FKD's nadofaragene

firadenovec for bladder cancer in the US, BioMarin's valoctocogene roxaparvovec for Haemophilia A in the US and EU) undergoing regulatory review in the US and EU. Filings were rejected/withdrawn for Akcea's volanesorsen (approved in the EU for familial chylomicronemia) and Sarepta's eteplirsen (approved in the US for Duchenne muscular dystrophy) in the US and EU respectively. In February 2021, FDA approved Sarepta Therapeutics' Amondys 45™ (casimersen) for the treatment of Duchenne muscular dystrophy.

With the approval of Novartis' Kymriah® and Gilead's Yescarta®, gene-modified cell therapies changed the treatment paradigm for patients with certain hematologic malignancies. With their curative potential, CAR T-cell therapies are giving hope to thousands of patients suffering from incurable diseases witnessing a rise in R&D activities in this space. Though, the gene-modified cell therapies space is dominated by large companies like Novartis, Gilead and BMS, smaller companies such as Bluebird Bio (Zynteglo® approved for thalassemia in EU and Orchard Therapeutics (Strimvelis® approved for adenosine deaminase deficiency related SCID in EU) also entered with approved products.

In March 2021, BMS received US FDA approval of Abecma® (idecabtagene vicleucel), which was the first gene-modified cell therapy for adult patients with multiple myeloma (MM) who have not responded to, or whose disease has returned after, at least four prior lines of therapy. As there is no cure for multiple myeloma, Abecma® approval provides a new treatment option for patients who have this uncommon type of cancer. While MM may be an uncommon cancer when considering all possible cancers, MM accounts for ~14% of blood cancers[5]. This cancer population is significant and represents a large increase in potential gene modified cell therapy recipients compared to target populations of other CAR-Ts (acute lymphoblastic leukemia (ALL), diffuse large B-cell lymphoma (DLBCL)). The entry of Abecma® for MM to the market is a significant for the RM sector. The approval of Abecma® marks a shift in the need to upscale manufacturing capacity, supply chain and clinical delivery capacity in the regenerative medicine value chain. Further discussion of the regenerative medicine value chain, manufacturing capabilities and addressing growth of the RM sector in Australia can be found in the Regenerative Medicine Catalyst Project Value Chain[6], Manufacturing and [7] Strategic Roadmap reports[8].

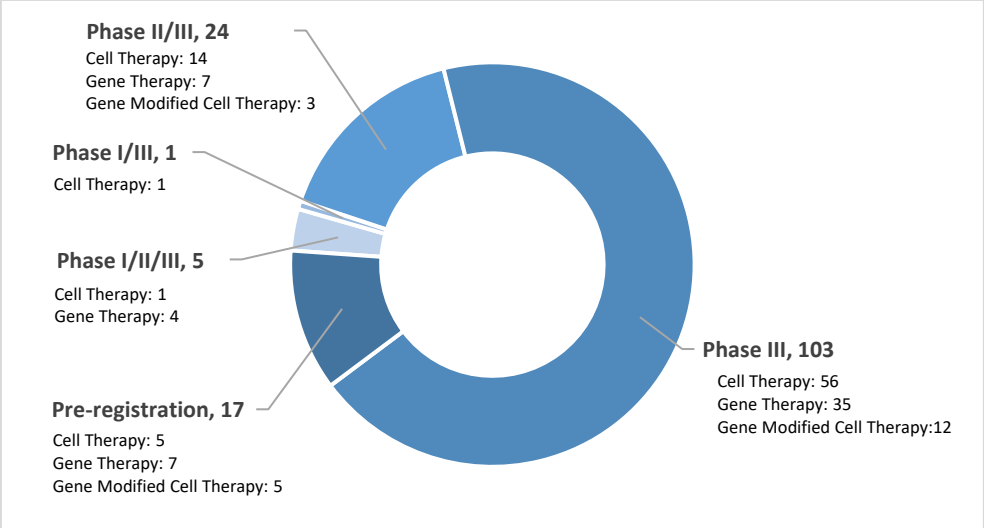
[5] Global CAR-T Cell Therapy Market, Market Size, Forecasts, Trials and Trends, 2021, BioInformant.

[6] Regenerative Medicine Catalyst Project. (2021). The Regenerative Medicine Value Chain - The Pathway from Discovery to Patient Delivery.

[7] Regenerative Medicine Catalyst Project. (2021). Australia's Regenerative Medicine Manufacturing Capacity & Capability.

[8] Regenerative Medicine Catalyst Project. (2021). Catalysing Regenerative Medicine in Australia - A Strategic Roadmap for the Regenerative Medicine Sector.

Figure 4: CGT – Number of Late-stage Active Pipeline Assets by Phase and Therapy Types



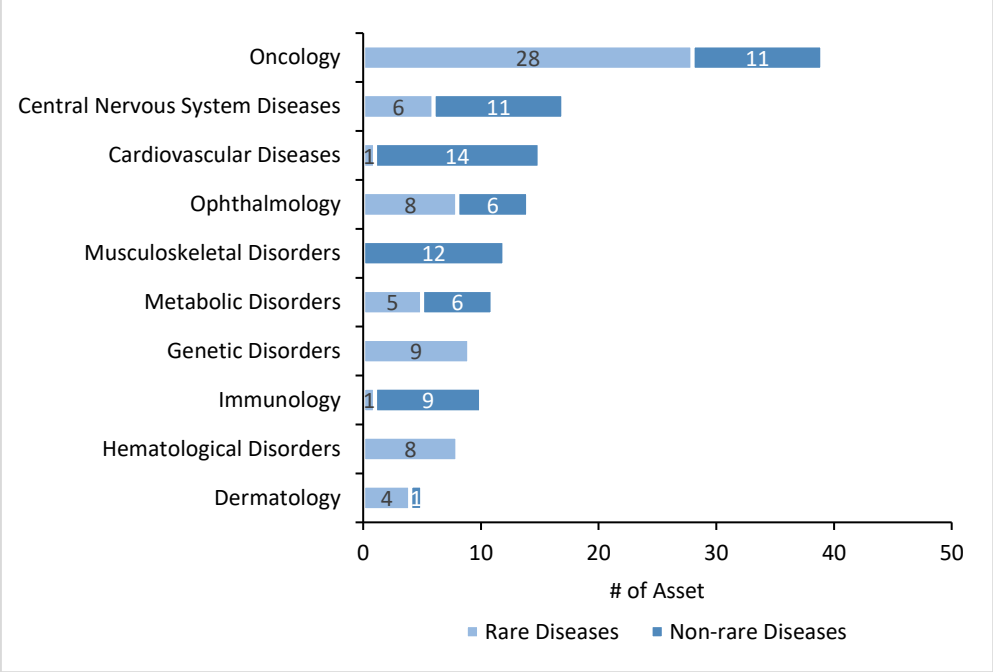
Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

In the CGT global pipeline, ~70% assets are in phase III of development and 11% of assets are undergoing regulatory review. Phase II/III accounted for 16% of the total pipeline. Five assets in Phase I/II/III and one asset in Phase I/III are also being evaluated in the CGT pipeline. The pipeline also includes three previously approved products for which filings are rejected/withdrawn for indications that are not approved in the US and EU (Mesoblast's remestemcel-L for graft versus host disease in the US, Akcea's villainesses sodium for familial chylomicronemia in the US and Sarepta's eteplirsen for Duchenne muscular dystrophy in EU).

2.B: CGT Late-stage Pipeline by Top Therapy Areas

Figure 5: CGT – Number of Late-stage Active Pipeline Assets for Top 10 Therapy Areas Including Rare Diseases



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets; The list of rare diseases (for CGT development) has been provided in Table 14 in the Appendix 3.

Oncology is the leading therapy area followed by central nervous system and cardiovascular diseases. Ophthalmology, musculoskeletal disorders, and metabolic disorders had more than 10 assets in late-stage development for CGT.

In oncology, cell therapies accounted for the highest number of assets in late-stage development followed by gene-modified cell therapies and gene therapies. Though Novartis and Gilead had strong presence in oncology, entry of BMS and smaller companies like Legend Biotech, FKD Therapies Oy, Gamida Cell Ltd and Tella Inc will intensify future competition in this space.

In central nervous system diseases space, large companies like Novartis and Biogen are already present. However, smaller companies such as Akcea Therapeutics Inc, Helixmith Co Ltd, Orchard Therapeutics and BrainStorm Cell Therapeutics Inc. are in the race targeting new neurological indications such as amyloid polyneuropathy, cerebral palsy, amyotrophic lateral sclerosis and metachromatic leukodystrophy.

A majority of cardiovascular diseases pipeline assets are cell therapies based and are dominated by smaller companies like Helixmith Co Ltd, Mesoblast, BioCardia, Inc. and Japan Regenerative Medicine Co Ltd. Most of the approved products are in the APAC region, creating a space for companies to enter into major markets. Novartis' gene therapy asset, inclisiran, is undergoing regulatory review awaiting approval in atherosclerosis, which was earlier rejected by the US FDA due to unresolved facility inspection-related conditions, however, the US FDA has not raised any concerns related to its efficacy or safety.

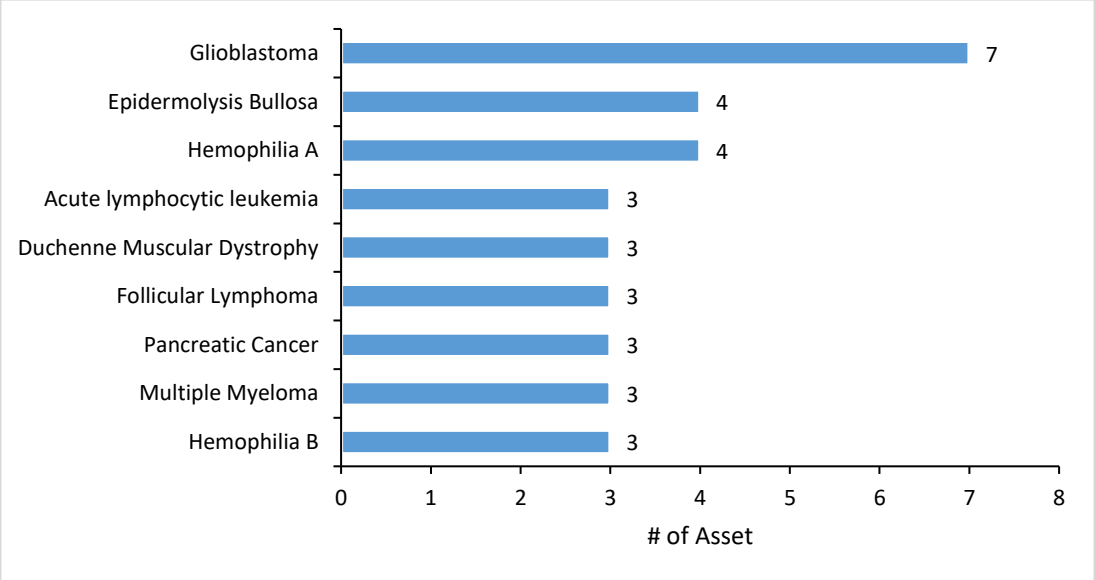
In the haematological disorders space, Bluebird Bio's Zynteglo®, a gene-modified cell therapy is the only approved therapy in EU for thalassemia. Many companies including the large companies are developing potential drug candidates to boost haemophilia treatment. There are six assets in late-stage development for haemophilia A and haemophilia B in the US, EU and other markets.

- There are five gene therapy assets in the pipeline including:
  - BioMarin's valoctocogene roxaparvovec in regulatory review for Haemophilia A in the US and EU and in Phase III in Australia;
  - Four assets in Phase III development: Pfizer's giroctocogene fitelparvovec for haemophilia A (US and other countries); Sanofi's fitusiran for haemophilia A and haemophilia B in the US, EU, Japan, Australia and other countries; Spark Therapeutics' dirloctocogene samoparvovec for haemophilia A in the US; UniQure's etranacogene dezaparvovec for hemophilia B in the US and EU; and
- Pfizer's fidanacogene elaparvovec (gene-modified cell therapy) in Phase III for haemophilia B in the US, EU, Japan, Australia and other countries.

Oncology is the leading therapy area with highest number of assets in late-stage development for rare disease followed by genetic disorders and ophthalmology and haematological disorders.

2.C: CGT Late-stage Pipeline for Rare Diseases

Figure 6: CGT – Number of Late-stage Active Pipeline Assets for Top 10 Rare Diseases



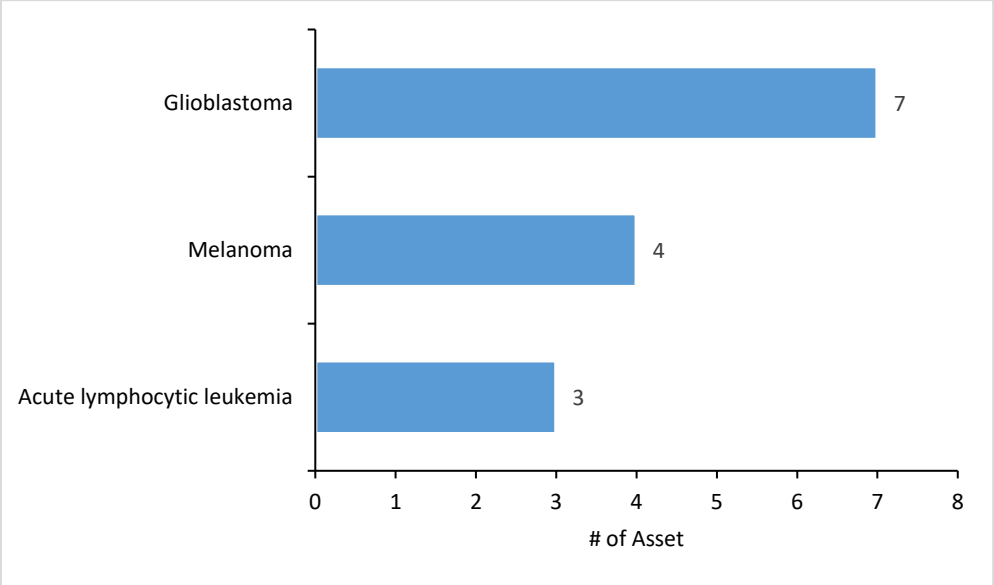
Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Of the top 10 rare disease in CGT global pipeline, oncology indications are predominantly investigated.

2.D: CGT Late-stage Pipeline: Top Indications for Top 3 Therapy Areas

Figure 7: CGT – Number of Late-stage Active Pipeline Assets for Top 3 Indications in Oncology

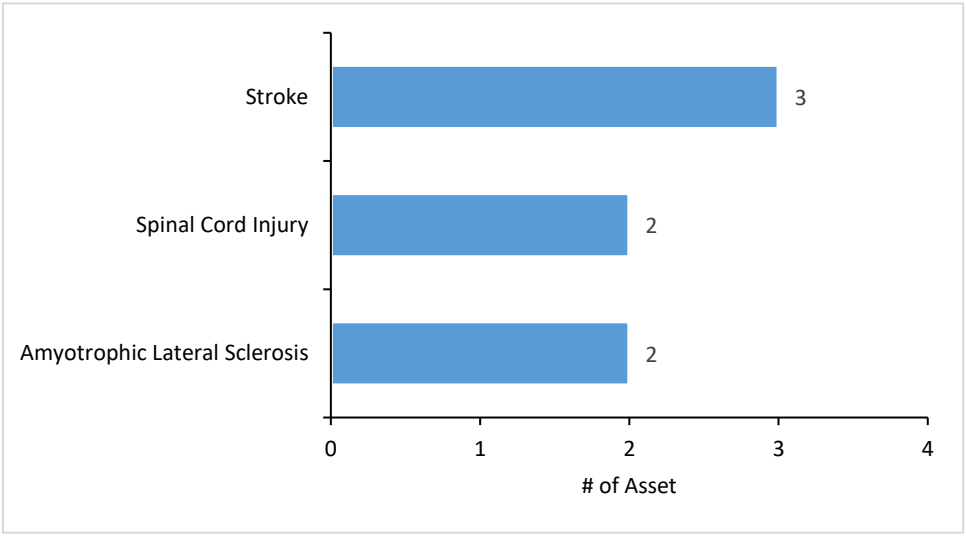


Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

The largest number of late-stage pipeline assets in oncology are seen in GBM, followed by melanoma and acute lymphocytic leukemia.

