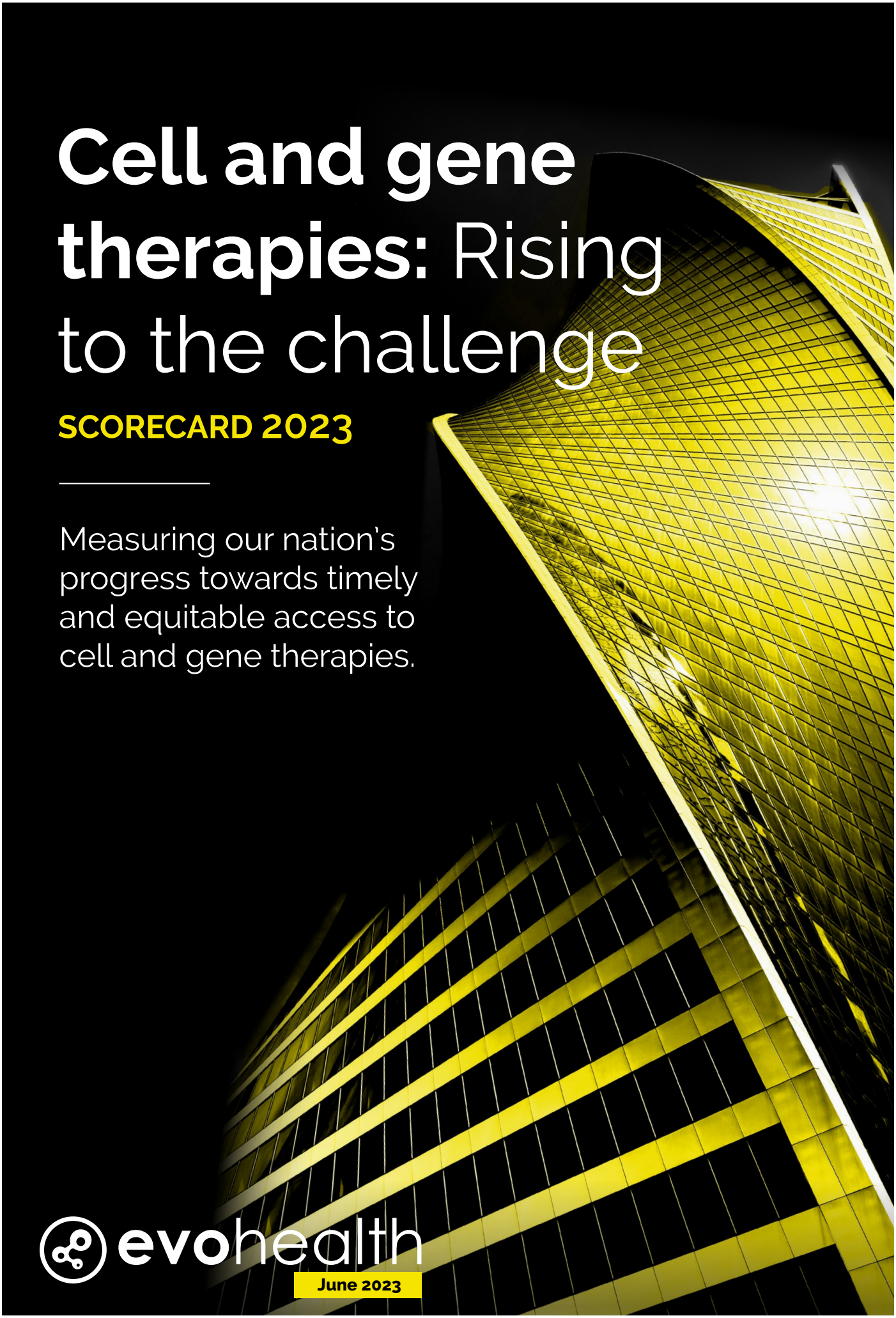
Cell and gene therapies: Rising to the challenge

SCORECARD 2023

Measuring our nation's progress towards timely and equitable access to cell and gene therapies.



evohealth

June 2023

Evohealth acknowledges that we work on the traditional lands of many Aboriginal clans, tribes, and nations.

We commit to working in collaboration with Aboriginal and Torres Strait Islander communities and peoples to improve health, emotional and social well-being outcomes in the spirit of partnership.

About Evohealth

The delivery of healthcare is complex.
Our focus is not.

Better health for all Australians.

Executive summary

We are fortunate to live in a time of rapidly evolving medical innovation. Significant advances are being made in research and development offering promise to patients living with incurable health conditions. Emerging therapies are available with the potential to cure or correct underlying causes of many life-altering and life-threatening conditions.

Cell and Gene Therapies, or CGTs, are at the forefront of this medical innovation. Unlike conventional medicines, these powerful new therapies target a patient's own immune cells or genes to deliver long-lasting therapeutic, or at times, curative benefits. CGTs have the potential to treat a range of health conditions such as some cancers, genetic disorders (e.g., cystic fibrosis, haemophilia, muscular dystrophy), chronic diseases (e.g., diabetes, heart disease) and more. CGTs are referred to as transformative due to their potential to significantly alter the course of traditionally burdensome diseases.

Cell and gene therapies give patients hope where no hope has existed before.

CGTs are very different to conventional medicines. They are also dominating Australia's innovative therapy pipeline, with more than 140 in various stages of development. We are at the beginning of a transformational change to how care will be delivered to thousands of patients.

Our research reveals that Australia's health system will struggle to deliver on the promise of these innovative therapies without significant change. If we want to harness their potential to improve the health of Australians, an urgent focus on system change is necessary.

Preparing the health care system for a new era in medical treatment

Australia has a strong history of prioritising health care. As a nation, we accept that care needs to be made readily available to our most vunerable. Amongst these people are those that need access to transformative therapies.

In July 2021, Evohealth launched the ***CGT: Rising to the challenge*** white paper. This paper examined Australia's preparedness for CGTs. Seven recommendations outlined critical and immediate actions to progress equitable and timely access to CGTs for Australians in need, namely:

Recommendations

1. **Leverage recommendations for CGTs from the National Strategic Action Plan for Rare Disease.**
2. **Establish an Office for Rare Diseases as a portfolio agency of the Department of Health and Aged Care (DoHAC).**
3. **Establish a CGT expert advisory group to provide input and advice to the Therapeutic Goods Administration (TGA), Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC).**
4. **Enhance the role of horizon scanning via the Health Technology Reference Group or equivalent.**
5. **The Minister for Health to establish a cross-functional working group including Department of Health (both Federal and State/Territory), industry, patients, and academics to consider current Health Technology Assessment (HTA) for CGTs.**
6. **Develop a national strategic approach to equitable and timely access to CGTs via the National Health Reform Agreement (NHRA) framework or another mechanism.**
7. **Develop incentives for CGTs to create opportunities for trials, manufacturing, and commercial success in Australia.**

Australia is falling behind our international counterparts in preparing for CGTs

Since the launch of the ***CGT: Rising to the challenge*** white paper, even more CGTs have become available. Several CGTs are already being used in Australian hospitals to treat eligible patients with certain forms of blood cancer, melanoma, spinal muscular atrophy and inherited retinal disease despite the lack of nationally coordinated preparation for these innovative therapies.

Internationally, there have been great strides made to prepare for incorporating CGTs into patient care through collaboration and Government initiatives. Yet, progress in Australia remains slow. Where Australia was a once global exemplar for evaluation of new medicines, with respect to preparedness for CGTs, we now lag behind our international counterparts. Our current Health Technology Assessment (HTA) processes are not contemporary, particularly for CGTs, and lack specialist expertise.

The United Kingdom (UK) is leading the way in reshaping the HTA landscape, demonstrating how innovations such as CGTs can be valued and made available to patients in the shortest possible time. Australia needs to take note, otherwise we will miss the direct opportunity to improve quality of life for our most vulnerable citizens.

With innovation comes change and change needs action

Australia's HTA landscape must evolve to ensure that vulnerable patients can access proven therapies – including CGTs – when they need them most. This scorecard has been developed to highlight where progress has been made and demonstrate where more work is needed by Government to equip our health care system for an impending wave of these innovative therapies.

This scorecard rates the pace of change in Australia against the seven recommendations of the 2021 ***CGT: Rising to the challenge*** white paper with 16 expert informed and endorsed indicators. These indicators are designed to be measured against progress in the coming years.

The rating for each indicator is underpinned by evidence sourced from peer reviewed publications, key local and international organisational websites and stakeholder engagement including a survey of relevant Patient Advisory Groups (PAGs). Valuable oversight and advice were provided by an expert Advisory Committee representing the patient voice, clinicians, industry, and academia.

Australia's progress in preparing our health system for CGTs

As shown in the scorecard on next page, Australia has made some progress towards implementing the seven recommendations in the ***CGT: Rising to the challenge*** white paper since 2021. Most notably, investment in and incentives for research, manufacturing, and commercialisation of CGTs is tracking well due to Government funding initiatives. But when it comes to progress towards other recommendations, efforts are sporadic and lack coordination at a national level. In addition, there remains uncertainty regarding how evaluation frameworks will be adapted to accommodate the unique challenges with funding CGTs.

CGT: Rising to the challenge Scorecard

1 Leverage recommendations, relevant to CGTs, from the National Strategic Action Plan for Rare Diseases.

Indicators	Progress
1.1 There is a national education program for consumers.	● ○ ○
1.2 There is a national education program for health professionals.	● ○ ○
1.3 There is a national workforce strategy to meet the future needs for management of CGTs.	● ○ ○
1.4 There is a publicly available framework for CGTs that explicitly considers equity in HTA.	● ○ ○
1.5 There is a national research strategy which considers CGTs.	● ● ○

2 Establish Office for Rare Diseases as a Portfolio Agency of Department of Health and Aged Care (DoHAC).

Indicators	Progress
2.1 There is an Office for Rare Diseases.	○ ○ ○
2.2 There are mechanisms or working groups which include State and Territory Governments and patient advisory groups to inform regulation and reimbursement process for CGTs.	○ ○ ○
2.3 There is a national register for rare diseases with national registry standards relevant to CGTs.	● ● ○

3 Establish a CGT expert advisory group to provide input and advice to TGA, PBAC, and MSAC.

Indicators	Progress
3.1 A CGT expert advisory group has been established either within the Office of Rare Diseases, DoHAC or another organisation.	● ● ○
3.2 The membership of each HTA includes a dedicated bioethicist.	○ ○ ○

○○○ Not achieved ● ○ ○ Some progress achieved ● ● ○ Partially achieved ● ● ● Fully achieved

4 Enhance the role of horizon scanning via the Health Technology Reference Group, or equivalent.

Indicator	Progress
4.1 There is a formalised Government process for conducting horizon scanning, that interfaces with regulation, reimbursement, and clinical infrastructure.	● ● ○

5 The Minister for Health to establish a crossfunctional working group including Departments of Health (both Federal and State/Territory), industry, patients, and academics to consider current HTA processes for CGTs.

Indicators	Progress
5.1 Patients are being treated equitably across jurisdictions for access to CGTs using transparent and sustainable arrangements.	● ● ○
5.2 HTA processes for CGTs have been reviewed	● ○ ○

6 Develop a national strategic approach to equitable and timely clinical care for CGTs via the NHRA framework.

Indicator	Progress
6.1 There is a national strategic and co-design approach to CGT access that considers: • Clinical infrastructure; • Administrative infrastructure; and • Post marketing infrastructure.	● ○ ○

7 Develop incentives for CGTs to create opportunities for trials, manufacturing, and commercial success in Australia.

Indicators	Progress
7.1 There are incentives for clinical trials to support CGT research.	● ● ○
7.2 There are incentives for manufacturing and commercial success for translating CGT research.	● ● ○

○○○ Not achieved ●○○ Some progress achieved ●●○ Partially achieved ●●● Fully achieved

Priorities for progress

With 140 CGTs in the pipeline, the Australian Government needs to act fast. The issue of how best to evaluate CGTs and make them available to patients is becoming critical. Vulnerable Australians and their families are counting on these therapies to change, and potentially save, lives.

Patient groups consulted for this project were unequivocal about the importance of CGTs as part of contemporary medicine. They expressed a strong desire for patient access to clinical trials or early access schemes for CGT so that vulnerable patients can access the best possible care when they need it most. Patient groups also emphasised the importance of a coordinated government approach to both ensuring equitable access to CGTs and building the preparedness of the health workforce and system to deliver CGTs in a timely manner.

CGTs are the future. **Australia has significant work to do, to rise to the challenge and prepare our HTA landscape for a new era of medicine.**

With so much to do, this scorecard has prioritised the critical indicators needed to prepare for the very near future.

To accelerate the rate of progress, we recommend Government focus on three key indicators in the next 12 months:

1. **Establish an Office for Rare Diseases**
2. **Explicitly consider equity for CGTs in the current HTA review**
3. **Establish a CGT expert advisory group to provide input and advice to TGA, PBAC and MSAC**

There is considerable support from the community to act on these key activities and the broader recommendations of the ***CGT: Rising to the challenge*** white paper. We know this because Evohealth and our expert Advisory Committee are not alone in calling for change. The recommendations in our white paper are consistent with a growing collective of voices seeking change to give hope to many of our most vulnerable citizens.

Collective voices

Over the last four years, there have been numerous reports of significance in Australia published by government, industry, research, and patient advocacy groups which address the multiple challenges with respect to equitable and timely access to innovative therapies. Analysis of these reports has revealed stakeholder agreement with the seven recommendations in the ***CGT: Rising to the Challenge*** white paper and the necessary activities required for progressing equitable and timely access to CGTs in Australia.

This show of collective voices reinforces the importance of prioritising progress on the recommendations in the ***CGT: Rising to the Challenge*** white paper.

Making safe and effective CGTs available to Australian patients in a timely and equitable manner delivers on the support that many Australians need. Vulnerable patients and their families do not have time to wait.

White paper evidence base:

- A scoping review of national and comparable international organistion's websites. Included were any Government or non-Government organisation involved in developing, manufacturing, trialling, approving, implementing, or evaluating a CTG for human use.
- An expert advisory group. Please see pages 13 for members
- A confidential, opt-in patient advisory group electronic survey. We reached out to 18 PAGs where CGTs are relevant to their patient base and received 13 responses.

Acknowledgements

Evohealth wishes to acknowledge the ongoing support from the organisations and individuals who contributed to both the *CGT: Rising to the challenge* white paper and this project. In particular, we would like to acknowledge the project Advisory Committee who provided critical oversight and input to the development of this report.

The Advisory Committee comprised the following members:

- Jessica Bean, Chairperson Patient Voice Initiative
- Tiffany Boughtwood, Australian Genomics
- Nettie Burke, Founder and Director of Good-Works Advocacy
- Andrew Bowskill, MTPConnect
- Louise Healy, Rare Voices Australia
- Professor Adam Jaffe, John Beveridge Professor of Paediatrics and Head of Discipline of Paediatrics and Child Health, UNSW Sydney
- Brendan Shaw, Health Economist, ShawView Consulting

Other

- Naomi Guest, Design
- Sasha Yudaev, Cover photograph
- Charlie Harris & Jack Bass, Case Study photograph

Contents

Disclaimer

This Report has been independently prepared by Evohealth Pty Ltd ACN 627 552 729 (**Evohealth**) on behalf of Novartis Australia Pty Ltd ACN 004244 160 (**Novartis Australia**).

This Report has been commissioned by Novartis to evaluate the current and future progress, in Australia on the seven recommendations in the ***CGT: Rising to the challenge white paper (2021).***

This Report is not intended to be and should not be used by any other person or entity other than a Recipient and Evohealth accepts no duty of care whatsoever to any such other person or entity.

While reasonable efforts have been made to ensure that the contents of this Report are factually correct, this Report is provided by Evohealth on a general basis only. Neither Evohealth or any of its directors, officers, employees, advisers, consultants, contractors, and agents make any representation or warranty, express or implied, as to the currency, accuracy, reliability, or completeness of the information referred to or contained in this Report and none of those persons or entities accepts any responsibility or liability (except a liability that cannot lawfully be excluded) for any reliance placed on the contents of this Report by any person. This Report does not purport to be comprehensive or to contain all the information a Recipient may desire or require in respect of its subject matter. The Recipient should make its own enquiries and obtain its own independent advice in relation to the information contained within this Report before making any decision or taking any action based on its contents.

To the maximum extent permitted by law, Evohealth and its directors, officers, employees, advisers, consultants, contractors and agents disclaim and exclude all liability for any loss, claim, demand, damages, costs and expenses of whatsoever nature (whether or not foreseeable): suffered or incurred by any person relying or acting on any information provided in, or omitted from, this Report or any other written or oral opinions, advice or information provided by any of them; or arising as a result of or in connection with information in this Report being inaccurate or incomplete in any way or by reason of any reliance thereon by any person; and whether caused by reason of any negligence, accident, default or however otherwise caused.

Each Recipient of this Report acknowledges and accepts each of the matters and conditions contained in this Disclaimer.

June 2023

Authors Renae Beardmore, Jodie Hillen, Karinna Saxby, Yukti Sharma and Laura Birchall.

Citation: Evohealth. 2023. Cell and Gene Therapies: Rising to the Challenge *Scorecard* 2023. Evohealth. Canberra.
https://evohealth.com.au/media/reports/2023_Scorecard_Rising_To_The_Challenge.pdf

Introduction

We live in a time of rapidly evolving medical innovation.

Significant advances are being made in research and development offering incredible promise to patients living with incurable conditions. Emerging therapies are available with potential to cure or correct many underlying causes of life-altering and life-threatening conditions. Cell and Gene Therapies (CGTs) are at the forefront of this medical innovation and are revolutionising medical therapy by offering potentially curative therapies for debilitating genetically inherited conditions, rare diseases, and cancer. But CGTs require unique consideration and infrastructure to ensure patients receive therapy in an equitable and timely manner.

In recognition of the central role of CGTs in the future of medical innovation and their unique challenges, Evohealth launched the ***CGT: Rising to the challenge*** white paper in 2021 (1). This paper identified seven recommendations for action to improve equitable and timely access to CGTs for Australians in need.

This scorecard evaluates progress towards achieving these seven recommendations using 16 expert endorsed indicators.

What are Cell and Gene Therapies?

CGTs correct abnormal cells or genetic material within a cell (2). They are complex health interventions involving advanced biochemical techniques (3).

Cell therapies involve the transfer of live healthy cells into a patient (either their own cells which have been modified in a lab or cells from a donor) to alleviate or cure a disease (4). For example, Chimeric Antigen Receptor T-cell or CAR-T cell therapy is currently used to treat blood cancers such as leukaemia and lymphoma. CAR-T therapy involves weaponising the immune system to recognise and destroy cancerous cells (4).

Gene therapies involve using a vehicle (viral vector) to deliver the correct genetic information to an abnormal cell. Once delivered, this genetic information recodes cells to produce the correct protein or protein levels which have been contributing to a disease or condition (5). Gene therapies are often referred to as transformative as they are designed to be delivered as a once-off intervention with curative results (5). Some innovative therapies use both techniques (4).

CGTs have several unique characteristics which have posed, and will continue to pose, challenges to our healthcare system and include: (1).

CGTs are not specifically a product, device or a service and can be a combination thereof;

CGTs have complex manufacturing and supply chains with associated costs;

CGTs can be transformative by significantly changing the course of disease;

Early diagnosis is often vital to achieve best outcomes; and

CGTs treating rare conditions have small markets.

Preparing for the CGT pipeline

Australia's health care system is designed to deliver conventional pharmaceuticals, such as medicines. CGTs are not medicines. With over 140 CGT products in the global pipeline for Australia it is clear there needs to be significant change in how care is delivered (6). **The time to act is now.**

Ensuring equitable and timely access to CGTs

Research reveals that Australians are willing to pay more to make the distribution of health more equitable (1). Importantly, this includes Australia's most disadvantaged by health status, such as those born with an inheritable chronic disorder or diagnosed with cancer. The Pharmaceutical Benefits Scheme (PBS) safety net threshold which caps the annual out of pocket expenses for Australians requiring multiple medicines is a good example of equity at work (1).

As well as addressing the direct costs to consumers and the health care system, equity also addresses the indirect costs for those living with rare or incurable diseases. Indirect costs are shared by individuals, families and society and include lifelong social, emotional, psychological and financial costs (1).

CGTs will require greater investment compared to conventional or biologic medicines. This investment acknowledges long term benefits and the potential to transform or cure a disease (7). Australia's current processes for evaluating health interventions for inclusion in national health funding schemes are not equipped to account for the potential long-term societal or patient benefits of these therapies and are therefore not equitable (1, 8, 9).

The seven recommendations from the ***CGT: Rising to the challenge*** white paper (Figure 1) target key areas for action to improve equitable and timely access to CGTs for Australians in need.

Summary of Recommendations

These recommendations will allow Australia to deliver on the promise of CGTs as a future of care for many Australians living with currently incurable cancers, viruses, and rare debilitating conditions.

1. Leverage recommendations from the National Strategic Action Plan for Rare Disease (which have been accepted by the Minister for Health in 2020).

2. Establish Office for Rare Diseases as a Portfolio Agency of Department of Health.

7. Develop incentives for CGTs to create opportunities for trials, manufacturing and commercial success in Australia.

We know that society is willing to pay more to make the distribution of health more even.

3. Establish a CGT expert advisory group to provide input and advice to the key evaluation bodies – the Therapeutic Goods Administration, Pharmaceutical Benefits Advisory Committee and Medical Services Advisory Committee.

6. Develop a national strategic approach to equitable and timely clinical care for CGTs via the National Health Reform Agreement framework.

4. Enhance the role of horizon scanning via the Health Technology Reference Group, or equivalent.

5.The Minister for Health to establish a cross-functional working group including Departments of Health (both Federal and State/Territory), industry, patients and academics to consider current Health Technology Assessment processes for CGTs.

Figure 1: Recommendations from the CGT: Rising to the challenge white paper (1).

Collective Voices

The 2021 ***CGTs: Rising to the challenge*** report is not alone in making the case for change.

In just the last four years, there have been numerous submissions to government and key reports published in Australia which present similar solutions to the multiple challenges of improving access to innovative and transformative therapies. Some reports target issues specific to speciality areas, such as CGTs for rare diseases, whilst others have addressed broader health system deficiencies. This cross-sector support from research, industry, Government, and patient advocacy groups presents an opportunity to harness a collaborative approach to advancing equitable and timely access to CGTs in Australia.

There is cross-sector support to prepare for a new future of care with CGTs.

This groundswell of collective voices reinforces the importance of prioritising progress on providing access to these transformative therapies. A summary of how the recommendations of these ten reports align with the intent of those in our ***CGT: Rising to the Challenge*** white paper is presented in Table 1.