Figure 8: CGT – Number of Late-stage Active Pipeline Assets for Top 3 Indications in Central Nervous System Diseases

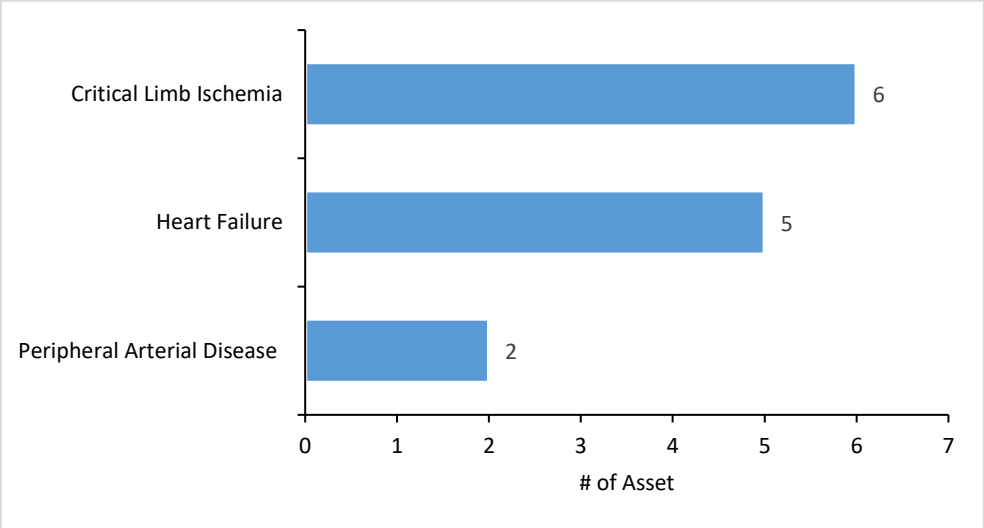


Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Among central nervous system diseases, stroke with three assets, is the leading indication followed by spinal cord injury and amyotropic lateral sclerosis with equal number of assets (two each) in late-stage development.

Figure 9: CGT – Number of Late-stage Active Pipeline Assets for Top 3 Indications in Cardiovascular Diseases



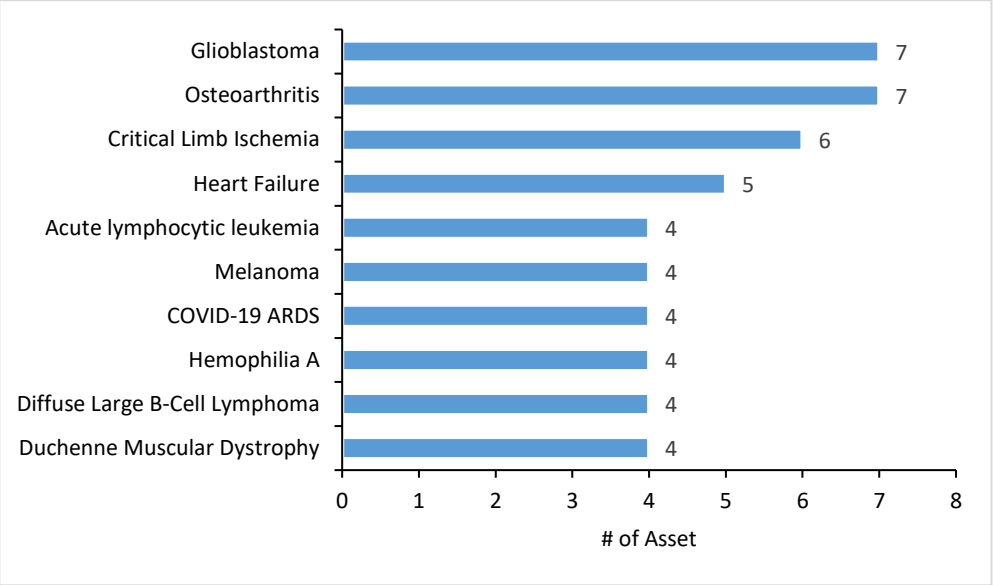
Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Among cardiovascular diseases, critical limb ischemia is the leading indication followed by heart failure and peripheral arterial disease.

2.E: CGT Late-stage Pipeline by Top Indications

Figure 10: CGT – Number of Late-stage Active Pipeline Assets for Top 10 Indications



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Of the 140 CGT global pipeline, GBM and osteoarthritis are the leading indications with equal number of assets (7 each) in development followed by critical limb ischemia and heart failure. Other indications such as Duchene's muscular dystrophy, diffuse large B-cell lymphoma, haemophilia A, COVID-19 Acute Respiratory Distress Syndrome (ARDS), melanoma and acute lymphocytic leukemia had equal number of assets (four each) in development.

Among top 10 indications, two gene therapy assets are undergoing regulatory review in major markets for GBM and haemophilia A.

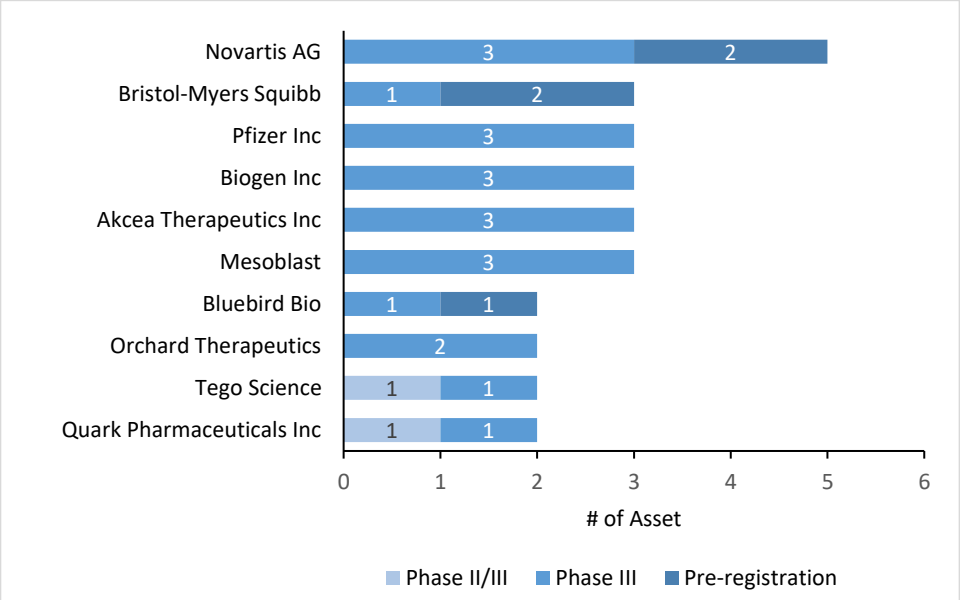
- In GBM, ERC's ERC-1671 is undergoing regulatory review in the EU for conditional approval in recurrent GBM.
- In haemophilia A, BioMarin's valoctocogene roxaparvovec is awaiting approval in the US and EU. If approved, valoctocogene roxaparvovec has the potential to redefine the treatment paradigm for people with haemophilia A

There are five late-stage cell therapy-based assets targeting COVID-19:

- Four assets targeting COVID-19 ARDS are in development (two each in the US and Iran)
- One asset from CellTex Therapeutics, targeting COVID-19 infection is in development in Mexico.

2.F: CGT Late-stage Pipeline by Top Sponsors

Figure 11: CGT – Number of Late-stage Active Pipeline Assets for Top 10 Industry Sponsors



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

The companies developing CGTs included both small biotechs and large biopharmaceutical firms. Industry-sponsored (>80%) assets vastly outnumbered non-industry sponsored assets.

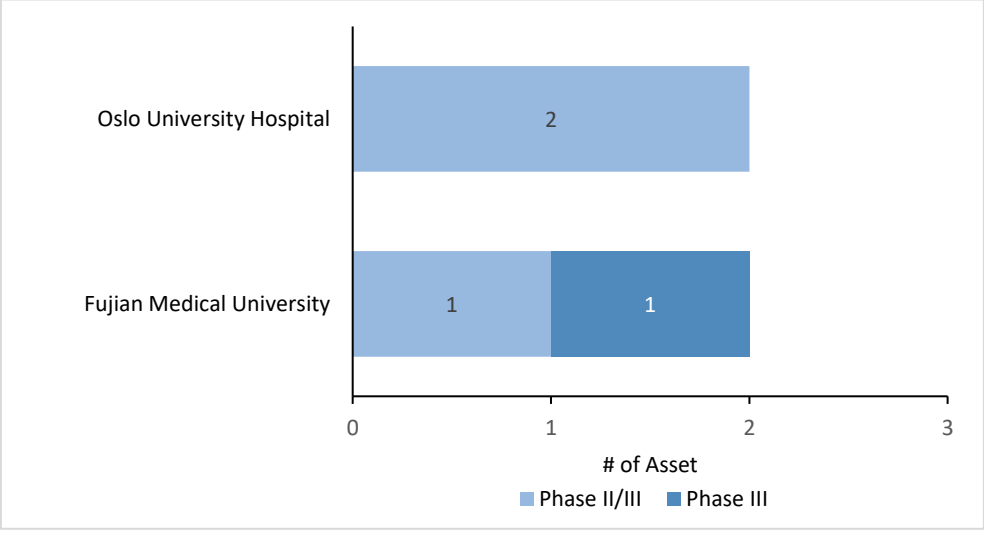
Among the top 10 industry sponsors, Novartis sponsored the highest number of assets followed by BMS, Pfizer Inc, Biogen Inc, Akcea Therapeutics Inc and Mesoblast with equal number of assets (three each) in late stages of development. Novartis and BMS (two assets each) led the race in terms of near approval (undergoing regulatory review) followed by Bluebird Bio. Mesoblast and Cynata Therapeutics Ltd are the two Australian sponsors featured in the global CGT pipeline.

As the CGT market becomes more established, both small biotechs and larger biopharmaceutical firms are seeking a larger share in this sector. In order to remain competitive, companies are entering into strategic alliances or acquiring small- to mid-size companies (Table 1. examples of strategic alliances and acquisitions) or assets.

Table 1: Examples of Strategic Alliances and Acquisitions

Deal Date	Partner/Acquirer	Alliance/Acquisition Entity	Deal Details
Licensing and Co-Development			
November 2020	Takeda	Arrowhead	ARO-AAT, a gene therapy asset to be co-developed and co-commercialized in the US by Takeda and Arrowhead under a 50/50 profit-sharing structure. Takeda receives exclusive license to commercialise ARO-AAT for alpha-1 antitrypsin-associated liver disease (AATLD) outside the US
November 2020	Novartis	Mesoblast	Novartis entered into an exclusive worldwide licensing and collaboration agreement with Mesoblast to develop, commercialise and manufacture remestemcel-L for the treatment of COVID-19 ARDS.
April 2020	Alnylam	Dicerna	Alnylam Pharmaceuticals, Inc. and Dicerna Pharmaceuticals, Inc. announced development and commercialisation collaboration on investigational RNAi therapeutics
Acquisitions			
May 2018	Novartis	AveXis	Novartis acquired AveXis, the developer of Zolgensma® which as approved as a gene therapy for spinal muscular atrophy (SMA).
October 2017	Gilead	Kite Pharma	Gilead acquired Kite Pharma, its Yescarta® (axicabtagene ciloleucel), became the first CAR-T therapy approved by the FDA for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.

Figure 12: CGT – Number of Late-stage Active Pipeline Assets by Top Non-industry Sponsors

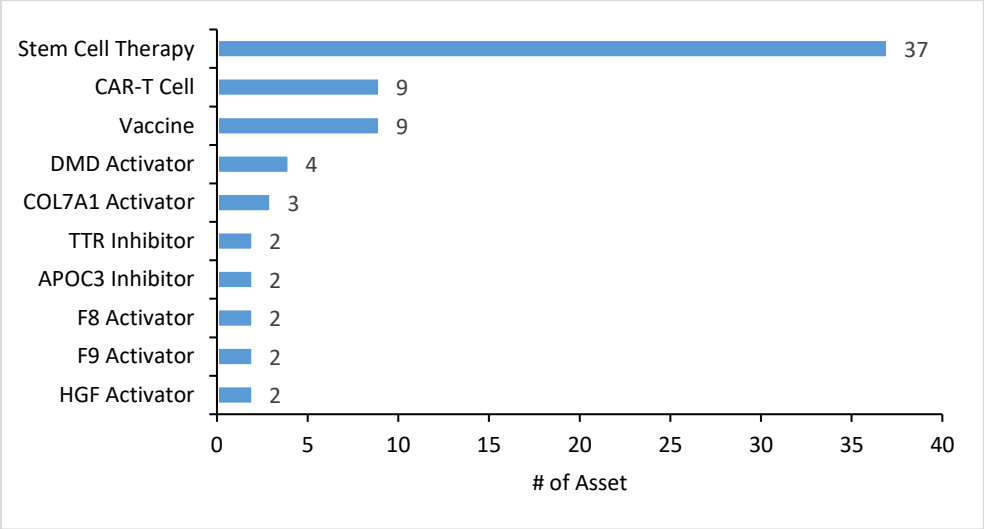


Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

As shown in Figure 25, Fujian Medical University (Fuzhou, Fujian, China) and Oslo University Hospital (Nydalen, Oslo, Norway) are the two leading non-industry sponsors involved in CGT global pipeline.

2.G: CGT Late-stage Pipeline by Mechanism of Action (MoA)

Figure 13: CGT – Number of Late-stage Active Pipeline Assets for Top 10 MoAs



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography)

Stem cell therapy-based MoAs outnumbered the rest of the MoAs. A stem cell therapy-based asset, Amesanar® from Rheacell GmbH & Co. KG is under regulatory review for venous leg ulcers in Germany and Mesoblast's remestemcel-L filing is rejected/withdrawn in the US for paediatric graft versus host disease (GVHD). CAR-T cells and vaccines are the second leading (nine products each) class or MoA in the CGT pipeline.

CAR-T cell therapies are the established treatment for variety of blood cancers, such as CD19 CAR-T for B-cell malignancies and BCMA CAR-T for MM.

- Many products are approved targeting CD19 CAR-T cell: Novratis' Kymriah®, Gilead's Yescarta® & Tecartus® and BMS' Breyanzi®
- BMS's Abecma® is approved targeting BCMA CAR-T Cell and Legend's ciltacabtagene autoleucel is under review in the US and EU for relapsed multiple myeloma and refractory multiple myeloma
- One asset from Fujian Medical University (Fuzhou, Fujian, China) targeting CD123/CLL1 CAR-T Cell is in Phase III for relapsed and refractory MM.

A majority of the vaccine-based assets in late-stage development are being investigated in GBM sponsored by smaller companies and non-industry sponsors (Tella's TLP-0001, Gradalis' gemogenovatucel-T, Northwest's DCVax-L and others). ERC's ERC-1671 is undergoing regulatory review in the EU for conditional approval in recurrent GBM.

2.H: CGT Late-stage Pipeline by Region

In terms of geographic spread, though the CGT pipeline is mostly focused on the US and EU regions, Table 2, suggests that the APAC is emerging as a key region supporting CGT research with several local companies, such as Tella Inc, Cynata Therapeutics Ltd, Stempeutics Research Pvt Ltd, Tego Science Inc and Seneca Biopharma Inc, having potential products expected to enter into the market in the next three to five years. A majority of the approved products in cell therapies are from companies based in the APAC region such as Mesoblast's Prochymal®, Tego's Rosmir®, Nipro's Stemirac® and others.

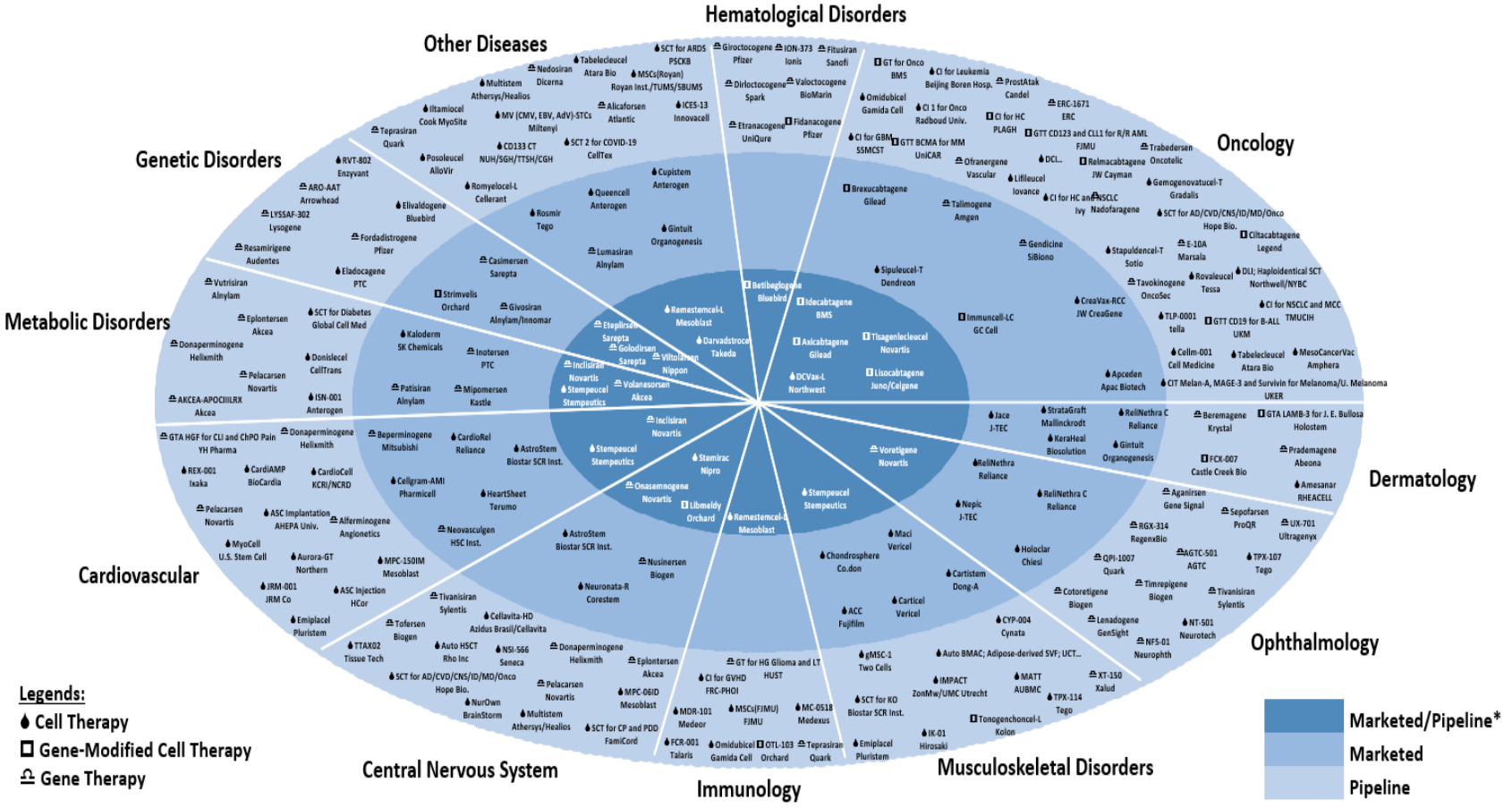
Table 2: CGT – Examples of Late-stage CGT Pipeline in the APAC Region

Drug Class and Name	Company	Indication	Phase	Country
Cell Therapies				
TPX-107	Tego Science,Inc	Corneal Defects	Phase III	South Korea
Stempeucel	Stempeutics Research Pvt Ltd	Knee Osteoarthritis; Diabetic Foot Ulcers	Phase III	India
NSI-566	Seneca Biopharma Inc	Paralysis Due to Ischemic Stroke	Phase II/III	China
TLP-0001	Tella Inc	Pancreatic Cancer	Phase III	Japan
CYP-004	Cynata Therapeutics Ltd	Knee Osteoarthritis	Phase III	Australia
Gene Therapies				
Donaperminogene seltoplasmid	Helixmith Co Ltd	Critical Limb Ischemia	Phase III	China
E-10A	Marsala Biotech Inc	Head And Neck Cancer Squamous Cell Carcinoma	Phase III	China
Gene-Modified Cell Therapies				
Relmacabtagene autoleucel	JW Cayman Therapeutics Co Ltd	Diffuse Large B-Cell Lymphoma	Pre-registration	China
Gene Therapy to Target BCMA for Multiple Myeloma	Shanghai Unicar-Therapy Bio-Medicine Technology Co Ltd	Multiple Myeloma	Phase III	China

2.I: CGT Late-stage Pipeline Competitive Assessment

The bulls eye chart represents the global RM pipeline competitive overview by therapy areas. It also provides information on therapy type, sponsor, and phase of development. Oncology is the leading therapy area followed by central nervous system and cardiovascular diseases.

Figure 14: CGT – Late-stage Active Pipeline Assets Competitive Assessment



Source: GlobalData; Pharma Intelligence Center Pipeline Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

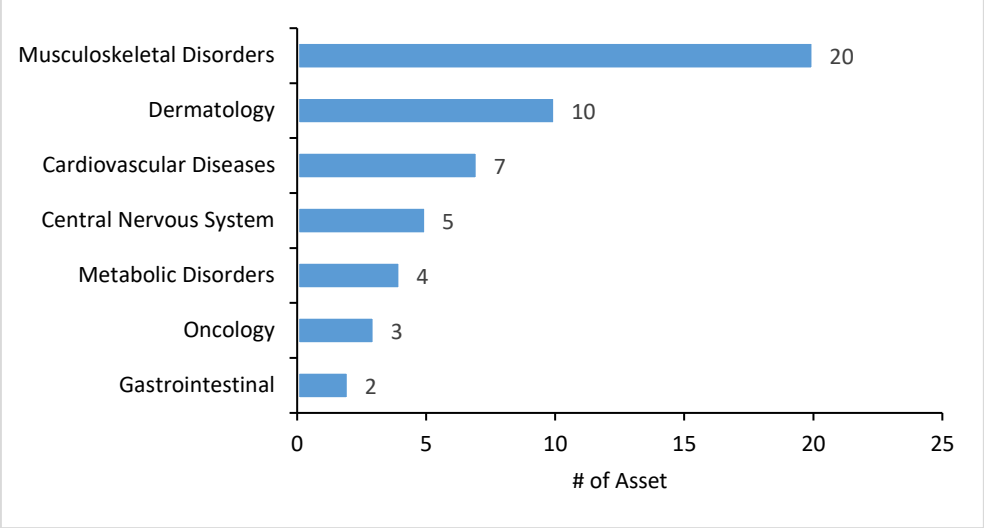
Note: Late-stage pipeline includes phase III and above assets (including marketed products which are in late-stage clinical development either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets. *Includes already approved and on-market assets in pipeline for additional indication/geography

ACC - Autologous cultured cartilage, ASC Implantation - Allogeneic stem cells implantation, ASC Injection - Adipose Stromal Cells Injection, Auto HSCT - Autologous Hematopoietic Stem Cell Transplantation, CI 1 for Onco - Cellular Immunotherapy 1 for Oncology, CI for GBM - Cellular Immunotherapy for Glioblastoma Multiforme, CI for GVHD - Cellular Immunotherapy for Graft Versus Host Disease, CI for HC - Cellular Immunotherapy for Hepatocellular Carcinoma, CI for HC and NSCLC - Cellular Immunotherapy for Hepatocellular Carcinoma and Non-Small Cell Lung Cancer, CI for Leukemia - Cellular Immunotherapy for Leukemia, CI for NSCLC and MCC - Cellular Immunotherapy for Non-Small Lung Cancer and Metastatic Colorectal Cancer, CIT Melan-A, MAGE-3 and Survivin for Melanoma/U. Melanoma - Cellular Immunotherapy to Target Melan-A, MAGE-3 and Survivin for Melanoma and Uveal Melanoma, DCI - Dendritic cell immunization, DLI; Haploidentical SCT - Donor Lymphocyte Infusion (DLI); Haploidentical Stem Cell Transplantation, Donaperminogene - Donor Lymphocyte Infusion (DLI); Haploidentical Stem Cell Transplantation, GT for HG Glioma and LT - Gene Therapy for High-Grade Glioma and Liver Transplantation, GT for Onco - Gene Therapy for Oncology, GTA HGF for CLI and ChPO Pain - Gene Therapy to Activate HGF for Critical Limb Ischemia and Chronic Post-Operative Pain, GTA LAMB-3 for J. E. Bullosa - Gene Therapy to Activate LAMB-3 for Junctional Epidermolysis Bullosa, GTT BCMA for MM - Gene Therapy to Target BCMA for Multiple Myeloma, GTT CD123 and CLL1 for R/R AML - Gene Therapy to Target CD123 and CLL1 for Relapsed and Refractory Acute Myeloid Leukemia, GTT CD19 for B-ALL - Gene Therapy to Target CD19 for B-Acute Lymphoblastic Leukaemia, IMPACT - Instant MSC Product Accompanying Autologous Chondron Transplantation (IMPACT), MATT - Microfragmented Adipose Tissue Transplant, MV (CMV, EBV, AdV)-STCs - Multivirus (CMV, EBV, AdV)-specific T cells, SCT 2 for COVID-19 - Stem Cell Therapy 2 for Coronavirus Disease 2019 (COVID-19), SCT for AD/CVD/CNS/ID/MD/Onco - Stem Cell Therapy for Autoimmune Disorders, Cardiovascular Disorders, CNS Disorders, Infectious Disease, Musculoskeletal Disorders and Oncology, SCT for ARDS - Stem Cell Therapy for Acute Respiratory Distress Syndrome, SCT for CP and PDD - Stem Cell Therapy for Cerebral Palsy and Pervasive Developmental Disorder, SCT for Diabetes - Stem Cell Therapy for Diabetes, SCT for KO - Stem Cell Therapy for Knee Osteoarthritis, MSCs - Mesenchymal Stem Cells, Auto BMAC; Adipose-derived SVF; UCT - Autologous Bone Marrow Concentrate (BMAC); Adipose-derived Stromal Vascular Fraction (SVF); Umbilical Cord Tissue (UCT)

BMS - Bristol-Myers Squibb, GC Cell - GREEN CROSS CELL, PTC - PTC Therapeutics Inc, J-TEC - Japan Tissue Engineering Co Ltd, HSC Inst. - Human Stem Cells Institute, J-TEC - Japan Tissue Engineering Co Ltd, AGTC - Applied Genetic Technologies, HCor - Hospital do Coracao, KCRI/NCRD - National Center for Research and Development, NUH/SGH/TTSH/CGH - National University Hospital; Singapore General Hospital; Tan Tock Seng Hospital; Changi General Hospital, SSMCST - Safe Save Medical Cell Sciences & Technology Co Ltd, FRC-PHOI - Federal Research Institute of Pediatric Hematology Oncology and Immunology, PLAGH - The General Hospital of the People's Liberation Army, TMUCIH - Tianjin Medical University Cancer Institute and Hospital, UKER - Universitatsklinikum Erlangen, Northwell/NYBC - New York Blood Center, PTC - PTC Therapeutics Inc, HUST - Huazhong University of Science & Technology, BMS - Bristol-Myers Squibb, YH Pharma - Yichang Humanwell Pharmaceutical , FJMU - Fujian Medical University, UKM - National University of Malaysia, JRM Co - Japan Regenerative Medicine Co Ltd, AUBMC - American University of Beirut Medical Center, Miltenyi - multiple company in company standards file, PSCKB - Parnia Stem Cell Knowledge-Based Co.

2.J: Tissue Engineered Products Pipeline by Top Therapy Areas

Figure 15: Tissue Engineered Products – Number of Late-stage Active Pipeline Assets for Top Therapy Areas



Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Of the total 43 assets in development for tissue engineered products, musculoskeletal disorders is the leading therapy area followed by dermatology and cardiovascular diseases.

The large pipeline for musculoskeletal disorders targets the increasing elderly population and people with disabilities associated with musculoskeletal conditions a population also expected to increase in the future. Since such diseases often result in the wastage of the muscle and bone, RM is becoming an emerging treatment option.

Lattice Biologics' Bone Scaffold + ECM (extra cellular matrix), Antibe's CGX-443, SurgaColl's ChondroColl™ and Collagen Solutions' ChondroMimetic® are undergoing regulatory review in the US and EU for musculoskeletal disorders such as osteoarthritis, bone fracture, bone deformities and others.

In dermatology, five assets are undergoing regulatory review targeting different indications in major markets as well as emerging markets such as Mexico, Kuwait, South Korea and Sri Lanka.

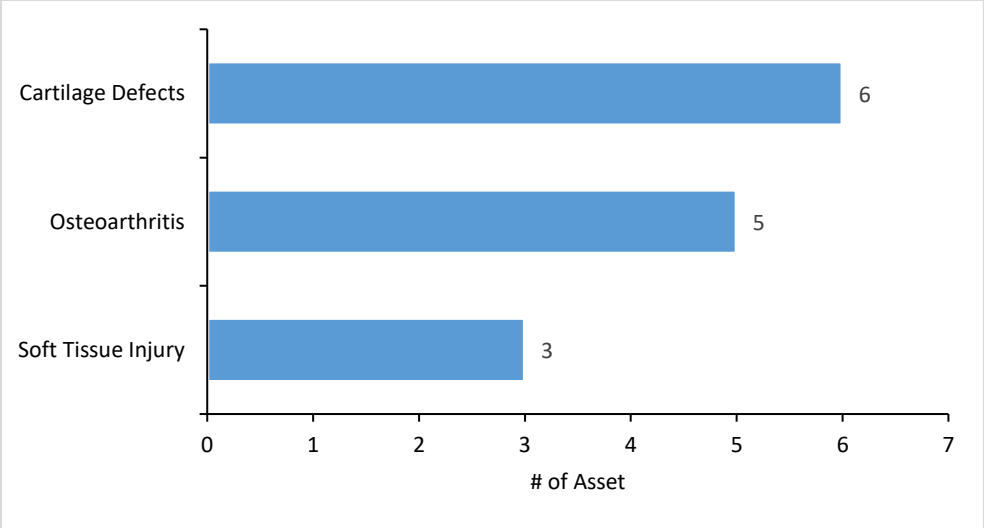
- Tempo's MAP Tissue Scaffold - Acute Wound for acute wounds in the US
- Elanix's First Cover Acute for acute wounds in EU
- MiMedx's EpiFix® Amniotic Membrane Allograft for venous leg ulcer, partial thickness wounds and burn wounds
- PolyNovo's NovoSorb® BTM - Wound Dressing for wounds and ulcer in Mexico, Kuwait, South Korea and Sri Lanka
- Avita's RECELL® System – Vitiligo for Vitiligo in Japan

In cardiovascular diseases, three assets are undergoing regulatory review targeting mostly in emerging markets except Tissue Regenix's Cardiopure™, which is for aortic valve disease and pulmonary valve disease and under review in the EU.

In oncology, three assets (BioAesthetics' Acellular NAC Graft™ and TeVido's TeVido Breast Graft in the US; Tensive's REGENERA Breast Implant in EU) are in clinical development for breast cancer.