Recommendations

Reports

Evohealth	CGT: Rising to the challenge	Leverage recommendations from the National Strategic Action Plan for Rare Disease	Establish Office for Rare Diseases as Portfolio Agency of Department of Health	Establish a CGT expert advisory group to provide input and advice to TGA, PBAC and MSAC	Enhance the role of horizon scanning via the Health Technology Reference Group, or equivalent
Government	The New Frontier Inquiry 2021 (10)	✓	✓	✓	✓
Government	National Strategic Action Plan for Rare Diseases (2020) (11)	✓	✓	✓	–
Patient Advisory Groups	Australian Patient Advocacy Alliance (APAA) Canberra Health Summit Consensus Statement 2019 (12)	–	–	–	✓
Patient Advisory Groups	Multiple submissions to the Standing Committee on Health, Aged Care and Sport including APAA, Rare Voices Australia (RVA) and Patient Voice Initiative (PVI) (13)	✓	✓	✓	–
Patient Advisory Groups	Multiple submissions to the review of the National Medicines Policy including APAA, RVA and PVI (14)	✓	✓	✓	✓
Research	Australia's Missing Link (2021) (15)	✓	–	–	–
Industry	Realising the full potential of genomics to personalise health care (2022) (16)	–	–	✓	–
Industry	Precision Medicine (2019) (17)	✓	–	✓	
Industry	Medicines Australia Strategic Agreement 2022-27 (18)	–	–	–	✓
Industry	McKell Institute Report 2021 (19)	✓	✓	–	–

*Table 1: Cross-sector support for **CGT: Rising to the challenge** white paper recommendations*

Recommendations

Reports

	CGT: Rising to the challenge	The Minister for Health to establish a cross-functional working group including Department (both Federal and State/Territory), industry, patients, and academics to consider current Health Technology Assessment (processes) for CGTs	Develop national strategic includeapproach to equitable and timely access to CGTs via the NHRA framework or another mechanism	Develop incentives for CGTs to create opportunities for trials, manufacturing, and commercial success in Australia
Evohealth				
Government	The New Frontier Inquiry 2021 (10)	✓	✓	✓
Government	National Strategic Action Plan for Rare Diseases (2020) (11)	✓	✓	—
Patient Advisory Groups	Australian Patient Advocacy Alliance (APAA) Canberra Health Summit Consensus Statement 2019 (12)	✓	✓	—
Patient Advisory Groups	Multiple submission to the Standing Committee on Health, Aged Care and Sport including APAA, Rare Voices Australia (RVA) and Patient Voice Initiative (PVI) (13)	✓	✓	✓
Patient Advisory Groups	Multiple submissions to the review of the National Medicines Policy including APAA, RVA and PVI (14)	—	✓	—
Research	Australia's Missing Link (2021) (15)	—	—	—
Industry	Realising the full potential of genomics to personalise health care (2022) (16)	✓	—	—
Industry	Precision Medicine (2019) (17)	—	—	✓
Industry	Medicines Australia Strategic Agreement 2022-27 (18)	✓	—	✓
Industry	McKell Institute Report 2021 (19)	✓	✓	✓

*Table 1: Cross-sector support for **CGT: Rising to the challenge** white paper recommendations*

Australia's National Medicines Policy

In December 2022, 20-years after implementation, the revised National Medicines Policy (NMP) was published (20). The NMP vision statement is: 'To achieve the world's best health, social and economic outcomes for all Australians through a highly supportive medicines policy environment.' To achieve this vision, there must be strong alignment with relevant state and federal health reform policies.

The NMP covers the life cycle of medicines in Australia, including CGTs, with a focus on equitable access and Quality Use of Medicines (QUM). All stakeholders (industry, researchers, clinicians, patients, and Governments) are responsible for the stewardship of the NMP. Two of the four pillars of the NMP are particularly relevant to timely and equitable access to CGTs in Australia:

Pillar 1:
Australians should have timely, reliable, and equitable access to medicines which are affordable to the community; and

Pillar 4:
Australia should have viable, collaborative, and innovative medicines industry sectors with the necessary skills to adapt to future needs.

Whilst broad in its approach, the NMP lends support to recommendations one, three and six in Table 1 above.

TGA action to accommodate CGTs in our regulatory framework

In 2021, MTPConnect was commissioned by the TGA to undertake stakeholder interviews and workshops to understand the necessary changes to the current regulatory framework to accommodate cell, gene, and tissue products. In July 2022, the TGA responded to the 19 recommendations in the MTPConnect report (21). The following TGA responses are relevant to the recommendations in this report.

- TGA will endeavour to clarify the pathways for clinical trial applications (CTA) through an education campaign;
- TGA will endeavour to work more closely with the Office of the Gene Technology Regulator (OGTR) to streamline processes for applicants and
- The TGA actively participates in horizon scanning and is looking to incorporate real-world evidence into the regulatory framework.

Measuring Progress

This scorecard has been designed to compare progress year on year against the recommendations of the *CGT: Rising to the challenge* white paper and other reports.

Sixteen indicators addressing core components of the seven recommendations were developed and endorsed by a project Advisory Committee with expertise in clinical practice, research, patient advocacy, health economics, regulatory and industry practices (see Acknowledgements on page 11). The scoring and criteria for progress on each indicator are in Appendix A. To inform progress in Australia, this scorecard also draws upon evidence from the international community with respect to initiatives and learnings for progress.

1 Leverage recommendations relevant to CGTs from the National Strategic Action Plan for Rare Diseases.

Recommendations from the National Strategic Action Plan for Rare Diseases were accepted by the Minister for Health in 2020 (22). This Action Plan includes any therapies for all rare diseases.

Five indicators measure progress for this recommendation:

1.1 There is a national education program for consumers;
1.2 There is a national education program for health professionals;
1.3 There is a national workforce strategy to meet the future needs of CGTs;
1.4 There is a publicly available framework for CGTs that explicitly considers equity in HTA; and
1.5 There is a national research strategy which considers CGTs.

Each are discussed in detail below.

1.1 There is a national education program for consumers.

Some progress achieved

1.2 There is a national education program for health professionals.

Some progress achieved

In Australia, consumer, and health professional education for CGTs is fragmented. Whilst some progress has been achieved in the development of educational materials for rare diseases, there is currently no comprehensive nationally coordinated education program targeting CGTs.

CGTs are complex and unique therapies (1). The fragmented approach to consumer and health care professional education may lead to inconsistencies in information across the health sector and compound confusion for both patients and clinicians.

> The implication of a lack of a national approach to education is that information may be inconsistent, incomplete, or inaccurate…. and not suited to Australian consumers. **(Consumer representative)**

> There continues to be widespread confusion regarding what CGTs actually are. **(Industry representative)**

In Australia, many currently available CGT educational materials address either screening or diagnosis of a rare disease. For example, the Haemophilia Foundation of Australia has developed a range of educational resources for patients and health professionals including a comprehensive booklet about genetic testing for females (23). In addition, both Australian Genomics and AusBiotech have developed consumer support materials for a range of genetic tests and related interventions (24, 25).

Government funded projects are underway to develop educational materials for rare diseases which may be relevant to CGTs. Two of these projects are:

- The Raise Awareness Rare Education (RARE) portal. As a direct response to the Action Plan the government funded RVA $1 million to develop an information portal. The portal includes education targeting both the workforce and consumers contextualised for the Australia health care system (26). In addition, the Government has also funded the University of New South Wales to undertake the RArEST project ($1.9 million). This project aims to improve health care practitioner awareness and management of rare diseases through education (27).
- The Sydney Children's Hospital Network (SCHN) are designing an education program for Adeno-Associated Virus (AAV) gene therapy (28). This program will include multidisciplinary team models of care and care standards for patients eligible to receive gene therapy via recombinant adeno-associated virus (rAAV) vectors. After trialling it at SCHN, it is intended that this program will be available to other health services in the future.

These two projects help to fill the information gap for some rare diseases but will not address information for CGTs for more common diseases. Nor do they provide a nationally coordinated and consistent approach to consumer and health professional CGT education for all diseases. As a result, only some progress has been achieved for these two indicators.

Global progress

Internationally there are a range of comprehensive CGT educational programs for consumers and health care professionals. These education programs include:

1. The **International Society for Cell and Gene Therapy (ISCT)** offers a number of education programs to support the CGT sector with a focus on the scientific, regulatory, and commercialisation communities (29).
2. The **National Organisation for Rare Diseases (NORD) Rare Disease Database in the US provides consumers with access to information regarding the diagnosis and treatment of rare diseases** including free webinars and factsheets (30). Information targeting health care professionals is also available on the NORD Physician Guides website (30). Patients can also access patient assistance programs for financial support to access diagnostics, treatments and carer support (31).
3. The **American Society of Cell and Gene Therapy (ASCGT)**, a national professional organisation for CGTs, provides education for consumers and professional development opportunities for health care professionals regarding CGT for any disease (4, 5).
4. In the UK, the **British Society for Gene and Cell Therapy (BSCGT)** delivers consumer friendly educational resources (32). BSCGT focus is the current generation in CGT therapies to promote translation of CGTs from bench to bedside.

1.3 There is a national workforce strategy to meet the future needs for management of CGTs.

Some progress achieved

Some progress has been achieved in Australia to improve workforce readiness, but there is no national approach specific to CGTs. Where progress has been made this is highlighted below.

In 2022, the Victorian Government Centre for Commercialisation of Regenerative Medicine Australia (CCRM Australia) and the Canadian Advanced Therapies Training Institute (CATTI) entered into an agreement to improve the curriculum standards for CGT training in Australia (33). This partnership will allow access to CATTI online and hands-on training for Australians working in the CGT development and commercialisation sectors.

Other training and accreditation programs are also underway. The Human Genetic Society of Australasia (HGSA) has formed a working group to provide strategic leadership for the accreditation of the profession of genetic counsellors (34). For clinicians, the Australian Association of Clinical Geneticists trains over 130 medical specialists in clinical genetics across Australia and New Zealand (ANZ). Training is under the auspices of the Royal Australian College of Physicians (35).

Through its Researcher Exchange and Development within Industry (REDI) scheme, MTPConnect also currently supports two projects which educate industry on the manufacturing and regulatory challenges with respect to innovative therapies including CGTs (36, 37).

Whilst these workforce programs demonstrate some progress, the current focus is on the research, manufacturing, and genetic counselling workforce. There remains a lack of workforce strategies for other health care providers. This was reinforced by the February 2022 Rare Voices Australia Rare Metabolic Disease Workforce white paper which highlighted the lack of a specialised workforce in Australia and called for a national strategic approach to meet international best practice (38).

'A coordinated Government approach to ensuring the health workforce and health system has capacity to deliver CGTs in a timely manner' was rated by Patient Advisory Groups as a top four priority for the next five years. **(Some progress achieved)**

Global progress

In the UK, workforce preparedness is well advanced and supported by the Innovate UK initiative. Innovate UK hosts multiple projects to encourage innovation across the science sectors (39). Through their CGT Catapult, funding has been provided to train individuals including clinicians to develop, manufacture and deliver CGTs (40, 41). For more information on UK and CGT, see the case study – **UK Cell and Gene Catapult**

1.4 There is a publicly available framework for CGTs that explicitly considers equity in HTA.

Some progress achieved

Our research from the ***CGT: Rising to the challenge*** white paper revealed that society accepts an equitable approach to accessing health care resources. CGTs often target rare disorders with a high unmet need. These patients need equity to be expressly considered to facilitate access to innovative therapies.

Our research reveals that severity and unmet needs are currently considered to an extent in the HTA process. However, explicit weightings are not being applied and there is a lack of transparency regarding consideration of equity.

Determining how equity is expressly considered during the HTA process is difficult. Whilst a review of Australia's HTA processes is underway and equity for certain groups is in scope, it is unclear how equity for CGTs will be explicitly considered (42). There will, however, be consideration of the methods used to evaluate reimbursement eligibility for therapies such as CGTs. With public consultation commencing in April 2023, there is an opportunity to advocate for the need for a transparent framework that specifically considers equity for CGTs in HTA.

In addition, many HTA bodies future discount the benefit of clinical interventions. In Australia discounting future states along with costs is mandated. Further discussion of the discount rate is included in 5.2.