2.K: Tissue Engineered Products Pipeline: Top Indications for Top 3 Therapy Areas

Figure 16: Tissue Engineered Products – Number of Late-stage Active Pipeline Assets for Top 3 Indication in Musculoskeletal Disorders

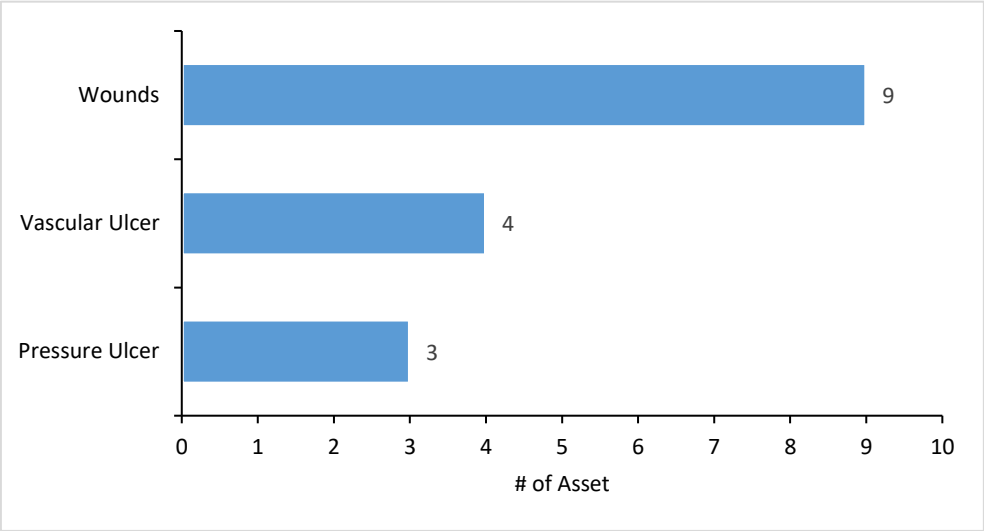


Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Among musculoskeletal disorders, cartilage defect is the leading indication followed by osteoarthritis and soft tissue injury.

Figure 17: Tissue Engineered Products – Number of Late-stage Active Pipeline Assets for Top 3 Indication in Dermatology

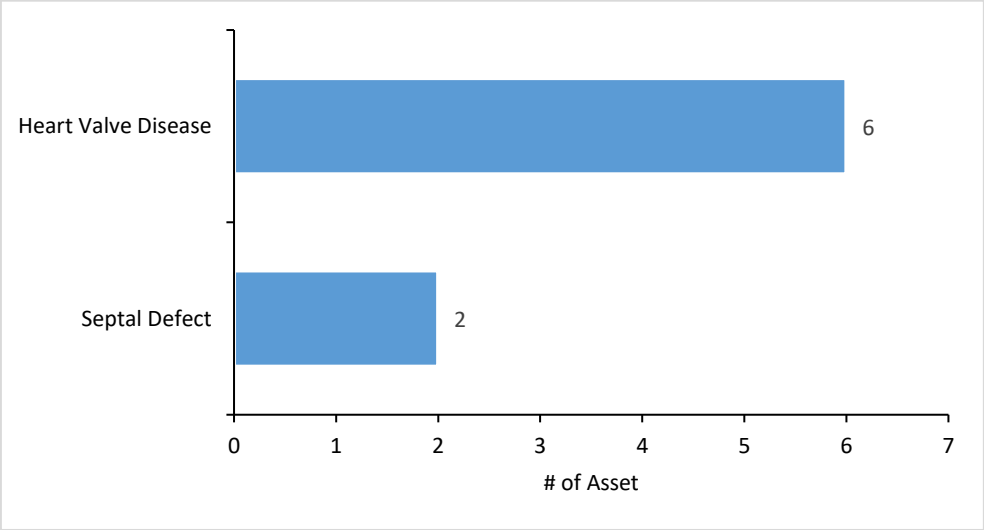


Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

The largest number of pipeline assets in dermatology are seen in wound management, followed by vascular ulcers and pressure ulcers.

Figure 18: Tissue Engineered Products – Number of Late-stage Active Pipeline Assets for Top 2 Indications in Cardiovascular Diseases



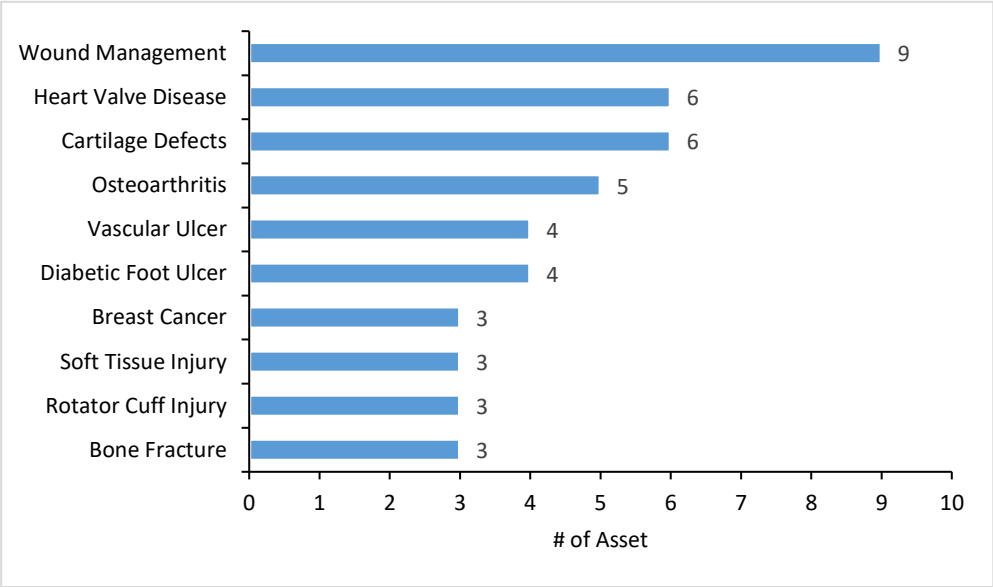
Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Among cardiovascular diseases, heart valve disease is the leading indication for product development.

2.L: Tissue Engineered Products Pipeline by Top Indications

Figure 19: Tissue Engineered Products – Number of Clinical-stage Active Pipeline Assets for Top 10 Indications



Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

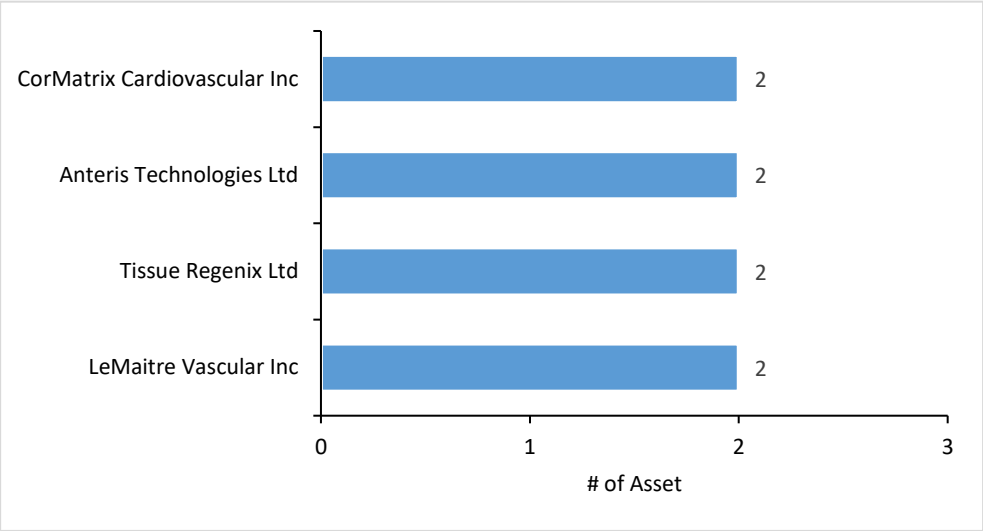
Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

The highest number of pipeline assets are seen in wound management followed by equal number of assets (six products each) for heart valve disease and cartilage defects.

Wound management includes acute wounds, burn wounds, chronic wounds, partial thickness wounds, surgical wounds and traumatic wounds. There are four assets undergoing regulatory review for wound management.

- MiMedx's EpiFix® Amniotic Membrane Allograft in Japan for burn wounds, and partial thickness wounds
- Elanix's First Cover Acute in EU for acute wounds
- Tempo's MAP Tissue Scaffold - Acute Wound in the US for acute wounds
- PolyNovo's NovoSorb® BTM - Wound Dressing in Mexico, South Korea, Kuwait, and Sri Lanka for various wounds

Figure 20: Tissue Engineered Products – Number of Clinical-stage Active Pipeline Products by Top Sponsors



Source: GlobalData; Medical Intelligence Center Drug Database [Accessed on 24/03/2021]; ClinicalTrial.gov; Company websites

Note: Clinical pipeline includes assests in clinical development and in approval process (including marketed products which are in clinical development/in approval process either for additional indication/geography); Since a single asset may be investigated for multiple indications/geographies/phases, the count of total assets could be higher than the actual number of pipeline assets

Industry-sponsored assets formed a majority of the tissue engineered products pipeline. All top industry sponsors had equal number of assets in clinical development (two each).

CorMatrix's Cor® PEDIATRIC Tricuspid ECM® Valve and Cor® TRICUSPID ECM® Valve Device are in clinical development for heart valve disease in the US.

Anteris' ADAPT® technology-based assets are undergoing regulatory review mostly for cardiovascular disease and neurological disease in emerging markets and its DurAVR™ asset category is in clinical development for aortic stenosis in the US and EU.

Tissue Regenix's Cardiopure™ asset category (Cardiopure™ - Aortic Heart Valve and Cardiopure™ - Pulmonary Heart Valve) are undergoing regulatory review in EU for aortic valve disease and pulmonary valve disease. OrthoPure® XT is under clinical development for ligament fractures in the US.

LeMaitre's CardioCel® asset category (CardioCel® - Hernia Repair, Cardiocel® - Mitral Valve Repair, Cardiocel® - Tri-Leaflet Aortic Valve Repair, Cardiocel® 3D and CardioCel® Neo) is undergoing regulatory review for cardiovascular disease and gastrointestinal diseases in many countries which are already approved in multiple countries including major markets. VascuCel® is undergoing regulatory review for carotid artery disease in China, Philippines, Taiwan, and Thailand and have already been approved in major markets.

2.M: Tissue Engineered Products Pipeline Competitive Assessment

Table 3: Tissue Engineered Products in Development

Drug Name	Company Name	Indication	Phase of Development	Geography
Acellular NAC Graft™	BioAesthetics Corp	Breast Cancer	Clinical	US
Actifit®	Orteq Sports Medicine Ltd	Meniscus Tear	Clinical	US
ADAPT®[1]	Anteris Technologies Ltd	Dural Tear; Aortic Valve Disease; Jugular Vein Distention; Cardiovascular Diseases	Clinical; In approval Process	Multiple country
Agili-C™	CartiHeal Ltd	Osteochondral Defects; Cartilage Defects	Clinical	US
Algisyl-LVR™	Lonestar Heart Inc	Chronic Heart Failure	Clinical	US
Biological Grafts	Biomatlante SA	Bone Fracture; Maxillofacial Fractures	Clinical	Europe
BioPoly® RS[2]	BioPoly RS LLC	Femoral Condyle Cartilage; Defect; Cartilage Lesions; Knee Fracture; Shoulder Fractures	Clinical	US
BioPoly® RS Partial Resurfacing Shoulder		Shoulder Fractures	Clinical	Europe; Indonesia; Malaysia; Singapore; Thailand
Bone Scaffold + ECM	Lattice Biologics Ltd	Bone Deformities	In approval Process	US
Braxon®	DECO Med Srl	Breast Deformity	Clinical	US
CardioCel®[3]	LeMaitre Vascular Inc	Congenital Heart Disease; Septal Defect; Hernia; Mitral Valve Disease; Aortic Valve Disease; Cardiovascular Diseases; Aortic Arch Syndrome; Heart Valve Disease	Clinical; In approval Process	Multiple country
Cardiopure™	Tissue Regenix Ltd	Aortic Valve Disease; Pulmonary Valve Disease	In approval Process	Europe
Cartilage Regeneration	ROKIT Healthcare Inc	Osteoarthritis; Achondroplasia	Clinical	Egypt
Cartiva® Synthetic Cartilage Implant – CMC	Cartiva Inc	Carpometacarpal Joint; Osteoarthritis	Clinical	US
Celgro® - Nerve Regeneration	Orthocell Ltd	Peripheral Nerve Injury	In approval Process	Australia
			Clinical	US; Japan
Celgro® - Tendon Regeneration	Orthocell Ltd	Tendon Injury	In approval Process	Australia; EU
			Clinical	US
CelGro® - General Surgery	Orthocell Ltd	Hernia	Clinical	Europe
CelGro® - Soft Tissue Repair	Orthocell Ltd	Soft Tissue Injury	Clinical	US
CelGro® SMRT Graft - Bone Repair	Orthocell Ltd	Bone Defects	Clinical	US; Australia
Celgro® SMRT Graft - Rotator-Cuff Tendon Repair	Orthocell Ltd	Rotator Cuff Injury	Clinical	US; EU; Australia
CGX-443	Antibe Therapeutics Inc	Maxillofacial Fractures; Bone Fracture	In approval Process	US
ChondroColl™	SurgaColl Technologies Ltd	Trauma; Osteoarthritis	In approval Process	Europe
ChondroMimetic®	Collagen Solutions	Cartilage Defects	Clinical	US, China

Drug Name	Company Name	Indication	Phase of Development	Geography
			In approval Process	Europe South Korea
		Osteoarthritis	Clinical	US, China
			In approval Process	Europe South Korea
Cor® PEDIATRIC Tricuspid ECM® Valve	CorMatrix Cardiovascular	Tricuspid Valve Disease	Clinical	US
CorMatrix Cor® TRICUSPID ECM® Valve Device	CorMatrix Cardiovascular	Tricuspid Valve Disease	Clinical	US
Cytal Wound Matrix	ACell Inc	Diabetic Foot Ulcer; Pressure Ulcer; Surgical Wounds; Traumatic Wounds; Venous Ulcers	Clinical	Multiple country
DurAVR™[4]	Anteris Technologies Ltd	Aortic Stenosis	Clinical	US, Europe
Epicel®	Vericel Corp	Burn Wounds	Clinical	China; Indonesia; Malaysia; Singapore; South Korea; Thailand
EpiFix®	MiMedx Group Inc	Venous Leg Ulcer; Partial Thickness Wounds; Diabetic Foot Ulcer; Burn Wounds	In approval Process	Japan
FibroFix™ Meniscus	Orthox Ltd	Meniscus Tear	Clinical	US
First Cover Acute	Elanix	Acute Wounds	In approval Process	Europe
Hyalofast®`	Anika Therapeutics Inc	Cartilage Defects	Clinical	US
Kerecis® Omega3 - Third-Degree Burns	Kerecis ehf	Burn Wounds	Clinical	US
MAP Tissue Scaffold - Acute Wound	Tempo Therapeutics Inc	Acute Wounds	In approval Process	US
NOVOCART® 3D	Aesculap Biologics LLC	Articular Cartilage Damage	Clinical	US
NovoSorb®[5]	PolyNovo Biomaterials Pty Ltd	Multiple indication	Clinical; In approval process	Multiple country
Ologen Biocornea	Aeon Astron Corporation	Corneal Diseases	In approval Process	Europe
OrthoPure® XT	Tissue Regenix	Ligament Fractures	Clinical	US
OTR4132MD	OTR3 SAS	Acute Ischemic Stroke	Clinical	Europe
Partial Larynx Scaffold	Videregen Ltd	Larynx Disease	Clinical	Europe
PEEK-OPTIMA™ Femoral Knee Replacement Device	Invibio Knee Ltd	Knee Fracture	Clinical	Global
RECELL®[6]	Avita Medical Inc	Vitiligo; Wounds; Surgical Wounds; Soft Tissue Injury; Traumatic Wounds	Clinical	US
		Vitiligo	In approval process	Japan
REGENERA Breast Implant	Tensive SRL	Breast Cancer	Clinical	Europe
RevaFlex™	Isto Biologics	Knee Arthritis; Cartilage Defects	Clinical	US
TeVido Breast Graft	TeVido BioDevices	Breast Cancer	Clinical	US

Drug Name	Company Name	Indication	Phase of Development	Geography
Transpose®[7]	InGeneron Inc	Facet Joint Syndrome; Rotator Cuff Injury; Venous Ulcers; Wrist Osteoarthritis	Clinical	US
VascuCel®	LeMaitre Vascular Inc	Carotid Artery Disease	In approval Process	China; Philippines; Taiwan; Thailand
Vergenix™[8]	Collplant Biotechnologies Ltd	Multiple indication	In approval Process; Clinical	Multiple country
3D Printing Scaffold	Univ. of Arizona	Bone Fracture	Clinical	Global

1: ADAPT® - Dura Mater Repair; ADAPT® - Half Pipe Conduit; ADAPT® - Jugular Vein; ADAPT® - Pediatric Leaflets; ADAPT® – Samurai; 2: BioPoly® RS Partial Resurfacing Femoral System; Biopoly® RS Partial Resurfacing Knee; BioPoly® RS Partial Resurfacing Patella; BioPoly® RS Partial Resurfacing Trochlea System 3: CardioCel®; CardioCel® - Hernia Repair; Cardiocel® - Mitral Valve Repair; Cardiocel® - Tri-Leaflet Aortic Valve Repair; Cardiocel® 3D; CardioCel® 3D Stage 1 Arch; CardioCel® Neo;4: DurAVR™ Heart Valve; DurAVR™ Leaflet Repair (RP); 5: Novosorb® - Bladder Sling; NovoSorb® - Breast Reconstruction; NovoSorb® BTM - Full Thickness Burn; Novosorb® BTM - Wound Dressing; 6: RECELL® - Soft Tissue Reconstruction; RECELL® - Trauma Wounds; RECELL® System – Vitiligo; 7: Transpose® RT System - Facet Joint Syndrome; Transpose® RT System - Rotator Cuff Tendinopathy; Transpose® RT System - Venous Stasis Ulcers; Transpose® RT System - Wrist Osteoarthritis; 8: Vergenix™ STR; Vergenix™ STR - Anterior Cruciate Ligament

Section 3: Estimated Likelihood and Timelines of Potential Entry of CGTs in Australia

3.A: CGT Late-stage Pipeline Assets Trials in the US and Australia

Analysis of CGT products likely to enter the Australian market in the next five years and the timelines for entry were undertaken. Clinical trials in Australia were one of parameter used to estimate products likelihood to enter the Australian market and below tables provides product clinical trials availability in the US and Australia.

Table 4: Cell Therapy Late-stage Pipeline Assets

Drug Name	Company Name	Indications	Phase of Development	Trials in US and Australia	
				US	Australia
DCVax-L	Northwest Biotherapeutics	Glioblastoma Multiforme	Phase III	✓	X
Elivaldogene autotemcel	Bluebird Bio	Adrenoleukodystrophy	Phase III	✓	✓
Emiplacel	Pluristem Therapeutics Inc	Muscle Injury	Phase III	✓	X
Iltamiocel	Cook MyoSite Inc	Female Stress Urinary Incontinence	Phase III	✓	X
MPC-150IM	Mesoblast	Chronic heart failure due to LV systolic dysfunction	Phase III	✓	X
MyoCell®	U.S. Stem Cell Inc	Congestive Heart Failure	Phase II/III	✓	X
NurOwn®	BrainStorm Cell Therapeutics Inc	Amyotrophic Lateral Sclerosis	Phase III	✓	X
Omidubicel	Gamida Cell Ltd	Acute Lymphocytic Leukemia; Chronic Myelocytic Leukemia; Myelodysplastic Syndrome	Phase III	✓	X
Remestemcel-L	Mesoblast	COVID-19 Acute Respiratory Distress Syndrome	Phase III	✓	X

Drug Name	Company Name	Indications	Phase of Development	Trials in US and Australia	
				US	Australia
RVT-802	Enzyvant Sciences	DiGeorge Syndrome	Pre-registration	✓	X
Stapuldencel-T	Sotio AS	Metastatic Hormone Refractory Prostate Cancer	Phase III	✓	X
StrataGraft®	Mallinckrodt Plc	Burn	Marketed	✓	X
Tabelecleucel	Atara Biotherapeutics	Post-Transplant Lymphoproliferative Disorder	Phase III	✓	✓

Table 5: Gene Therapy Late-stage Pipeline Assets

Drug Name	Company Name	Indications	Phase of Development	Trials in US and Australia	
				US	Australia
Alicaforsen sodium	Atlantic Healthcare	Pouchitis	Phase III	✓	X
Beremagene geperpavec	Krystal Biotech	Dystrophic Epidermolysis Bullosa	Phase III	✓	X
Casimersen	Sarepta Therapeutics Inc	Duchenne muscular dystrophy	Marketed	✓	✓
Donaperminogene seltoplasmid	Helixmith Co Ltd	Diabetic Neuropathic Pain	Phase III	✓	X
Etranacogene dezaparvovec	UniQure NV	Hemophilia B	Phase III	✓	X
Fitusiran	Sanofi	Hemophilia A; Hemophilia B	Phase III	✓	✓
Givosiran	Alnylam Pharmaceuticals Inc	Acute Intermittent Porphyria	Marketed	✓	✓
Golodirsen	Sarepta Therapeutics Inc	Duchenne muscular dystrophy	Marketed	✓	X
Inclisiran	Novartis	Atherosclerosis	Pre-Registration	✓	X
Lumasiran	Alnylam Pharmaceuticals Inc	Primary Hyperoxaluria Type I	Marketed	✓	X
QPI-1007	Quark Pharmaceuticals Inc	Non-Arteritic Anterior Ischemic Optic Neuropathy	Phase II/III	✓	✓
Timrepigene emparvovec	Biogen Inc	Choroideremia	Phase III	✓	X
Tofersen sodium	Biogen Inc	Amyotrophic Lateral Sclerosis	Phase III	✓	✓
Valoctocogene roxaparvovec	BioMarin Pharmaceutical Inc	Hemophilia A	Pre-Registration	✓	✓
Viltolarsen	NS Pharma Inc	Duchenne muscular dystrophy	Marketed	✓	X
Vutrisiran	Alnylam	Familial Amyloid Neuropathies	Pre-registration	✓	✓

Table 6: Gene Modified Cell Therapy Late-stage Pipeline Assets

Drug Name	Company Name	Indications	Phase of Development	Trials in US and Australia	
				US	Australia
Ciltacabtagene autoleucel	Legend Biotech Corp	Relapsed and Refractory Multiple Myeloma	Pre-Registration	✓	✓
Idecabtagene vicleucel	Bristol-Myers Squibb	Relapsed and Refractory Multiple Myeloma	Marketed	✓	X
Lisocabtagene maraleucel	Juno Therapeutics	Diffuse Large B-Cell Lymphoma; Follicular Lymphoma; Non-Hodgkin Lymphoma; Primary Mediastinal B-Cell Lymphoma; Relapsed or Refractory Large B-cell Lymphoma	Marketed	✓	X
Tonogenchoncel-L	Kolon TissueGene	Knee Osteoarthritis	Phase III	✓	X

3.B: CGT Late-stage Pipeline Assets Ranking and Estimate of Approval in Australia

Analysis of CGT products likely to enter the Australian market in the next five years and the timelines for entry were undertaken. Likelihood to enter the Australian market was based on estimates of the likelihood of approval, companies' presence in Australia and clinical trials of the product in Australia. Timelines for entry were based on RM approved products average timings of phase III completion, phase III to regulatory filing, filing to approval and average approval gap US vs Australia.

Based on these estimates the following products were considered to be the most likely to enter the Australian market.

- Cell Therapy: StrataGraft® (Mallinckrodt Plc) and RVT-802 (Enzyvant Sciences Ltd) in 2023; Omidubicel (Gamida Cell Ltd) and Stapuldencel-T (Sotio AS) in 2024
- Gene Therapy: Vutrisiran (Alnylam Pharmaceuticals Inc) in 2023; Fitusiran (Sanofi) and Etranacogene dezaparvovec (UniQure NV) in 2025
- Gene Modified Cell Therapy: Lisocabtagene maraleucel (Juno Therapeutics Inc) in 2023; Ciltacabtagene autoleucel (Legend Biotech Corp) in 2024

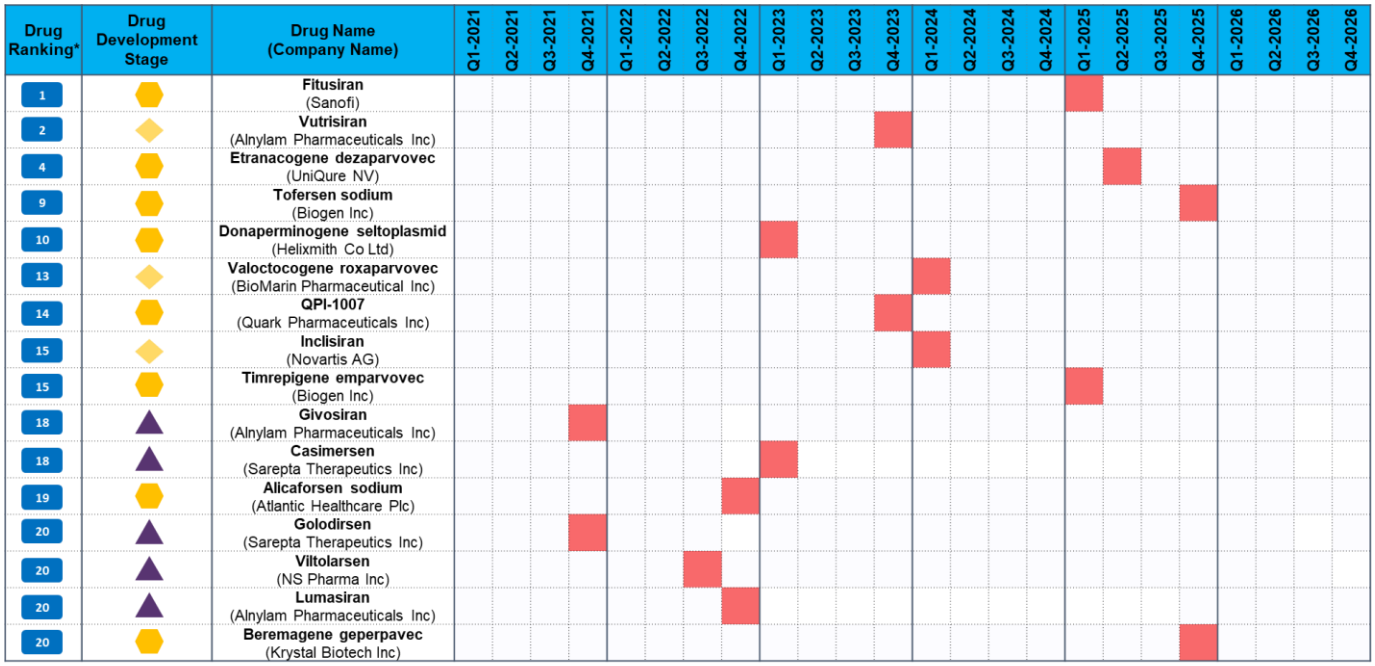
Table 7: Cell Therapy Late-stage Pipeline Assets Approval Estimate

Drug Ranking*	Drug Development Stage	Drug Name (Company Name)	Q1-2021	Q2-2021	Q3-2021	Q4-2021	Q1-2022	Q2-2022	Q3-2022	Q4-2022	Q1-2023	Q2-2023	Q3-2023	Q4-2023	Q1-2024	Q2-2024	Q3-2024	Q4-2024	Q1-2025	Q2-2025	Q3-2025	Q4-2025	Q1-2026	Q2-2026	Q3-2026	Q4-2026
4	▲	**StrataGraft®** (Mallinckrodt Plc)																								
4	⬢	**Omidubicel** (Gamida Cell Ltd)																								
4	⬢	**Stapuldencel-T** (Sotio AS)																								
5	◆	**RVT-802** (Enzyvant Sciences Ltd)																								
14	⬢	**Tabelecleucel** (Atara Biotherapeutics Inc)																								
17	⬢	**DCVax-L** (Northwest Biotherapeutics Inc)																								
17	⬢	**NurOwn®** (BrainStorm Cell Therapeutics Inc)																								
18	⬢	**Remestemcel-L** (Mesoblast Ltd)																								
18	⬢	**Elivaldogene autotemcel** (bluebird bio Inc)																								
19	⬢	**MyoCell®** (U.S. Stem Cell Inc)																								
19	⬢	**Iltamiocel** (Cook MyoSite Inc)																								
19	⬢	**Emiplacel** (Pluristem Therapeutics Inc)																								
20	⬢	**MPC-150IM** (Mesoblast Ltd)																								

▲ Marketed ◆ Pre-Registration ⬢ Phase III

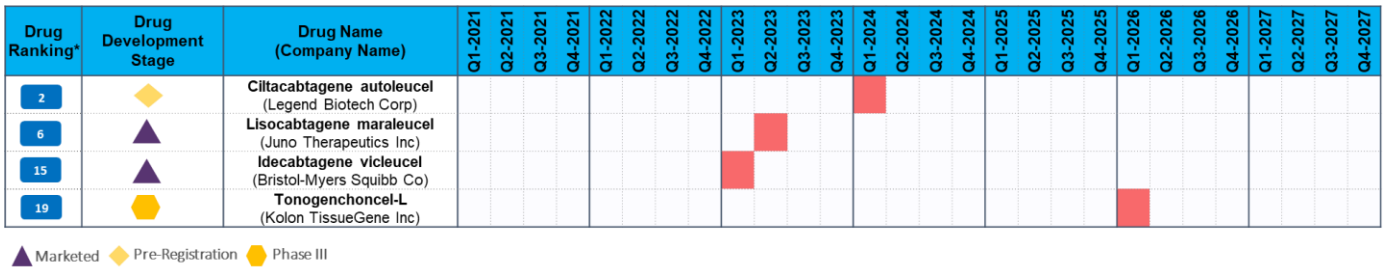
Note: Assets shown in the table represents those which are estimated to be approved in the next five years. The actual approval date may vary depending on multiple factors including but not limited to trial results, company's development plans and regulatory decisions. *Ranking indicates higher probability of approval (based on factors such as drug likelihood of approval, company's presence in Australia and clinical trials in Australia) and it is independent of the approval timelines; Higher ranking indicates higher probability of approval (1=high; 20=low). Phase III includes assets which are in development in Phase II/III, Phase I/II/III, Phase III and Phase III (planned).

Table 8: Gene Therapy Late-stage Pipeline Assets Approval Estimate



Note: Assets shown in the table represents those which are estimated to be approved in the next five years. The actual approval date may vary depending on multiple factors including but not limited to trial results, company's development plans and regulatory decisions. *Ranking indicates higher probability of approval (based on factors such as drug likelihood of approval, company's presence in Australia and clinical trials in Australia) and it is independent of the approval timelines; Higher ranking indicates higher probability of approval (1=high; 20=low). Phase III includes assets which are in development in Phase II/III, Phase I/II/III, Phase III and Phase III (planned).