> The review of the HTA framework is an opportunity to address systematic deficiencies with respect to innovative therapies, including CGTs. **(Australian health economist)**

The HTA review is happening at a crucial time as the CGT pipeline is expected to grow exponentially over the next decade. This is an opportunity to incorporate CGT specific processes to ensure there is equitable access to CGTs in Australia.

A coordinated Government approach to ensuring equitable access to CGTs' was rated by Patient Advisory Groups as a top four priority for the next five years. **(Some progress achieved)**

Global progress

There are several examples internationally of how equity is being considered for innovative therapies but not specific to CGTs. The UK, Norway, Netherlands, Canada, and Sweden have adjusted their existing HTA processes through a range of strategies including weighting for disease severity and unmet need when evaluating for access through their national health schemes (43, 44).

In the US, the Institute for Clinical and Economic review (ICER) provides independent advice to the Food and Drug Administration (FDA) on pricing models for innovative therapies to improve equitable access. ICER has recently completed a review of methodological changes to update their value-based framework and inform future international HTA assessment processes (45). The review includes five key recommendations for HTA bodies to improve consideration of which three have particular significance to CGTs. HTA bodies should:

- Directly engage with patient groups to ensure diverse representation. In some cases, this may include an advisory group with expertise for a particular intervention;
- Deliberate on and include the economic impact of multiple importance societal values when addressing equity; and
- Identify health system structures which need to be addressed so inequities are not amplified when introducing innovative interventions.

In 2021, following extensive community consultation, the UK National Institute for Health and Care Excellence (NICE) revised their HTA processes (46). In February 2022, they released a single guidance manual which includes highly specialised technologies. Changes relevant to CGTs include:

- Defining explicit criteria for routing technologies into the Highly Specialised Technologies Programme (HSTP);
- Applying a "severity modifier" to give more weight to severe and debilitating conditions; and
- A willingness-to-pay threshold adjustment for the HSTP.

Many CGTs will be eligible for the HSTP. This process will allow a more tailored evaluation pathway and combined with severity weightings, may enable higher willingness to pay thresholds for some of these therapies.

NICE also considered 'health inequality' and 'rarity of disease' weighting in their HTA review. While NICE is yet to incorporate such changes, potential adjustments have been tabled for exploration in the future. The discount rate used during HTA was also in scope of the review. Currently it is 3.5 per cent in the UK and no recommended changes were made. NICE noted that "almost all Advanced Therapy Medicinal Products (ATMPs) considered by NICE have been recommended using the current methods" and thus the impact of discounting specifically for ATMPs does not warrant a change to current methods (32, 33),

1.5 There is a national research strategy which considers CGTs.

Partially achieved

There is not a streamlined national approach to research specific to CGTs. There has been some progress however, with a range of research activities currently underway. The Federal Government funds research into rare diseases and innovative therapies through the following channels:

- The Medical Research Future Fund (MRFF) – medical research into rare diseases, not specific to CGTs (22).
- Australian Genomics (previously The Australian Genomics Health Alliance) – 24 strategic priority areas which cover both genomic and health system translation research (47).
- The Federal Government's Genomics Health Futures Mission (GHFM) – grants prioritising research specifically related to genomics (48).

Outside of Federal Government initiatives, Rare Voices Australia have developed research priorities which consider unmet need in rare diseases however these are not specific to CGTs (49).

Whilst the Federal Government supports research programs in this field, there is yet to be a national research strategy specific to CGTs, therefore this indicator was rated as partially achieved.

> It is likely that Australian Genomics will play a role in aligning investments and grants with strategic priorities, including Indigenous health. **(Researcher)**

Global progress

Overseas, there are both global and country-specific strategies to coordinate research into rare diseases however, like the Australian landscape, none of these are CGT specific. Globally, the International Rare Diseases Research Consortium (IRDiRC) has developed consensus on policies and guidelines for rare disease research with the goal of providing international governance (50). Advice is provided on a range of research activities including diagnostics, patient registries, clinical models, and intellectual property.

Two examples of country specific strategies were identified in Ireland and the US. In 2018, Ireland established the "Rare disease research partnership (RAinDRoP)" to engage students and established researchers to identity research priorities for rare diseases (51). Their focus is twofold (52):

1. Ensure there is coherent research informed by people living with rare diseases and
2. Identify research priorities that align with multiple stakeholders' views.

The National Institute of Health Research Programs in the US promotes translational research on rare diseases, with an emphasis on diagnostics and interventions (53).

2 Establish Office for Rare Diseases as Portfolio Agency of Department of Health.

The second recommendation from the ***CGT: Rising to the challenge*** white paper seeks the establishment of an office responsible for the consideration of rare diseases as a portfolio agency of the Federal Department of Health (now the Department of Health and Aged Care) (DoHAC). Functions of the office include informing regulation and reimbursement processes and governance of patient registries (1). To measure progress of this recommendation three indicators were developed:

2.1 There is an Office for Rare Diseases;
2.2 There are mechanisms or working groups which include State and Territory Governments and patients to inform regulation and reimbursement process for CGTs; and
2.3 There is a national register for rare diseases with national registry standards relevant to CGTs.

2.1 There is an Office for Rare Diseases.

Not achieved

This indicator has not been achieved. As shown in Table 1, several reports have called for the establishment of an Office for Rare Diseases including the ***New Frontier Inquiry, National Strategic Action Plan for Rare Diseases*** and ***McKell Institute Report***. However, there is currently no Office for Rare Diseases in Australia, nor any plans identified to establish one.

Global progress

Internationally there has been significant progress made on the establishment of an Office for Rare Diseases or equivalent in the US and Ireland. The US legislated the Rare Disease Act in 2002 which permitted the establishment of an Office for Rare Diseases (53). In Ireland, the National Rare Disease Office (NRDO) operates in partnership with the Royal College of Physicians of Ireland and the government's Health and Safety Executive (54).

2.2 There are mechanisms or working groups which include State and Territory Governments and patients to inform regulation and reimbursement process for CGTs.

Not achieved

This indicator has not been achieved as there are no mechanisms or working groups that include patients and State/Territory Governments tasked with informing HTA processes for CGTs.

In 2019, Australia developed an HTA Consumer Evidence and Engagement Unit under the Technology Assessment and Access Division within DoHAC (55). The HTA Consumer Evidence and Engagement Unit engages both patient and consumer groups during individual submissions to the PBAC and MSAC, not broader HTA processes. The Patient Voice initiative identified that patients were not aware of the Unit and did not understand how they can contribute to the HTA process (55).

Global progress

There are several countries with mechanisms or working groups to inform regulation and reimbursement, with progress being made in the UK. In the UK, the National Institute for Health and Care Research (NIHR) Innovation Observatory engages patients and carers perspectives when setting regulatory application priorities for (56). The Rare Disease Advisory Group (RDAG) in Scotland, Wales and Northern Ireland provides Clinical Priorities Advisory Group (CPAG) which in turn makes recommendations to the NHS in England on prioritisation of funding for services, treatments and technologies (57). RDAG membership includes representatives from the Royal Colleges, a geneticist, NHS staff and the Department of Health.

2.3 There is a national register for rare diseases with national registry standards relevant to CGTs.

Partially achieved

Development of registry standards is currently underway in Australia. Rare Voices Australia and Monash University have recently published a review of Australian rare disease registries and are working towards a national approach to data collection and reporting (58). This program works toward partial achievement of this indicator.

There is also increased collaboration in the linkage and sharing of health care administrative databases more broadly (59). Data linkage is challenging across all health sectors. However, its success will improve analytical power for monitoring effectiveness and safety of health interventions. For example, linkage of Medicare records holding information on genetic testing and inpatient hospital data can inform the impact of genetic disease on health service utilisation including use of CGTs (60).

Global progress

In the US, the National Centre for Advancing Translation Science (NCATS) recently launched a website called the Rare Disease Registry Program (RaDaR) (61). The website is an initiative aimed at providing best practice guidance on setting up registries specific to rare diseases (61). Also in the US, the National Organisation for Rare Disorders (NORD) developed the 'IAMRARE' Registry Program with input from the FDA, NIH, patients and subject matter experts (62).

The UK BioBank and the 100,000 Genomes project improve rare disease data collection (63). Specific to CGTs these projects are important for genetic sequencing and genetic markers. The 100,000 Genomics Project is a British initiative which sequences and studies the role of gene in health and disease. The 100,000 Genomics Project works closely with the NHS and is the largest genomic health care data resource globally. This project identifies the location of genetic variants contributing to diseases (64).

3 Establish a CGT expert advisory group to provide input and advice to TGA, PBAC, and MSAC.

The third recommendation from the ***CGT: Rising to the challenge*** white paper acknowledges the importance of establishing an expert advisory committee for CGTs. This advisory committee will have a similar role to that provided by the Australian Technical Advisory Group on Immunisation (ATAGAI) and TGA's Advisory Committee on Biologicals (ACB). Membership of the proposed committee should include clinicians and State and Territory representatives (1).

To measure progress of this recommendation two indicators have been developed, namely:

3.1 A CGT expert advisory group has been established either within the Office of Rare Diseases, DoHAC or another organisation; and
3.2 The membership of each HTA includes a dedicated bioethicist.

3.1 A CGT expert advisory group has been established either within the Office of Rare Diseases, DoHAC or another organisation.

Partially achieved

It is important to note that the ***New Frontiers*** report acknowledges the need for expert input into CGTs. The Government response to the recommendations in this report is currently underway and presents an opportunity to establish such a group. In recognition of this process this indicator has been rated as 'some progress achieved'.

Stakeholders have acknowledged that access to leading expertise on CGTs is a key challenge. Specialist expertise is important. Research revealed that there is currently a reliance on "knowing the right person" or using informal networks to access subject matter expertise. This indicates that there are insufficient mechanisms in place to connect CGT experts with decisions about the establishment of regulatory and reimbursement pathways.

In Australia, there are two groups focusing on the CGT landscape which may provide access to experts in the future:

1. The Regenerative Medicine Advisory Group (RMAG) was formed in 2016 and provides advice on both recent and upcoming issues and innovations in the regenerative medicine sector in Australia and overseas (65). RMAG facilitates engagement within the sector under a universal definition of regenerative medicines.

2. The TGA formed the ACB in 2012 and this committee provides independent advice to the Minister for Health and the TGA on the safety and efficacy of biologicals including some cell therapies classified as biologicals (66).

Global progress

Globally, there has been significant progress towards the establishment of CGT expert advisory groups. Australia falls short of international examples. The UK has expert advisory groups in the CGT landscape. The Cell and Gene Therapy Advisory Committee (CGTAC) emphasises the importance and the benefits of CGTs to patients and the broader UK economy (67). CGTAC membership includes a number of stakeholders including key organisations such as the Cell and Gene Therapy Catapult (67).

In the US, the FDA's Cellular, Tissue, and Gene Therapy Advisory Committee consists of 13 voting members (68). Formally known as the Biological Response Modifiers Advisory Committee, these subject matter experts are involved in the review of safety and efficacy of CGTs.

3.2 The membership of each HTA includes a dedicated bioethicist.

Not achieved

This indicator has not been achieved. There is no dedicated bioethicist in either the PBAC or MSAC. While there are members with qualifications in bioethics, there is no formal mechanism for ensuring ethics forms part of the consideration (69, 70).

Global progress

Both the US and UK are exemplars of progress that has been made internationally.

For example, in the US there is direct ethics input into the HTA process from the Cellular, Tissue and Gene Therapies Advisory Committee (68). The specialist expertise of this committee assists regulators with identifying ethical issues. Furthermore, the working group is involved in the development of CGT processes and regulatory frameworks. In the US the Cellular, Tissue, and Gene Therapies Advisory Committee in the FDA also have a dedicated bioethicist.

The UK's Gene Therapy Advisory Committee (GTAC) and the Advanced Therapy Medicinal Products committee incorporates the Ethics Academy (71). The gene therapy expert advisory committee collaborate with other Government agencies and the GTAC Secretariat under the Department of Health for England . However, the GTAC is not directly involved in the HTA process.

4 Enhance the role of horizon scanning via the Health Technology Reference Group, or equivalent.

The fourth recommendation from the ***CGT: Rising to the challenge*** white paper encourages the re-establishment of horizon scanning via the Health Technology Reference Group or equivalent (1). This recommendation is also consistent with the findings of the review of Council of Australian Governments (COAG) Councils and Ministerial Forum (1).

The HTA Reference group will be involved in identification of priority areas and populations who have unmet needs (1). It will liaise with HTA bodies and undertake assessment to provide timely access to care for patients (1).

To measure progress of this recommendation one indicator has been developed, namely:

4.1 There is a formalised Government process for conducting horizon scanning that interface with regulation, reimbursement, and clinical infrastructure.

4.1 There is a formalised Government process for conducting horizon scanning, that interfaces with regulation, reimbursement, and clinical infrastructure.

Partially achieved

While there are no formalised processes for horizon scanning, that interfaces with regulation, reimbursement, and clinical infrastructure as per the indicator, there is partial progress in this area. In 2003, a committee under the COAG was established to undertake horizon scanning. This committee was disbanded in 2017. In 2021, Medicines Australia together with the Commonwealth Government announced the five-year Strategic Agreement which includes an annual horizon scanning forum (60).

The purpose of this forum is to identify 'therapeutic advancements' that will go through regulatory and reimbursement processes in the next 18-24 months. The inaugural forum was held in December 2022 with a report pending.

In line with the strategic plan, Bristol Myers Squibb (BMS) and AusBiotech have also contributed to the progress of this indicator:

- BMS recently published a report exploring current horizon scanning activities in the Australian system (56). The independent third party report was informed by 25 PAGs and funded by the Commonwealth Government (56).
- AusBiotech published the Australia's Regenerative Medicine Global Tracker (6). This tracker scans all products in the global pipeline including CGTs.

Global progress

Horizon scanning is prioritised in the UK. The National Institute for Health Research Innovation Observatory (NIHR) undertakes regular horizon scanning (72, 73).

5 The Minister for Health to establish a cross-functional working group including the Department of Health (Federal and State/Territory), industry, patients, and academics to consider current Health Technology Assessment processes for CGTs.

The fifth recommendation from the ***CGT: Rising to the challenge*** white paper encourages the opportunity to align HTA with the expectations of society. This recommendation puts an emphasis on the equity of access for the most vulnerable citizens (1).

To measure progress of this recommendation two indicators have been developed, namely:

5.1 Patients are being treated equitably across jurisdictions for access to CGTs using transparent and sustainable agreements; and

5.2 HTA processes for CGTs have been reviewed.

5.1 Patients are being treated equitably across jurisdictions for access to CGTs using transparent and sustainable arrangements.

Partially achieved

Ensuring there is a standardised approach to early access to CGTs regardless of a patient's geographical location is important. Whilst some CGTs have been made available in Australia, stakeholders noted that there are often delays in patient access due to malalignment of State/Territory and Federal delivery and funding frameworks. For example, The newborn blood screening program is funded by States and Territories, however, CGTs for inheritable diseases are funded by the Commonwealth (74).

Stakeholders identified that coordination of delivery of CGTs is uncertain and differs between jurisdictions. Hospitals were considered inexperienced for delivery and patient follow-up for CGTs.

In addition, co-dependent submissions for CGTs involve dual submissions to both the PBAC (for the intervention) and MSAC (for the companion diagnostics) and this can lead to delays in HTA approval.

A coordinated Government approach to patient access to clinical trials or early access schemes was rated by Patient Advisory Groups as a top four priority for the next five years. **(Partially achieved)**

Global progress

The UK has adopted a hub and spoke approach to the coordination of delivery of CGT care throughout the NHS. For example, in the UK the Advanced Therapy Treatment Centres (ATTC) have a nationally coordinated approach for the delivery of CGTs (75). The ATTC provide Model of Care frameworks through three ATTCs within the UK.

5.2 HTA processes for CGTs have been reviewed

Some progress achieved

A review of the HTA processes in Australia is currently underway (42). The committee responsible for this review includes Government, industry, the health sector, and patients. As part of this review, the committee will consider methods for evaluating current funding pathways for emerging technologies (including CGTs). The HTA review committee's Terms of Reference have been published with public consultation opening in April 2023 (42), therefore, this indicator has been rated as 'some progress achieved'.

To complement this, the PBAC has undertaken a review on the discount rate to assess if the current rate of five per cent aligns with international best practice (76). After considering stakeholder input and advice from industry and government sub-committees, the PBAC recommended not to change the base. However, it was noted that the PBAC should highlight in their guidelines that it does consider a range of base-rates (zero to three per cent) in certain circumstances. In addition, the PBAC recommended should the base-discount rate be no lower than 3.5 per cent per year in the HTA review. A response to the PBAC recommendation will be included in the HTA review which is currently underway.

Global progress

Globally there has been significant progress made on this indicator. For example, in the UK, NICE has put forward consideration to include Precision Medicines (including CGTs) as a priority in their methods review. Both Germany and France have implemented post 'listing' data collection to inform annual health technology reassessments for gene therapies (77). The Institute for Clinical and Economical Research (ICER) has also developed guidelines for short term and transformative therapies specifically including CGTs (78).

6 Develop national strategic approach to equitable and timely clinical care for CGT via the NHRA framework.

CGTs have complex in-hospital patient delivery protocols for relatively small populations and as such can only be delivered in select locations, often referred to as Centres of Excellence. The Australian population is geographically dispersed and consequently some patients will need to travel within and across States to access care. This provides challenges for our existing hospital funding models and State-based clinical protocols.

To address these challenges, recommendation six seeks that, under the NHRA, the Federal Government coordinates the standardisation of CGT processes across States and Territories. Standardisation of co-designed referral pathways, patient care pathways, and data collection will improve coordination of cross-border care and build efficiencies into State and Territory health budgets.

To measure progress of this recommendation one indicator has been developed, namely:

6.1 There is a national strategic and co-design approach to CGT access that considers clinical infrastructure, administrative infrastructure and post-marketing infrastructure.

6.1 There is a national strategic and co-design approach to CGT access that considers:
- Clinical infrastructure;
- Administrative infrastructure and
- Post marketing infrastructure.

Some progress achieved

There has been some progress towards a national strategic approach to future-proof clinical and administrative infrastructure for innovative therapies, including CGTs. There is, however, little evidence of infrastructure to support post marketing exercises unique to CGTs.

At a national level, the 2020-25 NHRA provided specific arrangements for ensuring all patients can access therapies in public hospitals (79). The shared funding arrangements between Federal and State/Territory Governments apply to high-cost in-patient therapies approved by the MSAC. State and Territory Governments, as system managers of public hospitals, will determine if, when and where these treatments are delivered.

Some Centres of Excellence have developed procedures and processes around the delivery of CGTs, including cross border arrangements. In NSW, the Ministry of Health is establishing a five-year plan (2023-2028) for delivery of immune effector cell (IEC) therapies (80). However, stakeholders reported that currently there is inequity in CGT access and challenges with some hospitals asserting that they did not have the budget at a certain point in time to be able to deliver the therapy.

In 2017, Australian Health Ministers endorsed the Newborn Bloodspot Screening (NBS) National Policy Framework (81). Health care providers offer newborn bloodspot screening to all babies in Australia. This blood test detects certain rare genetic conditions and metabolic disorders and aims to identify those who could benefit from early intervention. It is envisioned that States and Territories will be able to contribute to this program to ensure timely access to diagnosed newborns.

Government support for research into rare diseases and novel therapies including monitoring of health outcomes was rated by Patient Advisory Groups as a top four priority for the next five years. **(Some progress achieved)**

Global progress

The UK and Europe have made significant progress towards this indicator. The CGT Catapult coordinates clinical, administration and post-marketing infrastructure in the UK (see case study on page 38 for more information). In Europe, Rare Impact undertook a review on improving patient access to cell and gene therapy for rare diseases and made eight recommendations including early dialogue with governments to ensure health system infrastructure resourcing requirements can be met for CGTs (82).

7 Develop incentives for CGTs to create opportunities for trials, manufacturing, and commercial success in Australia.

There have been previous significant Government investments in the research and development of innovative therapies. However, there is a need to ensure incentives cover the lifecycle of a product and are targeted at patient access to CGTs. Recommendation seven seeks Government support for sector incentives across the lifecycle of a CGT including funding that is targeted at patient access.

Two indicators were developed to evaluate progress towards achieving Recommendation seven, namely:

7.1 There are incentives for clinical trials to support CGT research; and
7.2 There are incentives for manufacturing and commercial success for translating CGT research.

7.1 There are incentives for clinical trials to support CGT research.

Partially achieved

In Australia, there are several projects underway to support both implementation and patient access to clinical trials. The Government continues to provide funding for clinical trials in innovative therapies and several organisations are coordinating efforts to streamline access to clinical trials. For example:

- The Federally funded Clinical Trials Activity initiative which addresses rare cancers, rare diseases and unmet needs will provide $750 million over 10 years from 2022-23 (83).
- A national research platform or 'one stop shop' is being developed by the Australian Commission on Safety and Quality in Health Care (ACSQHC). The stakeholder consultation phase is complete and implementation is due early 2023 (84, 85). This research platform will provide a cross jurisdictional database for clinical trial approvals, registries, and outcomes. It is envisaged that this platform will also facilitate patient recruitment.
- The Murdoch Children's Research Institute (MCRI) and the Australian Friedreich Ataxia Stem Cell and Gene Therapy Consortium are collaborating to fast track clinical trials in Australia and internationally (86).
- The Australian Clinical Trials Alliance (ACTA) has provided guidance on establishing and administering a clinical trial network. There are currently 74 members in Australia each working towards improving the quality of clinical trial outcomes through large-scale efficiencies (87, 88).
- The Sydney Children's Hospital Network supported the streamlining of approval processes for CGTs. It suggested decreasing the time it took to obtain a licence from the Office of the Gene Technology Regulator (OGTR) as this was seen as a barrier to bringing clinical trials to Australia (55).
- The Centre for Biopharmaceutical Excellence (CBE) was launched in September 2022 supported by the MTPConnect REDI initiative (89). This is a consultancy service to provide advice to industry on a range of pre-marketing activites and commercialisation.

The above programs demonstrate that progress on this indicator has been partially achieved.

Global progress

Again, the UK is the most advanced country in terms of supporting clinical trials to be undertaken either within the UK or with international collaborators. The CGT Catapult clinical trials database provides information about CGT trials being conducted within the UK. For more information, see our case study – ***UK: Rising to the challenge of CGTs.***

7.2 There are incentives for manufacturing and commercial success for translating CGT research.

Partially achieved

There are multiple projects underway to support manufacturing and commercial success for translating CGT research in Australia. However, there remains a piece-meal approach as several initiatives are not CGT specific and can be either Federal or State-based. This indicator is therefore partially achieved.

To address the issue, AusBiotech's Regenerative Medicines Consortium Programme has published a strategic roadmap, Catalysing Regenerative Medicines in Australia, which highlights priority action areas for industry and government. This is a 12-month programme funded by an MTPConnect grant (90). To date this consortium has also published several reports addressing workforce planning, a sustainable funding model, regulatory and investment opportunities.