Table 9: Gene Modified Cell Therapy Late-stage Pipeline Assets

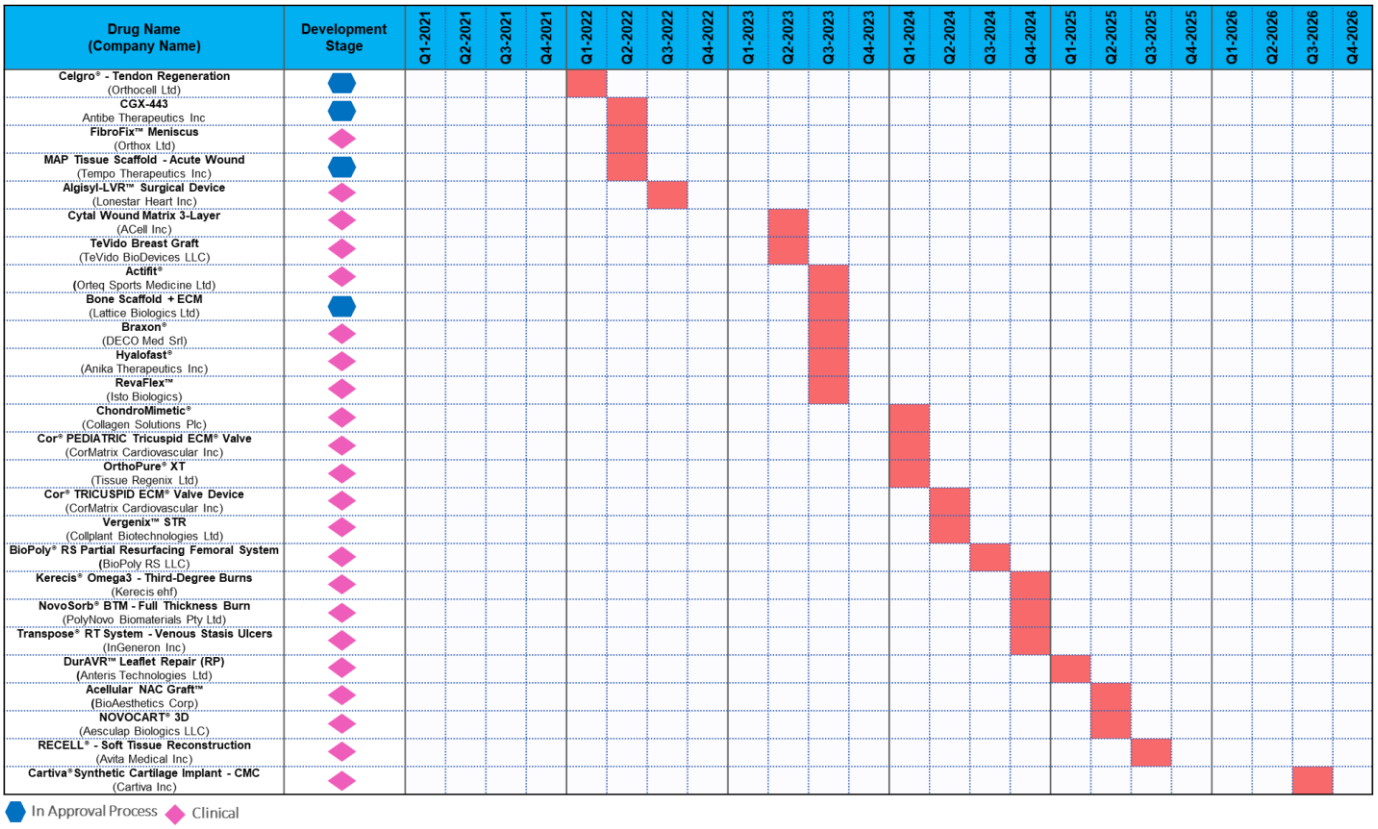


Note: Assets shown in the table represents those which are estimated to be approved in the next five years. The actual approval date may vary depending on multiple factors including but not limited to trial results, company's development plans and regulatory decisions. *Ranking indicates higher probability of approval (based on factors such as drug likelihood of approval, company's presence in Australia and clinical trials in Australia) and it is independent of the approval timelines; Higher ranking indicates higher probability of approval (1=high; 20=low). Phase III includes assets which are in development in Phase II/III, Phase I/II/III, Phase III and Phase III (planned).

Section 4: Estimated Likelihood and Timelines of Potential Entry of Tissue Engineered Products in Australia

Table 10: Tissue Engineered Products Approval Estimate

Estimates of potential entry in Australia of tissue engineered products were calculated using estimated approval date for the product in the US and average approval gap US vs Australia. The three tissue engineered products likely to enter the market in Australia in the next 12 months are CelGro® - Tendon Regeneration *(Orthocell Ltd)*, CGX-443 *(Antibe Therapeutics Inc)* and MAP Tissue Scaffold - Acute Wound *(Tempo Therapeutics Inc).*



Note: Assets shown in the table represents those which are estimated to be approved in the next five years. The actual approval date may vary depending on multiple factors including but not limited to trial results, company's development plans and regulatory decisions.

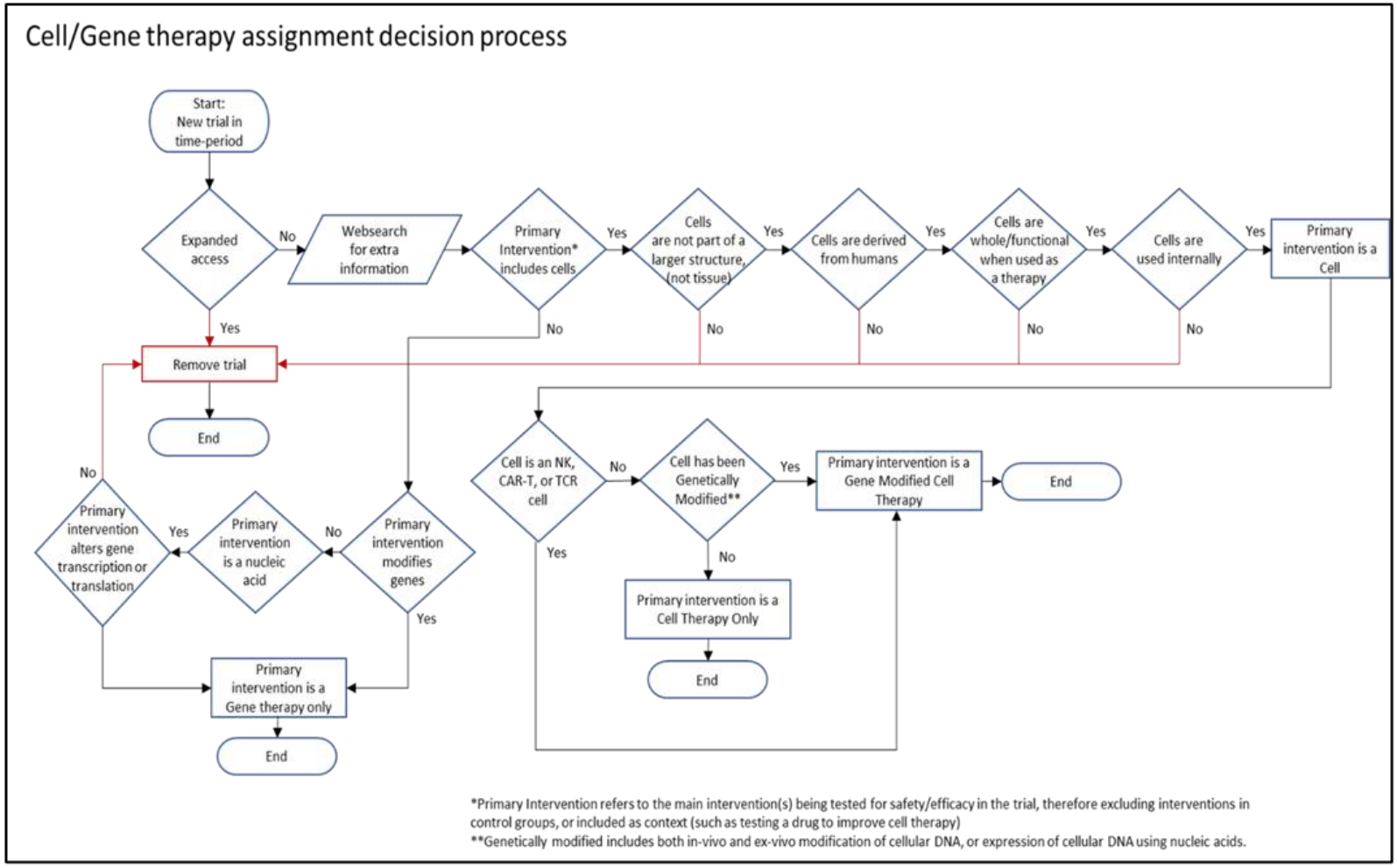
Methodology

RM pipeline data are extracted from GlobalData's (GD) proprietary *Pharma Intelligence Center: Drug Database and Medical Intelligence Center: Drug Trials Database* on 24 March 2021 with the following scope:

- **Molecule Type:** Cell therapy; gene therapy; gene modified cell therapy; antisense RNAi oligonucleotide; antisense oligonucleotide.
- **Inclusion:** Includes gene therapies, cellular therapies including (CAR-T, CAR-NK etc), stem cell therapies, other cell therapies utilising differentiated cell types, direct cell reprogramming, tissue engineering, biomaterials, and 3D bioprinting.
- **Trial Phases:** Pre-registration; Filing rejected/withdrawn; Phase III (also include Phase II/III and Phase I/II/III); Marketed.
- **Therapy Area:** All.
- **Target Geography:** Global.
- **Study Period:** All regenerative medicines pipeline products that could potentially enter Australia in the next five years (January 2026).
- **Exclusion:** Transplants, including bone marrow transplants or heart transplants; Blue-sky research into regenerative medicine; Pre-clinical; Medical devices (other than tissue scaffolds).

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 Pipeline Analysis and its Definitions:

1. Drug Name: Includes generic name or brand of a drug. If these are not available for a pipeline drug, the developer lab code has been used and in case drug lab code is not available, a descriptive name based on molecule type and indication(s) has been used.
2. Generic Name: A standardised non-proprietary designation for a drug. Novel pharmaceuticals must be submitted to the appropriate organisation for generic name designation in each country which the manufacturer seeks market approval. Pharma Intelligence Center Drugs refer to the United States Adopted Name (USAN), if available, and the International Non-proprietary Name (INN) if it is not. For Drugs, which do not have approved generic names, this field is blank.
3. Brand Name: It is the proprietary, trademark-protected name of a marketed drug.
4. Alias Name: The names besides the generic and brand names used to identify a drug during development.
5. Company Name: Company name refers to details the registered legal entity name of a company.
6. Indication: Disease or condition for which the drug has or is seeking approval to treat, prevent, cure, or mitigate.
7. Therapy Area: Disease or condition for which the drug has or is seeking approval to treat, prevent, cure, or mitigate.
8. Development Stage: Development stage is the current stage of development or marketing status for a drug.
    a. Pharmaceuticals
        i. Phase I: Phase I trials are conducted to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients. A Drug will be considered to be in Phase I Drug Stage when it has at least one development program for which a patient has been initiated into a Phase I clinical trial.
        ii. Phase II: Phase II trials include controlled clinical studies conducted to evaluate effectiveness of the drug for a particular indication or indications in patients with the same disease/s. The trials are conducted in several hundred subjects, mostly randomized, placebo-controlled, sometimes compared with the active comparator and are often blinded. These are also to assess common short-term side effects and risks. A Drug will be considered to be in Phase II Drug Stage when it has at least one development program for which a patient has been initiated for at least one Phase II or Phase I/II clinical trial.
        iii. Phase III: Phase III trials are expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained. Phase III studies are usually randomised with double blind testing in several hundred to several thousand patients. The large-scale testing in Phase III trials provides a more thorough understanding of the efficacy of the drug and the range of possible adverse reactions to assess risk-benefit profile for the investigational drug. A Drug will be considered to be in Phase III Drug Stage when it has at least one development program for which a patient has been initiated for at least one Phase III or Phase II/III clinical trial.
        iv. Pre-registration: In the pre-registration stage, all the necessary clinical trials have been completed and the drug is waiting for registration or approval for use by a governing body.
        v. Marketed/pipeline: Already approved and on-market assets in pipeline for additional indication/geography.
    b. Medical
        i. Clinical: Indicates that the pipeline medical device is in clinical studies to validate its safety and efficacy on subjects (humans), based on trials announcements on major registries and by developers. Like pharma pipeline in medical there is no further segment by phase is available.
        ii. In Approval Process: The medical device is “In approval process” in case it is filed for approval with the regulatory agency, based on developer statements only, or government announcements.
        iii. Marketed/pipeline: Already approved and on-market assets in pipeline for additional indication/geography.

9. Drug Geography: It is the geographical region or country that the drug is marketed in or for which the drug is being developed for approval:
    a. The pipeline drug geography as “Global” is a geographical placeholder, which is tagged for pipeline drugs where the company or institution have not yet specified the exact geographical region or country for which they intend to pursue market approval.
10. Product Geography: It is the geographical region or country that the drug is marketed in or for which the drug is being developed for approval.
11. Gene Therapy Vector: Captured as available in GD’s Pharma Intelligence Center.
12. Approval Date: The first date when a drug has been approved by the regulatory authority for use; "E" indicates estimated approval date.
13. Launch Date: The date of product launch; "E" indicates estimated launch date.
14. Designation Type: The regulatory designation assigned to a drug for a specific regulatory designation type pathway intended for regulatory authority approval by the country or region associated. This information is captured as available in Pharma Intelligence Center for US, EU and Japan. Wherever it is available marked as “Yes” and if not available marked as “NA”.
15. Agreement Date: Date on which the deal is finalized and includes deals from 2015 onward.
16. Deal Type: Identifies the various types of deals that have taken place.
17. Acquirers/Investors/Surviving Entity/Licensee/Partners/Grantor/Client: These are the funding side of a deal. An acquirer is a company that acquires rights to another company or business relationship through a deal. An investor is any person or other entity (such as a firm or mutual fund) who commits capital with the expectation of receiving financial returns. A licensee is any business, organisation, or individual that has been granted legal permission by another entity to engage in an activity.
18. Issuer/Licensor/Target/Vendor/Grantee/Service Provider: Within a deal, the Issuer/Licensor/Target are the companies that have issued their own securities, granted a license or were the target entity in a mergers and acquisitions attempt.
19. Drug Description: Provide drug detailed information.
20. Drug-Specific likelihood of approval (LoA): It is the probability of a drug being approved rather than failing at a stage prior to approval in the US.
21. Rare Disease: In the US, a rare disease is defined as a condition that affects fewer than 200,000 people in the US.
22. Note: Some tissue engineered products had multiple entries with different indications, in this analysis those products had been considered as one product (example: ADAPT® is available as ADAPT® - Dura Mater Repair, ADAPT® - Half Pipe Conduit, ADAPT® - Jugular Vein, ADAPT® - Paediatric Leaflets, ADAPT® – Samurai, hence we had considered all of them under ADAPT® as one product); Oncolytic virus has not been considered in CGT pipeline analysis.

Estimated Likelihood and Timelines of Potential Entry of CGTs in Australia

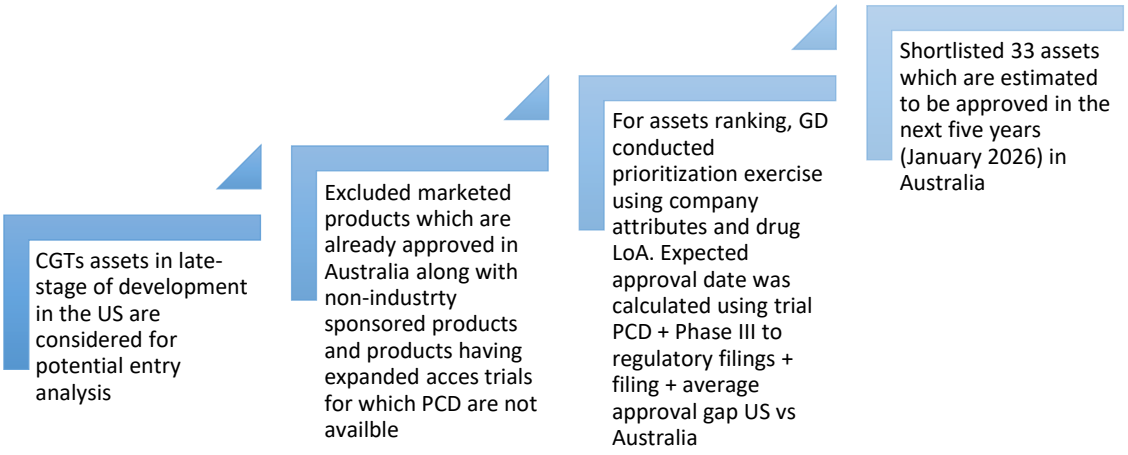
GD provided analysis for ranking* the late-stage CGTs assets and estimated their potential entry in Australia. Asset ranking was based on broad two parameters and its sub-parameters:

1. Likelihood of approval
   - Drug-Specific LoA.
2. Company attributes:
   - Multinational company;
   - Previously commercialised product in Australia:
   - Clinical trials in Australia.