Nationally, the TGA's Clinical Trial Notification (CTN) scheme has been designed to facilitate clinical trials for unapproved therapeutic goods (91). Under this scheme, trials which have already been approved by an overseas regulator, such as the EMA or the FDA, are automatically approved to also conduct trials in Australia. The alternative scheme, the Clinical Trial Application (CTA) process, was viewed as less favourable than the CTN scheme as it involved significant administrative burden due to processes that were distinct to overseas regulators. Unfortunately, some Class 4 biologicals (another definitional distinction unique to Australia), such as the gene modified cell therapy CAR-T, are not able to go through the CTN pathway and must go through CTA. This is considered a barrier to expediting access to patients through trials. The TGA has responded to stakeholder requests in the 2021 MTPConnect report, supported by Evohealth, on the CGT regulatory framework, stating that it will endevour to provide education to industry regarding the CTA process and will work with the OGTR to streamline this process (21).

Two Federal tax incentives provide financial incentives for manufacturing and commercialisation. The Research and Development tax incentive was established in July 2011 and provides non-refundable tax offsets for eligible Australian-based research activities (92). Eligible activities include those that are experimental in nature with the objective of generating new knowledge. From July 2022, the Patent Box initiative provides a concessional tax rate to encourage innovation in the medical and biotechnology industry (93).

The NSW government is very active in the CGT manufacturing and commercialisation in Australia. The NSW Government has committed to build a clinical-grade viral vector manufacturing facility in the Westmead Health district (94). This facility will be the first of its kind in Australia with the capacity to produce at scale and meet the growing local and international demand for viral vectors in gene therapy clinical trials in Australia and internationally. In addition, the NSW government is providing support to the State's leading universities, research institutions and hospitals to for mRNA research. This will support workforce training in the development and manufacturing of mRNA technologies to treat infectious diseases, cancers, and genetic diseases (95).

State based initiatives include the NSW Health CGT grants to support commercialisation (96).

Global progress

Both the US and UK have national programs which specifically target manufacturing and commercialisation of CGTs.

In the US, the Therapeutics for Rare and Neglected Diseases (TRND) Program has developed a suite of guidance tools to make investment in the development of gene therapy for small markets more appealing to companies (97).

In partnership with NICE, the NHS has launched a £340 million Innovative Medicines Fund (IMF). Together with the existing £340 million Cancer Drugs Fund, the IMF will secure a totoal of £680 million of protected NHS funding to fast-track products that are not considered cost-effective under tradition HTA processes. Through the fund, patients can have managed access until sufficient evidence is generated for these products to be funded under traditional schemes (98).

The UK Regenerative Medicine Platform operates five interdisciplinary and cross-institutional research hubs. The focus is on bridging the gap between scientific discovery and clinical application. This work provides new tools, protocols, engineering solutions and knowledge to the sector and community (99).

The Cost of Inaction

Australia has made some progress towards achieving the seven recommendations of the *CGT: Rising to the Challenge* white paper. Current evidence reveals that we still have significant challenges ahead to meet international progress so that Australians have the same access to innovation as citizens in comparable countries.

Overall, Australia is lagging with respect to equitable and timely access to CGTs due to systematic deficiencies in our processes for funding approval and clinical application of these novel therapies. There are mechanisms within our health system which could be adapted to meet these needs. Where mechanisms do not currently exist, there are examples of initiatives relevant to CGTs which, given momentum, could lead to exponential progress in this space.

Several countries have made swift progress in the CGT space through governance, leadership, and collaborative networks. This has led to positive outcomes for both patients and industry whilst growing local economies. In ten years since its inception, the UK CGT Catapult has created a collaborative network of national and international stakeholders to provide ten therapies for delivery through the NHS whilst upskilling 5,000 people . See our case study – UK: Rising to the challenge of CGTs for a detailed overview of how the UK has become a world leader in CGTs.

To progress towards a better future for many Australians, there needs to be significant investment in shifting health governance frameworks to align with societal expectations and address the future of medical treatment. If Australia continues to lag internationally, we not only miss the direct opportunity to improve the quality of life for our most vulnerable citizens, but we may also miss multiple opportunities to meaningfully contribute to solutions for future global medical challenges.

Case Study
UK: Rising to the challenge of CGTs

The UK CGT ecosystem is complex with multiple independent agencies collaborating to specifically consider CGTs.

The main organisation providing national frameworks from research to implementation of CGTs is the CGT Catapult, however, within specific regulatory agencies and the National Health Service itself, various aspects relevant to CGTs are considered. A full process flow diagram outlining some key interactions is provided in Appendix B.

Cell and Gene Therapy Catapult

Since its inception in 2012, the CGT Catapult has made tremendous progress in supporting timely access to CGTs (100). The CGT Catapult provides numerous mechanisms to facilitate CGT research translation, commercialisation and their ultimate implementation into clinical trials and practice. This includes generating research funding for priority areas, building workforce capacity, development of clinical models of care. A high-level overview of the coordinated approach taken by the CGT Catapult is provided in Figure 2 below.

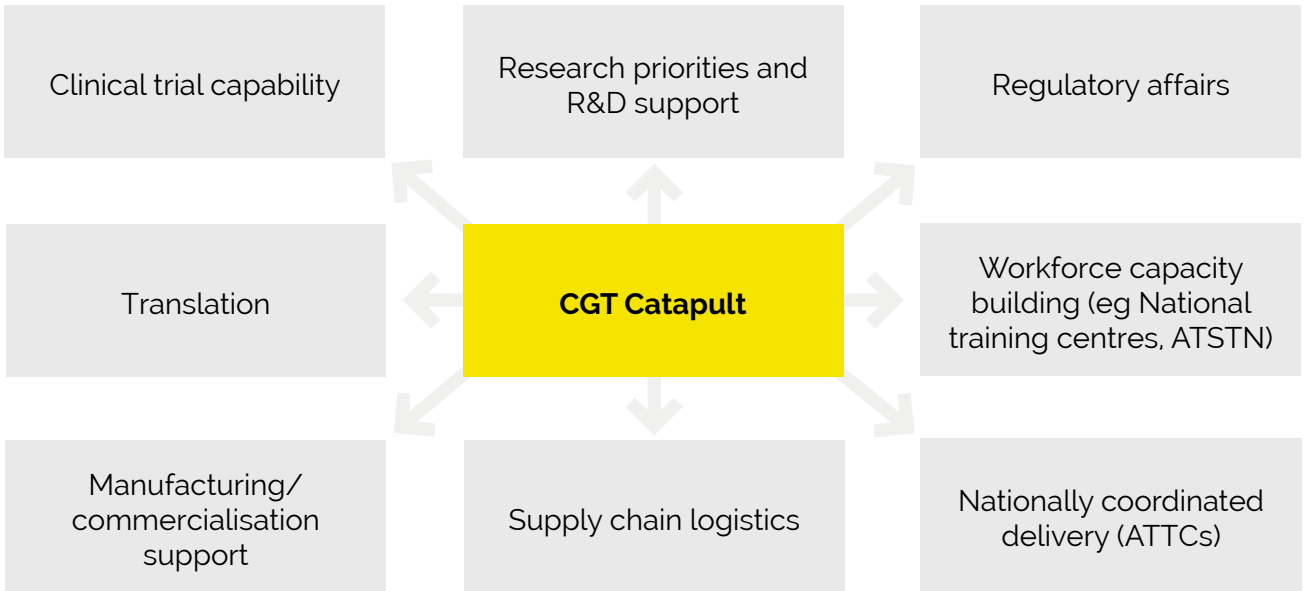


Figure 2 – CGT coordination roles

Innovate UK has established a national network of Catapults to support development and commercialisation of products The CGT Catapult provides national leadership to promote the advancement of CGTs and has established partnerships with various organisations that span the lifecycle of CGTs; from clinical trials through to treatment delivery and patient access.

As of 2022, the CGT catapult has been successful in supporting 163 projects through collaboration with local and international industry, academia, regulators, and consumer representatives (100). The CGT Catapult also conducts annual reviews to monitor progress in the CGT space.

Research, translation, and industry support

The CGT catapult has developed research priority areas for CGTs and provides funding to accelerate translation, including the provision of funding for spin off companies and small medium enterprises (SMEs). The Catapult has also developed the Process Analytical Technologies (PAT) Consortium which comprises various industry representatives in the manufacturing stage. Working together, they are developing processes for expediting manufacturing processes to facilitate commercialisation of CGTs. This knowledge sharing recognises some of the distinct challenges associated with CGTs such as the need for multi-site manufacturing (101). The CGT Catapult monitors progress in this space via production time and costs, the amount of Good Manufacturing Practice (GMP) certified spaces, and industry manufacturing activity.

Horizon Scanning

At the beginning of a CGT lifecycle, information on clinical trials and product development, is fed into the national horizon scanning body, National Institute for Health and Care Research (NIHR) Innovation Observatory (102). The observatory interacts with patient representatives, pharmaceutical companies as well as the regulatory and HTA agencies to ensure all stakeholders are aware of upcoming innovations prior to their market authorisation, including CGTs. The NIHR is the gateway for industry into the UK HTA process. The observatory also provides advice to NICE regarding the eligibility of new CGTs for the Highly Specialised Technology (HST) appraisal process. Specific jurisdictions also provide input to the HTA processes.

At the delivery level, the Accelerated Access Collaborative (AAC) also provides roles of horizon scanning for the UK's universal health care scheme, the National Health Service (NHS), and advises service providers to help expedite adoption of health innovations. An AAC Scorecard has also been developed to monitor the impact of the AAC, which includes monitoring jobs created and the number of patients/sites accessing treatments and diagnostics.

Accelerated and Equitable Access

While not always specific to CGTs, equity is considered throughout the lifecycle from market approval through to reimbursement and delivery, particularly for CGTs that target small patient populations with severe conditions and unmet needs. At the market approval stage, the Medicines and Healthcare products Regulatory Agency (MHRA) can consider the Innovative Licencing and Access Pathway (103). This pathway can allow for early market entry and considers whether the intervention is for a life-threatening or seriously debilitating condition as well as if there is significant unmet need.

At the HTA stage, equity is explicitly considered via routing technologies into the aforementioned HST Programme as well as by applying a 'severity modifiers' to health gains for severe and debilitating conditions (104). These modifies also consider the comparative standard of care and thus 'unmet need' (105). The HST Programme has a different willingness-to-pay threshold (43). All else equal, these processes provide a framework for treatments targeting populations with severe conditions to be prioritised when considering public reimbursement. Innovative medicines for rare disease will be considered under the IMF, including CGTs (98). Early access schemes may also be considered. To facilitate accelerated access in the UK, outcomes-based funding has been employed for some CGTs, such as CAR-T cell therapies. Aside from ongoing follow-up reported in trials, real world evidence collection, via registries and other national datasets, have been used to inform outcomes based funding (106).

Other CGTs not considered cost effective via the traditional pathway may also fall under the remit of 'Specialised Services' and be funded by specific hospitals across the country. Prioritisation of services for the Specialised Services arm is informed by engagement with the CPAG and the Rare Diseases Advisory Group (RDAG). This ensures priority groups, including patients with rare diseases and unmet need, are considered. The commissioning of Specialised Services is prioritised and reviewed annually.

System readiness and upskilling

Subsequent to public funding, novel CGTs may be eligible for Innovation and Technology Payments to facilitate their implementation into clinical practice (107). These aim to reduce financial and procurement barriers.

Nationally coordinated delivery of CGTs, and the associated Model of Care frameworks, also occurs via three Advanced Therapy Treatment Centres (ATTCs) strategically positioned in the UK. Up-skilling of NHS staff also occurs through these ATTCs as well as development of administrative and data collection processes (108). Specific training programmes have been developed for Advanced Therapies such as the Advanced Therapy Skills Training Network (ATSTN).