Each parameter and its sub-parameters weightage and scores had been provided in below tables.

Estimated potential entry in Australia is calculated using trial primary completion date (PCD) + Phase III to regulatory filings + filing + average approval gap US vs Australia

GD adopted following approach for assets ranking and estimated potential entry in Australia:



*Ranking indicates higher probability of approval (based on drug and market attributes) and it is independent of the approval timelines

Asset Ranking Parameters Weightage	
Drug Likelihood of Approval (LoA)	60%
Company Attributes	40%
• Multinational company	20%
• Previously commercialised product in Australia	50%
• Clinical trials in Australia	30%

Asset Ranking Parameters Score		
Drug Likelihood of Approval (LoA)		
Drug-Specific LoA (%)	0	0
Drug-Specific LoA (%)	1-30%	1
Drug-Specific LoA (%)	31%-50%	3
Drug-Specific LoA (%)	>50%	5
Company (Market) Attributes		
• Multinational company	Yes	5
	No	1
• Previously commercialised product in Australia	Yes	5
	No	1
• Clinical trials in Australia	Yes	5
	No	1

Score definition: 5= High; 3= Medium; 1=Low

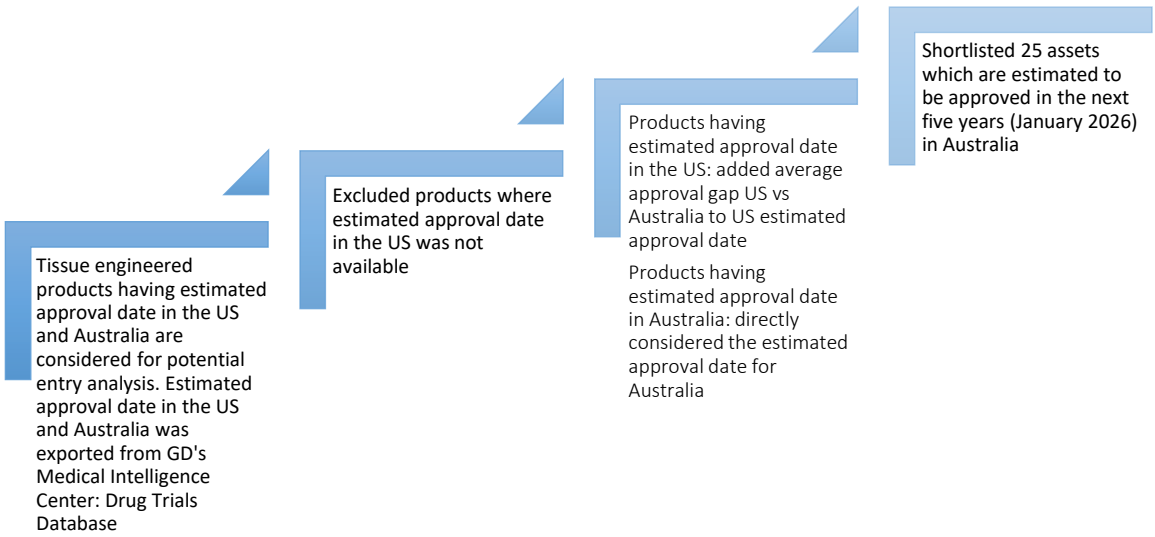
Timelines Estimates (US)	Months	Days
Phase II completion to Phase III initiation	9	270
Average Phase III completion	28	840
Phase III PCD date to regulatory filings	20.5	615
FDA filing to approval	7.2	216
Average approval gap US vs Australia	24.4	732

Source for timelines estimates: Timelines estimates are based on GD's internal analysis along with RM approved products average phase III completion, Phase III to regulatory filing, filing to approval and average approval gap US vs Australia

Estimated Likelihood and Timelines of Potential Entry of Tissue Engineered Products in Australia

GD provided tissue engineered products potential entry estimate in Australia and adopted following approach.

Estimated potential entry in Australia is calculated using average approval gap US vs Australia



Average approval gap considered US vs Australia: 11.2 months (336 days) based on GD's internal analysis.

References

GlobalData's Pharma Intelligence Center and Medical Intelligence Center: Drug Database identifies pipeline assets from various sources, in addition to company websites other sources includes journals, grants, publications, press releases, investor presentations, news, deals, conferences, filings, regulatory and financial registries and databases including clinicaltrials.gov.

1. Pharma Intelligence Center and Medical Intelligence Center: Drug Database
2. Clinical Trial.gov
3. Regulator websites – The U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)
4. Company websites
5. FDA approves StrataGraft for the treatment of adults with thermal burns
6. Sarepta Therapeutics announces FDA approval of AMONDYS 45™ (casimersen) injection for the treatment of Duchenne muscular dystrophy (DMD) in patients amenable to skipping Exon 45
7. FDA approves first cell-based gene therapy for adult patients with multiple myeloma
8. Mesoblast hit by FDA rejection, request to run another trial
9. Rejected by the FDA, Ionis and Akcea's Waylivra finds new life with EU approval
10. A Brief Introduction to CAR T-Cell Therapy Part 1: Background & Current Development Landscape
11. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS
12. Takeda and Arrowhead Collaborate to Co-Develop and Co-Commercialize ARO-AAT for Alpha-1 Antitrypsin-Associated Liver Disease
13. Novartis secures exclusive rights for potential acute respiratory distress syndrome cell therapy
14. Alnylam and Dicerna Form RNAi Therapeutics Collaboration on Alpha-1 Antitrypsin Deficiency-Associated Liver Disease and Complete Cross-License Agreement for Primary Hyperoxaluria Programs
15. Novartis enters agreement to acquire AveXis Inc. for USD 8.7 bn to transform care in SMA and expand position as a gene therapy and Neuroscience leader
16. Gilead Sciences to Acquire Kite Pharma for $11.9 Billion
17. Musculoskeletal conditions
18. The National Organization for Rare Disorders

Appendices

Appendix 1. RM Category Definitions

Table 11: Alliance for Regenerative Medicine (ARM) Therapy Categories used in this Pipeline Analysis

ARM 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 are available to the patient immediately at the time of need. Many cell-based therapies currently being developed utilize human induced pluripotent stem cells (hiPSCs). Unlike pluripotent human embryonic stem cells (hESCs), these are adult cells that have been genetically reprogrammed to a pluripotent state, and therefore are capable of becoming one of many types of cells of the adult body. This technology may enable the development of an unlimited supply of specific types of human cells needed for therapeutic purposes.	- 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, bone, and cartilage) - Lymphocytes - Dendritic cells - Pancreatic islet cells - Cytotoxic T Lymphocyte - Embryonic - Natural killer cell - Pluripotent stem cell - Regulatory T Cell - TCR - Tumor Infiltrating Lymphocyte - Vaccine; δT cell - Other Stem Cell; Other Cell
Gene Therapy	Gene therapy seeks to modify, delete, 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 gene into the body in order to fight disease. Gene therapy may be performed in vivo, in which a gene is directly 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 patient. Typically, gene therapy developers introduce new genes into patient cells, or correct genetic codes, 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	- 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)

ARM Categories of Regenerative Medicine*	Definitions	Examples
	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 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.	- Nucleases such as Cas9 and Cas 12a that derive from the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas) - 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 utilize any of a number of potential materials, from naturally occurring proteins to biocompatible synthetic polymers. Certain tissue engineering therapies may utilize 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.

Appendix 2. RM Marketed Products and Companies

Table 12: CGT Marketed Products and Companies

Product Name	Brand Name	Company Name
AstroStem	AstroStem®	Biostar Stem Cell Research Institute
Autologous cultured cartilage	JACC®	Fujifilm Corp
Axicabtagene ciloleucel	Yescarta®	Gilead Sciences
Beperminogene perplasmid	Collategene®	Mitsubishi Tanabe Pharma
Betibeglogene autotemcel	Zynteglo®	Bluebird Bio
Brexucabtagene autoleucel	Tecartus®	Gilead Sciences
Carticel	Carticel®	Vericel Corp
Casimersen	Amondys 45™	Sarepta Therapeutics
Chondrosphere	Spherox®	Co.don AG
Darvadstrocel	Alofisel®	Takeda Pharmaceutical Company Limited
DCVax-L	DCVax-L®	Northwest Biotherapeutics
Eteplirsen	Exondys 51®	Sarepta Therapeutics
Gintuit	Apligraf®	Organogenesis
Givosiran	Givlaari®	Alnylam
Golodirsen	Vyondys 53™	Sarepta Therapeutics
HeartSheet	HeartSheet®	Terumo Corp
Holoclar	Holoclar®	Chiesi Farmaceutici
Idecabtagene vicleucel	Abecma®	Bristol-Myers Squibb
Inclisiran	Leqvio®	Novartis
Inotersen sodium	Tegsedi®	Akcea Therapeutics Inc
Jace	Jace®	Japan Tissue Engineering Co Ltd
Atidarsagene autotemcel	Libmeldy™	Orchard Therapeutics
Lisocabtagene maraleucel	Breyanzi®	Bristol-Myers Squibb
Lumasiran	Oxlumo™	Alnylam
Maci	Maci®	Vericel Corp
Nepic	Nepic®	Japan Tissue Engineering Co Ltd
Nusinersen	Spinraza®	Biogen Inc
Onasemnogene abeparvovec	Zolgensma®	Novartis
Patisiran	Onpattro®	Alnylam
Remestemcel-L	Temcell®	JCR Pharmaceuticals Co Ltd
Sipuleucel-T	Provenge®	Dendreon Pharmaceuticals
Stemirac	Stemirac®	Nipro Corp
StrataGraft	StrataGraft®	Mallinckrodt Plc
Strimvelis	Strimvelis®	Orchard Therapeutics
Talimogene laherparepvec	Imlygic®	Amgen

Product Name	Brand Name	Company Name
Tisagenlecleucel	Kymriah®	Novartis
Viltolarsen	Viltepso®	NS Pharma Inc
Volanesorsen sodium	Waylivra®	Akcea Therapeutics Inc
Voretigene neparvovec	Luxturna®	Novartis

Table 13: Tissue Engineered Marketed Products and Companies

Product Name	Company Name
Actifit	Orteq Sports Medicine Ltd
Actifuse Shape	Baxter International Inc
ADAPT products	Anteris Technologies Ltd
Agili-C Cylindrical Implant	CartiHeal Ltd
Algisyl-LVR Surgical Device	Lonestar Heart Inc
Alloderm Select	Allergan Ltd
AUGMENT Bone Graft	Wright Medical Group NV
Aurix System	Nuo Therapeutics Inc
BioDFence	BioD LLC
BioPoly RS Partial Resurfacing products	BioPoly RS LLC
BonAlive Granules	BonAlive Biomaterials Ltd.
Braxon	DECO Med Srl
Bridge-Enhanced ACL Repair Implant	Miach Orthopaedics Inc
BST-CarGel	Smith & Nephew Plc
CardioCel products	LeMaitre Vascular Inc
Cartiva Synthetic Cartilage Implant - CMC	Cartiva Inc
Celgro products	Orthocell Ltd
ChondroMimetic	Collagen Solutions Plc
Collage Osteoconductive Scaffold	Orthofix Inc
CorMatrix products	CorMatrix Cardiovascular Inc
Cytal Wound Matrix products	ACell Inc
Dermagraft - Diabetic Foot Ulcer	Organogenesis Inc
DermaPure	Tissue Regenix Ltd
Epicel	Vericel Corp
EpiFix Amniotic Membrane Allograft	MiMedx Group Inc
FibroFix Meniscus	Orthox Ltd
Gentrix Surgical Matrix Hiatal	ACell Inc
HairWave	Indiba SA
Hyalofast	Anika Therapeutics Inc
Hyalograft 3D Autograft	Anika Therapeutics Inc

Product Name	Company Name
INFUSE Bone Graft	Medtronic Plc
INSTRUCT	CellCoTec
KAINOS+	Signus Medizintechnik GmbH
LifeCell Tissue Matrix	Allergan Ltd
MatriStem Pelvic Floor Matrix	ACell Inc
MIRODERM	Miromatrix Medical Inc
NOVOCART 3D	Aesculap Biologics LLC
NovoSorb products	PolyNovo Biomaterials Pty Ltd
Omnigraft	Integra LifeSciences Holdings Corp
Orthopure XT	Tissue Regenix Ltd
Osteomatrix+	Bioventus Inc
Osteomesh	Osteopore International Pte Ltd
Osteoplug	Osteopore International Pte Ltd
OsteoTE	PolarityTE Inc
RECELL products	Avita Medical Inc
ReGenerCel	Avita Medical Inc
ReNovaCell	Avita Medical Inc
SaluCartilage	SaluMedica LLC
SkinTE	PolarityTE Inc
STR GRAFT	Biorez Inc
Tornier BioFiber Scaffold	Tornier Inc
Transcyte	Organogenesis Inc
Transpose RT System products	InGeneron Inc
VascuCel	LeMaitre Vascular Inc
Vergenix products	Collplant Biotechnologies Ltd

Appendix 3. Late-stage Assets for Rare Diseases

Table 14: CGT Late-stage Pipeline Assets for Rare Diseases

Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Axicabtagene ciloleucel	Gilead Sciences Inc	Follicular Lymphoma	Oncology	Pre-Registration	US
Cellm-001	Cell Medicine Cooperation	Glioblastoma	Oncology	Phase III	Japan
Cellular Immunotherapy for Glioblastoma Multiforme	Safe Save Medical Cell Sciences & Technology Co Ltd	Glioblastoma	Oncology	Phase III	Taiwan
Cellular Immunotherapy for Glioblastoma Multiforme	Oslo University Hospital	Glioblastoma	Oncology	Phase II/III	Norway

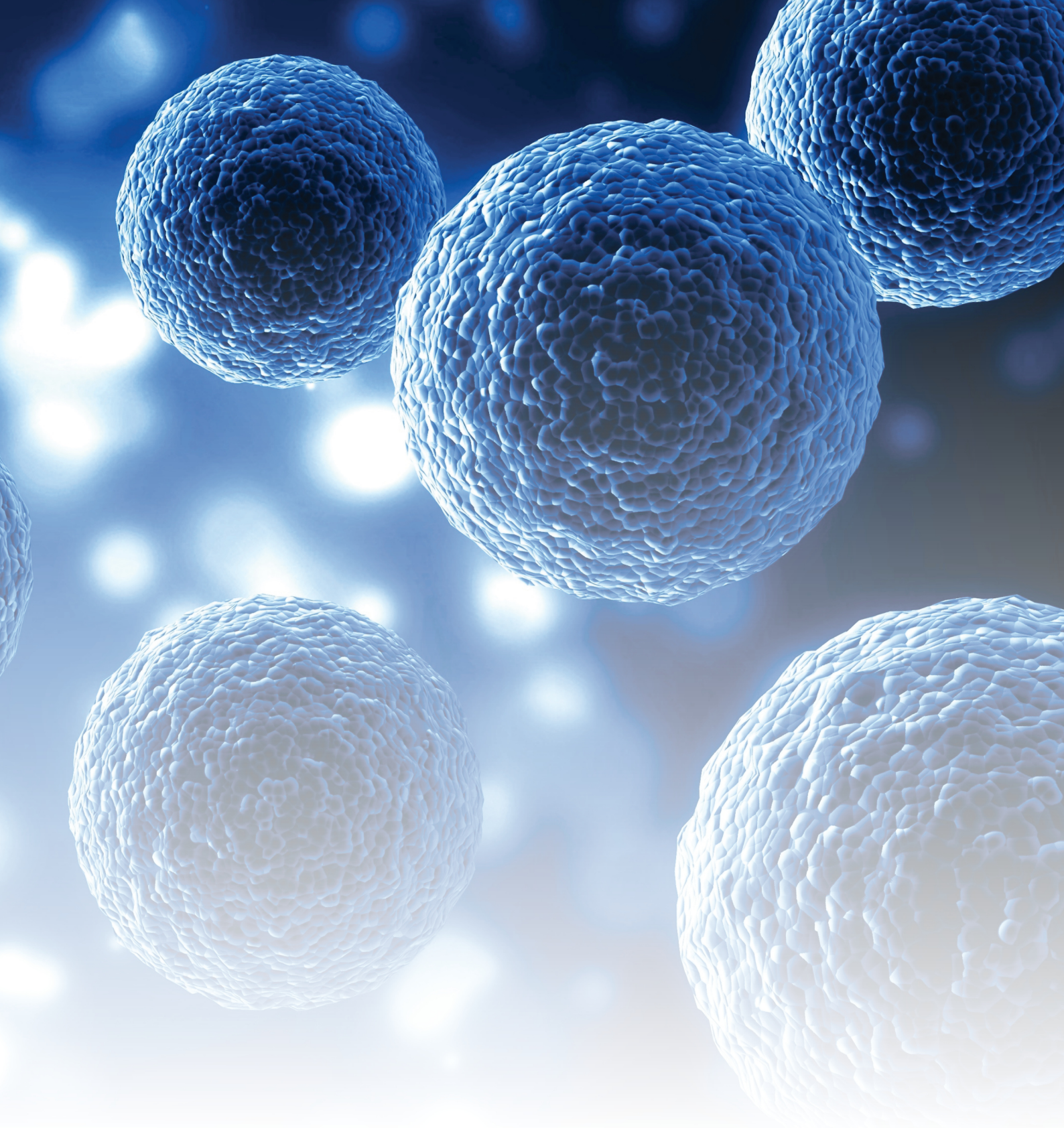
Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Cellular Immunotherapy for Hepatocellular Carcinoma	The General Hospital of the People's Liberation Army	Hepatocellular Carcinoma	Oncology	Phase II/III	China
Cellular Immunotherapy for Hepatocellular Carcinoma and Non-Small Cell Lung Cancer	Ivy Life Sciences Co Ltd	Hepatocellular Carcinoma	Oncology	Phase II/III	Taiwan
Cellular Immunotherapy to Target Melan-A, MAGE-3 and Survivin for Melanoma and Uveal Melanoma	Universitatsklinikum Erlangen	Uveal Melanoma	Oncology	Phase III	Germany
Ciltacabtagene autoleucel	Legend Biotech Corp	Multiple Myeloma	Oncology	Pre-Registration	US; EU
Ciltacabtagene autoleucel	Legend Biotech Corp	Multiple Myeloma	Oncology	Phase III	Australia; Japan
DCVax-L	Northwest Biotherapeutics Inc	Glioblastoma	Oncology	Phase III	US; Canada; EU
Dendritic cell immunization	Oslo University Hospital	Glioblastoma	Oncology	Phase II/III	Norway
Donor Lymphocyte Infusion (DLI); Haploidentical Stem Cell Transplantation	Northwell Health; New York Blood Center	Acute lymphocytic leukemia; Acute myeloid Leukemia; Myelodysplastic Syndrome; Chronic Myelogenous Leukemia	Oncology	Phase III	US
ERC-1671	ERC Belgium SA	Glioblastoma	Oncology	Pre-registration	EU
Gemogenovatucel-T	Gradalis Inc	Ewing Sarcoma	Oncology	Phase III	US
Gene Therapy to Target BCMA for Multiple Myeloma	Shanghai Unicar-Therapy Bio-Medicine Technology Co Ltd	Multiple Myeloma	Oncology	Phase III	China
Gene Therapy to Target CD123 and CLL1 for Relapsed and Refractory Acute Myeloid Leukemia	Fujian Medical University	Acute Myeloid Leukemia	Oncology	Phase III	China
Gene Therapy to Target CD19 for B-Acute Lymphoblastic Leukaemia	National University of Malaysia	Acute lymphocytic leukemia	Oncology	Phase II/III	Malaysia
Idecabtagene vicleucel	Bristol-Myers Squibb Co	Multiple Myeloma	Oncology	Pre-Registration	EU
Idecabtagene vicleucel	Bristol-Myers Squibb Co	Multiple Myeloma	Oncology	Phase III	Japan; Global
Lisocabtagene maraleucel	Bristol-Myers Squibb Co	Diffuse Large B-Cell Lymphoma; Follicular Lymphoma; Primary Mediastinal B-Cell Lymphoma	Oncology	Pre-Registration	EU
MesoCancerVac	Amphera BV	Malignant Pleural Mesothelioma	Oncology	Phase II/III	EU
Nadofaragene firadenovec	FKD Therapies Oy	Malignant Pleural Mesothelioma	Oncology	Phase III	US; EU; Australia; Russia; Canada
Ofranergene obadenovec	Vascular Biogenics Ltd	Glioblastoma	Oncology	Phase III	US; Canada; Israel

Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Omidubicel	Gamida Cell Ltd	Acute Myeloid Leukemia	Oncology	Phase III	US; EU; Israel; Singapore
Omidubicel	Gamida Cell Ltd	Acute Lymphocytic Leukemia; Chronic Myelocytic Leukemia; Myelodysplastic Syndrome	Oncology	Phase III	US; EU; Israel; Singapore
Relmacabtagene autoleucel	JW Cayman Therapeutics Co Ltd	Diffuse Large B-Cell Lymphoma	Oncology	Pre-registration	China
Rovaleucel	Tessa Therapeutics Ltd	Nasopharyngeal Cancer	Oncology	Phase III	US; Malaysia; Singapore; Taiwan; Thailand
Stem Cell Therapy for Autoimmune Disorders, Cardiovascular Disorders, CNS Disorders, Infectious Disease, Musculoskeletal Disorders and Oncology	Hope Biosciences LLC	Pancreatic Cancer	Oncology	Phase III	US
Tabelecleucel	Atara Biotherapeutics Inc	Post-Transplant Lymphoproliferative Disorder	Oncology	Phase III	Australia; US
Tisagenlecleucel	Novartis AG	Follicular Lymphoma	Oncology	Phase III	US; EU; Japan; Australia
TLP-0001	Tella Inc	Pancreatic Cancer	Oncology	Phase III	Japan
Trabedersen	Oncotelic Inc	Pancreatic Cancer	Oncology	Phase III (planned)	Unspecified
Trabedersen	Oncotelic Inc	Glioblastoma	Oncology	Phase III (planned)	Unspecified
Donor Lymphocyte Infusion (DLI); Haploidentical Stem Cell Transplantation	Northwell Health; New York Blood Center	Acute lymphocytic leukemia; Acute myeloid Leukemia; Myelodysplastic Syndrome; Chronic Myelogenous Leukemia	Oncology	Phase III	US
Cellavita-HD	Azidus Brasil; Cellavita Pesquisa Científica Ltda	Huntington Disease	Central Nervous System	Phase II/III	Brazil
Eplontersen sodium	Akcea Therapeutics Inc	Transthyretin-Mediated Amyloid Polyneuropathy	Central Nervous System	Phase III	US; EU; Argentina; Japan; New Zealand; Taiwan; Turkey
LibmeldyTM	Orchard Therapeutics Plc	Metachromatic Leukodystrophy	Central Nervous System	Phase III	US
NurOwn®	BrainStorm Cell Therapeutics Inc	Amyotrophic Lateral Sclerosis	Central Nervous System	Phase III	US
Onasemnogene abeparvovec	Novartis Gene Therapies	Spinal Muscular Atrophy	Central Nervous System	Pre-Registration	South Korea; Switzerland
Tofersen sodium	Biogen Inc	Amyotrophic Lateral Sclerosis	Central Nervous System	Phase III	Australia; US; EU; Japan; Canada; South Korea

Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Aurora-GTTM	Northern Therapeutics Inc	Pulmonary Arterial Hypertension	Cardiovascular	Phase II/III	Canada
AGTC-501	Applied Genetic Technologies Corp	Retinitis Pigmentosa	Ophthalmology	Phase II/III (planned)	Unspecified
Cotoretigene toliparvovec	Biogen Inc	Retinitis Pigmentosa	Ophthalmology	Phase III	US; EU; Canada
Lenadogene nolparvovec	GenSight Biologics SA	Leber Optic Atrophy	Ophthalmology	Pre-registration	EU
Lenadogene nolparvovec	GenSight Biologics SA	Leber Optic Atrophy	Ophthalmology	Phase III	US
NFS-01	Neurophth Therapeutics Inc	Leber Optic Atrophy	Ophthalmology	Phase II/III	China
NT-501	Neurotech Pharmaceuticals Inc	Macular Telangiectasia Type 2	Ophthalmology	Phase III	Australia; US; EU
Sepofarsen	ProQR Therapeutics NV	Leber Congenital Amaurosis	Ophthalmology	Phase I/II/III	US; EU; Canada
Timrepigene emparvovec	Biogen Inc	Choroideremia	Ophthalmology	Phase III	US; EU; Canada
UX-701	Ultragenyx Pharmaceutical Inc	Wilson Disease	Ophthalmology	Phase I/II/III (planned)	US
AGTC-501	Applied Genetic Technologies Corp	Retinitis Pigmentosa	Ophthalmology	Phase II/III (planned)	Unspecified
AKCEA-APOCIIILRX	Akcea Therapeutics Inc	Familial Chylomicronemia	Metabolic Disorders	Phase III	US, EU, Global
Eplontersen sodium	Akcea Therapeutics Inc	Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR CM)	Metabolic Disorders	Phase III	Australia; US; EU; Argentina; Canada; Israel
Inclisiran	Novartis AG	Homozygous Familial Hypercholesterolemia (HoFH)	Metabolic Disorders	Pre-registration	US
Volanesorsen sodium	Akcea Therapeutics Inc	Familial partial lipodystrophy	Metabolic Disorders	Phase III	US; EU; Global
Vutrisiran	Alnylam Pharmaceuticals Inc	Familial Amyloid Neuropathies	Metabolic Disorders	Pre-registration	US
Vutrisiran	Alnylam Pharmaceuticals Inc	Familial Amyloid Neuropathies	Metabolic Disorders	Phase III	Australia; EU; Japan; Canada; South Korea; Malaysia; Mexico; Taiwan
Vutrisiran	Alnylam Pharmaceuticals Inc	Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR CM)	Metabolic Disorders	Phase III	Australia; US; EU; Canada; Japan; South Korea; Malaysia; Thailand; Saudi Arabia; Moldova; Lebanon
ARO-AAT	Arrowhead Pharmaceuticals Inc	Alpha-1 Antitrypsin Deficiency	Genetic Disorders	Phase II/III	US; EU
Eladocagene exuparvovec	PTC Therapeutics Inc	Aromatic L-Amino acid Decarboxylase deficiency (AADC-d)	Genetic Disorders	Pre-registration	EU
Elivaldogene autotemcel	Bluebird Bio Inc	Adrenoleukodystrophy	Genetic Disorders	Phase III	US; Australia
Elivaldogene autotemcel	Bluebird Bio Inc	Adrenoleukodystrophy	Genetic Disorders	Pre-Registration	EU

Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Fordadistrogene movaparvovec	Pfizer Inc	Duchenne muscular dystrophy	Genetic Disorders	Phase III	EU; Canada; Israel; South Korea; Russia
Golodirsen	Sarepta Therapeutics Inc	Duchenne muscular dystrophy	Genetic Disorders	Phase III	EU; Australia
LYSSAF-302	Lysogene SAS	Mucopolysaccharidosis III (MPS III)	Genetic Disorders	Phase II/III	US; EU
Resamirigene bilparvovec	Audentes Therapeutics Inc	X-Linked Myotubular Myopathy	Genetic Disorders	Phase I/II/III	US; EU; Canada
RVT-802	Enzyvant Sciences Ltd	DiGeorge Syndrome	Genetic Disorders	Phase III	EU; South Korea; China
RVT-802	Enzyvant Sciences Ltd	DiGeorge Syndrome	Genetic Disorders	Pre-registration	US
Viltolarsen	Nippon Shinyaku Co Ltd	Duchenne muscular dystrophy	Genetic Disorders	Phase III	EU; Australia; Global
ARO-AAT	Arrowhead Pharmaceuticals Inc	Alpha-1 Antitrypsin Deficiency	Genetic Disorders	Phase II/III	US; EU
Eladocagene exuparvovec	PTC Therapeutics Inc	Aromatic L-Amino acid Decarboxylase deficiency (AADC-d)	Genetic Disorders	Pre-registration	EU
OTL-103	Orchard Therapeutics Plc	Wiskott-Aldrich Syndrome	Immunology	Phase III	Italy
Betibeglogene autotemcel	Bluebird Bio Inc	β-thalassemia	Hematological Disorders	Phase III	US
Dirloctocogene samoparvovec	Spark Therapeutics Inc	Hemophilia A	Hematological Disorders	Phase III	US
Etranacogene dezaparvovec	UniQure NV	Hemophilia B	Hematological Disorders	Phase III	US; EU
Fidanacogene elaparvovec	Pfizer Inc	Hemophilia B	Hematological Disorders	Phase III	Australia; US; EU; Japan; Israel; Canada; South Korea; Saudi Arabia; Taiwan; Turkey
Fitusiran	Sanofi	Hemophilia A; Hemophilia B	Hematological Disorders	Phase III	Australia; US; EU; Canada; China; India; Japan; South Korea; Malaysia; South Africa; Taiwan; Turkey
Giroctocogene fitelparvovec	Pfizer Inc	Hemophilia A	Hematological Disorders	Phase III	US; South Korea; Taiwan; Turkey
ION-373	Ionis Pharmaceuticals Inc	Alexander's Disease (Factor VII Deficiency)	Hematological Disorders	Phase II/III	Australia; US; EU; Japan; Canada; Argentina; Israel
Valoctocogene roxaparvovec	BioMarin Pharmaceutical Inc	Hemophilia A	Hematological Disorders	Phase III	Australia; Global
Valoctocogene roxaparvovec	BioMarin Pharmaceutical Inc	Hemophilia A	Hematological Disorders	Pre-Registration	US; EU
Beremagene geperpavec	Krystal Biotech Inc	Epidermolysis Bullosa	Dermatology	Phase III	US
FCX-007	Castle Creek Biosciences Inc	Epidermolysis Bullosa	Dermatology	Phase III	US

Drug Name	Sponsor Name	Rare Disease	Therapy Area	Development Stage	Geography
Gene Therapy to Activate LAMB-3 for Junctional Epidermolysis Bullosa	Holostem Terapie Avanzate SRL	Epidermolysis Bullosa	Dermatology	Phase II/III	EU
Prademagene zamikeracel	Abeona Therapeutics Inc	Epidermolysis Bullosa	Dermatology	Phase III	US
Mesenchymal Stem Cell Therapy	Royan Institute; Tehran University of Medical Sciences; Shahid Beheshti University of Medical Sciences	COVID-19 Acute Respiratory Distress Syndrome	Respiratory	Phase II/III	Iran
Nedosiran sodium	Dicerna Pharmaceuticals Inc	Primary Hyperoxaluria Type I; Primary Hyperoxaluria Type II	Genito Urinary System And Sex Hormones	Phase III	Australia; US; EU; Japan; Canada; Israel



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

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