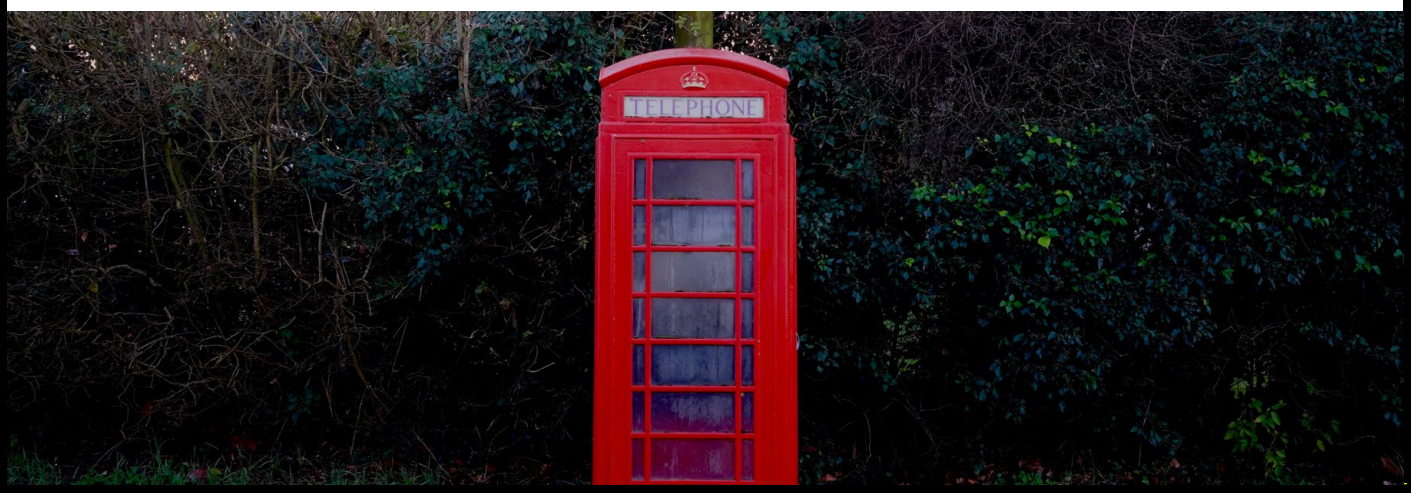
1. Similar priority pathways exist within the European Medicines Agency (EMA) and are being considered by the Therapeutic Goods Association (TGA).
2. Specifically, Quality-adjusted Life Years (QALYs), whereby the eligibility is determined based on the absolute QALY shortfall experienced by the patient population relative to the general population.

The following presents key outcomes as monitored in the 2022 CGT Catapult Annual Report (100):

- **Ten CGTs reimbursed** on the NHS
- ATTC NHS readiness toolkit accessed **over 17,000 times**
- **48 Phase 3** clinical trials conducted
- **6,900** jobs created
- **5,000 people** upskilled in Advanced Therapies
- **59 international collaborations**
- **154 company collaborations**
- **23 companies supported** that are operating CGT clinical trials
- **26 GMP manufacturing facilities** in the UK, with a 39,000 m2 GMP footprint
- **£5.5 billion pounds** raised for CGT Catapult activities

Challenges

The UK has positioned itself as a world leader in provision of CGTs. However, like other markets, the UK continues to face challenges with respect to uncertainty around long term outcomes, small patient populations and trials, decentralised manufacturing and delivery, payer sustainability, and comprehensive and consistent national data collection (77, 101, 106). The CGT Catapult goes a long way in recognising some of the unique challenges posed by CGT and demonstrates how improvements can be made in this space as well as identifying ongoing priorities.



Next Steps

Australia has a long history of prioritising health care. As a nation, we accept that care needs to be made readily available to our most vulnerable. Amongst these are the patients that need access to transformative therapies.

The existing health care system does not always enable this access due to the inherent differences between CGTs and conventional medicines. This presents a challenge. In 2021, Evohealth's white paper, CGTs: Rising to the Challenge, presented several recommendations to comprehensively address the gaps in enabling future of medical innovation.

In this scorecard we have updated this research and examined what progress, if any, has been made. In doing this we found that many other stakeholders share the same view. These ***Collective Voices*** from government, industry, research, and patient advocacy shared not only the same concerns regarding the current State of preparedness for CGTs but advocate for similar recommendations to the Evohealth white paper.

We also asked patient groups to prioritise actions for change. Their top priorities were:

- Ensuring the health workforce and health system has the capacity to deliver CGTs in a timely manner;
- A coordinated Government approach to ensuring equitable access to CGTs patient access to clinical trials or early access schemes; and
- Government support for research into rare diseases and novel therapies including monitoring of health outcomes.

CGTs: Rising to the challenge

Australia, once the exemplar of HTA globally, now lags when it comes to preparedness for CGTs. The UK is leading the way, demonstrating how these innovations can be valued and made available to patients in the shortest possible time.

There is much to do for Australia to rise to the challenge. The indicators presented in this scorecard are designed to be remeasured again in the future. To accelerate the rate of progress, we recommend Government to focus on three key areas in the next 12 months:

1 Establish an office for Rare Diseases

The establishment of an Office for Rare Diseases was recommendation one in both the ***CGT: Rising to the Challenge*** white paper and the The New Frontier Inquiry report which received bipartisan support. Establishing this office would achieve significant change toward many of the indicators in this scorecard. The office would coordinate many functions highlighted in the Evohealth report, thereby rising to the challenge towards enabling access to CGTs.

2 Explicitly consider equity for CGTs in the current Health Technology Assessment (HTA) review

Many CGTs will target rare diseases or patient groups with high unmet need. At times, the patient population will be small which will be challenging to evaluate with traditional HTA processes. Transparently considering equity in HTA will align Australia's with that of UK, Norway, Netherlands, Sweden, and Canada, amongst others.

The HTA review terms of reference, released in March 2023, include consideration of equity for several groups including patients with rare and under-recognised conditions (42). However, the HTA review terms of reference are extensive and CGTs will need explicit consideration as they do not fit into current HTA pathways. The first round of consultations will commence in April 2023.

3 Establish a CGT expert advisory group to provide input and advice to TGA, PBAC and MSAC

Much of what has been achieved in the UK has been because they recognise CGTs as having differing requirements from conventional medicines. This would not have been possible without input from those experienced in the unique attributes that make CGTs different. Establishing an expert advisory group to contribute to the considerations of Australia's regulatory and reimbursement framework, will support timely consideration of CGTs.

Abbreviations

Abbreviations	Meaning
AAC	Accelerated Access Collaborative
AAV	Adeno-Associated Virus
ACB	Advisory Committee on Biologicals
ACSQHC	Australian Commission on Safety and Quality in Health Care
ACTA	Australian Clinical Trials Alliance
ANZ	Australia and New Zealand
ASCGT	American Society of Cell and Gene Therapy
ATAGAI	Australian Technical Advisory Group on Immunisation
ATMPs	Advanced Therapy Medicinal Products
ATPs	Advanced Therapy Products
ATSTN	Advanced Therapy Skills Training Network
ATTC	Advanced Therapy Treatment Centers
BIA	British Infection Association
BMS	Bristol Myers Squibb
BSCGT	British Society for Gene and Cell Therapy
CAR-T	Chimeric Antigen Receptor T-cell
CATTI	Canadian Advanced Therapies Training Institute
CCRM	Centre for Commercialisation of Regenerative Medicine
CDF	Cancer Drugs Fund
CGT	Cell and Gene Therapy
CGTAC	Cell and Gene Therapy Advisory Committee
COAG	Council of Australian Governments
CPAG	Clinical Priorities Advisory Group
CTA	Clinical Trial Application
CTN	Clinical Trial Notification

Abbreviations	Meaning
DoHAC	Department of Health and Aged Care (formerly Department of Health)
EMA	European Medicines Agency
FDA	Food and Drug Administration
GHFM	Genomics Health Futures Mission
GMP	Good Manufacturing Practice
HGSA	Human Genetic Society of Australasia
HSTP	Highly Specialised Technology Program
HTA	Health Technology Assessment
ICER	Institute for Clinical and Economic Review
IMF	Innovative Medicines Fund
IRDiRC	International Rare Disease Research Consortium
ISCT	International Society for Cell and Gene Therapy
MBS	Medical Benefits Schedule
MCRI	Murdoch Children's Research Institute
MHRA	Medicines and Healthcare Products Regulatory Agency
MoC	Model of Care
MRFF	Medical Research Future Fund
MSAC	Medical Services Advisory Committee
NBS	Newborn Bloodspot Screen
NCATS	National Centre for Advancing Translation Science
NHMRC	National Health and Medical Research Council
NHRA	National Health Reform Agenda
NHS	National Health Scheme
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NMP	National Medicines Policy
NORD	National Organisation for Rare Diseases
NRDO	National Rare Disease Office

Abbreviations	Meaning
OGTR	Office of the Gene Technology Regulator
PAT	Process Analytical Technologies
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PMPRB	Patented Medicine Prices Review Board
PREMs	Patient Reported Experience Measures
PROMs	Patient Reported Outcome Measures
QUM	Quality Use of Medicines
rAAV	Recombinant Adeno-associated virus
RaDaR	Rare Disease Registry Program
RAinDRoP	Rare disease research partnership
RARE	Raise Awareness Rare Education
RDAG	Rare Disease Advisory Group
REDI	Researcher Exchange and Development within Industry
RMAG	Regenerative Medicine Advisory Group
RVA	Rare Voices Australia
SCHN	Sydney Children's Hospital Network
SME	Small or medium enterprise
TGA	Therapeutic Goods Administration
TRND	Therapeutics for Rare and Neglected Diseases

Appendix A

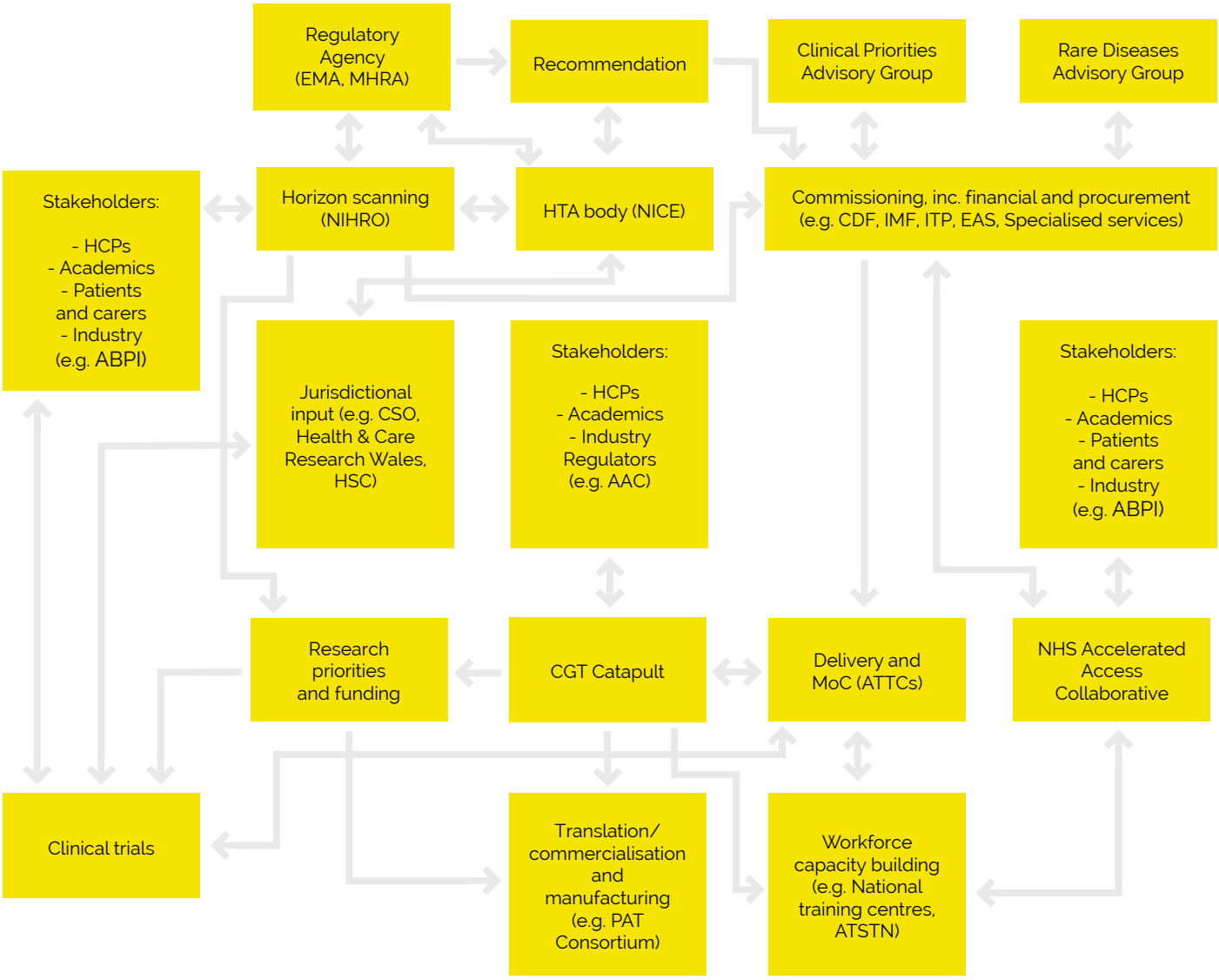
Endorsed criteria for scoring progress on the seven recommendations.

Score	Definition
Not achieved 	There is **no evidence** of progress or planned progress towards achieving this recommendation.
Some progress acheived 	There is **evidence of at least one activity**, **specific to CGTs**, which may support progress towards achieving this recommendation in the future. This includes existing activities prior to the launch of the white paper. For example: this would be the rating for the indicator: **'There is a national education program for consumers'**, as there is evidence of educational materials either developed or in development for specific conditions however, there lacks a nationally coordinated approach.
Partially achieved 	There is **recent evidence** of progress towards this recommendation. For example: this would be the rating for the indicator: **'There is a national research strategy which considers CGTs'**, as there is the NHMRC MRFF targeted grants scheme for CGTs.
Fully achieved	This recommendation has been **achieved**.

Appendix B

Process Flow Diagram of key bodies and stakeholders associated with enabling access to Cell and Gene Therapies in the UK.

The UK has made tremendous progress towards equitable and timely access to CGTs across their full life cycle. A high-level overview of important aspects of the CGT ecosystem and how the various committees and organisations interact with each other is presented below. Full details of each of the agencies and their interdependencies is provided in extensive detail in the CGT Catapult and on distinct agency websites. Additional detail on specific agencies is provided in the main report.



Legend:
AAC - Accelerated Access Collaborative
ABPI - Association of the British Pharmaceutical Industry
ATSTN - Advanced Therapies Skills Training Network
ATTC - Advanced Therapy Treatment Centre of the British Pharmaceutical Industry
CSO - Chief Scientist Office (CSO) Scotland
CDF - Cancer Drugs Fund
EAS - Early Access Scheme
EMA - European Medicines Agency
HCPs - Healthcare providers
HTA - Health Technology Assessment
HSC - Health and Social Care Research and Development Northern Ireland
IMF - Innovative Medicines Fund
ITP - Innovation and Technology Payment
MHRA - Medicines Health and Regulatory Agency
MoC - Model of Care
NHS - National Health Service
NICE - National Institute for Health and Care Excellence

Appendix C

Evohealth reached out to 18 patient advisory groups (PAG). We received 13 PAG responses and we have incorporated these findings into the report. The PAG's that Evohealth contacted include:

- Consumer Health Forum
- Cystic Fibrosis Australia
- Fara Australia
- Fight Duchenne Foundation
- Genetic Alliance
- Genetic Cures Australia
- Genetic Support Network Victoria
- Haemophilia Foundation Australia
- Leukaemia Australia
- Lymphoma Australia
- Macular Disease Foundation Australia
- Myeloma Australia
- Rare Cancers Australia
- Rare Voices Australia
- Save our Sons Duchenne
- SMA (Spinal Muscular Atrophy) Australia
- Thalassaemia and Sickle Cell Australia
- Vision Australia

References

1. Beardmore R, Saxby K. Cell and Gene Therapies: Rising to the Challenge. Canberra: Evohealth; 2020.
2. American Society of Cell and Gene Therapy (ASCGT). Gene & Cell Therapy Education United States: American Society of Cell and Gene Therapy (ASCGT); 2022 [9/6/2022]. Available from: https://asgct.org/.
3. O'Sullivan G, Philips JG, Rasko JE. Clinical gene technology in Australia: building on solid foundations. Medical Journal of Australia. 2022;217(2):65-70.
4. American Society of Gene and Cell Therapy. Gene and Cell Therapy FAQ's: ASGCT; 2022 [Available from: https://asgct.org/education/more-resources/gene-and-cell-therapy-faqs.
5. American Society of Gene and Cell Therapy. Patient Education. Gene Therapy Basics: ASGCT; 2022 [Available from: https://patienteducation.asgct.org/gene-therapy-101/gene-therapy-basics.
6. GlobalData. Australia's Regenerative Medicine Global Pipeline Tracker.: Ausbiotech; 2021.
7. Sharpe M, Barry J, Kefalas P. Clinical Adoption of Advanced Therapies: Challenges and Opportunities. J Pharm Sci. 2021;110(5):1877-84.
8. O'Shea R, Ma SA, Jamieson RV, Rankin NM. Precision medicine in Australia: now is the time to get it right. Medical Journal of Australia. 2022;271(1):559-63.
9. Chisholm O, Critchley H. Future directions in regulatory affairs. Frontiers in Medicine. 2023;9.
10. House of Representatives Standing Committee on Health ACaS. The New Frontier - Delivering better health for all Australians. Canberra. Australia: Commonwealth of Australia; 2021.
11. Australian Government. Department of Health. National Strategic Action Plan for Rare Diseases. Canberra. Australia.: Department of Health; 2020.
12. Australian Patient Advocacy Alliance. 2019 Canberra Health Summit. Consensus Statement.; 2019.
13. House of Representatives Standing Committee on Health ACaS. Inquiry into approval processes for novel drugs and novel medical technolgies in Australia. Canberra, ACT.: Parliament of Australia; 2021 [01/07/2022]. Available from: https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/~/link.aspx?_id=653148D7DE9E43338CC0DFD4626F4429&_z=z.
14. Department of Health and Aged Care. Review of the National Medicines Policy. Published responses. Canberra, ACT: Australian Government.; 2021 [Available from: https://consultations.health.gov.au/technology-assessment-access-division/national-medicines-policy-review/consultation/published_select_respondent.
15. Association of Australian Medical Research Institutes. Australia's Missing Link: A National Health And Medical Research Strategy. Melbourne, Victoria: aamri; 2021.
16. 16. InGeNA, Health Technology Analysts. Realising the full potential of genomics to personalise healthcare. Future directions for health technology assessent in Australia. Melbourne, Victoria: Australasian Institute of Digital Health; 2022.
17. MTP Connect. Precision Medicines. Roundtable White paper. Clayton, Victoria: MTPConnect; 2019.
18. Commonwealth of Australia, Medicines Australia Ltd. Strategic Agreement in realtion to reimbursement, health technology assessment and other matters. Canberra. Australia: Department of Health; 2021.
19. Jackson A, Geatches L. Funding Rare Disease Therapies in Australia. Ensuring Equitable Access to Health Care for all Australians. Sydney, Australia: The McKell Institute; 2021.
20. Department of Health and Aged Care. National Medicines Policy 2022. Canberra, ACT: Australian Government; 2022.
21. Therapeutic Goods Administration (TGA). Report on 'Cell, Gene and Tissue Regulatory Framework in Australia: Stakeholder Perspectives' - TGA response. Canberra, AUS: Australian Government; 2022 [Available from: https://www.tga.gov.au/report-cell-gene-and-tissue-regulatory-framework-australia-stakeholder-perspectives-tga-response.

22. Department of Health and Aged Care. What we're doing about rare diseases. Canberra: Australian Government.; 2022 [20/6/2022]. Available from: https://www.health.gov.au/health-topics/chronic-conditions/what-were-doing-about-chronic-conditions/what-were-doing-about-rare-diseases.
23. Haemophilia Foundation Australia. Publications Victoria: Haemophillia Foundation Australia; 2022 [15/6/2022]. Available from: https://www.haemophilia.org.au/publications.
24. AusBiotech. Publications. Human germline genome editing: fact sheet . 2020.
25. Australian Genomics. Consent and patient support materials Victoria: Australian Genomics; 2022 [Available from: https://www.australiangenomics.org.au/categories/consent/.
26. Rare Voices Australia. Rare Awareness Rare Education (RARE) Portal 2022 [15/6/2022]. Available from: https://rarevoices.org.au/rare-awareness-rare-education-r-a-r-e-portal/.
27. Hutchinson Y. Funding supports Australians living with a rare disease. Sydney, NSW: Universit of New South Wales; 2021 [Available from: https://newsroom.unsw.edu.au/news/health/funding-supports-australians-living-rare-disease.
28. KidsResearch. Network leads gene therapy education program 2022 [Available from: http://www.kidsresearch.org.au/news/network-leads-gene-therapy-education-program.
29. International Society for Cell and Gene Therapy. Key Translational Programs. Vancouver: ISCT; 2021 [Available from: https://www.isctglobal.org/about/key-programs.
30. National Organisation for Rare Diseases (NORD). Rare Disease Database and Online Physician Guides US: NORD; 2022 [Available from: https://rarediseases.org/about/what-we-do/programs-services/.
31. National Institute for Health Research Innovation Observatory. Patient Assistance Programs United Kingdom2023 [28/03/2023]. Available from: https://rarediseases.org/patient-assistance-programs/.
32. British Society of Cell and Gene Therapy. Education Cardiff: BSCGT; 2022 [9/6/2022]. Available from: https://www.bsgct.org/Education.aspx.
33. Centre for Commercialisation of Regenerative Medicine (CCRM) Australia. CCRM Australia and CATTI collaborate on training initiative 2022 [9/6/2022]. Available from: https://ccrmaustralia.com.au/2022/01/25/ccrm-australia-and-catti-collaborate-on-training-initiative/.
34. Australian Genomics. Professional regulation for the genetic counselling workforce in Australia and New Zealand. Victoria: Australian Genomics; 2022 [Available from: https://www.australiangenomics.org.au/professional-regulation-for-the-genetic-counselling-workforce-in-australia-and-new-zealand/.
35. Human Genetics Society of Australasia. Australasian Association of Clinical Geneticists. NSW: HGSA; 2022 [16/6/2022]. Available from: https://www.hgsa.org.au/aacg.
36. Centre for Biopharmaceutical Excellence. GMP Uplift Victoria: CBE; 2022 [Available from: https://cbe-ap.com.au/training/gmp-uplift.
37. The Association of Regulatory and Clinical Scientists. Foundations Bootcamp. North Sydney: ARCS Australia.; 2022 [Available from: https://www.arcs.com.au/events/foundations-bootcamp.
38. Jackson A, Geatches L, Helwani F. Rare Metabolic Disease Workforce White Paper: Towards a Strengthened Rare Disease Workforce for Australia. Victoria: Rare Voices Australia; 2022.
39. Catapult Network. Welcome to the Catapult Network UK: Innovate UK.; 2022 [16/6/2022]. Available from: https://catapult.org.uk/.
40. Catapult Cell and Gene Therapy. 2021 UK Cell and Gene Therapy Skills Demand Survey Report. London; 2021.
41. Cell and Gene Therapy Catapult. CGT Catapult works closely with NHS through Accelerated Access Collaborative to offer pioneering cell and gene treatments. London: Cell and Gene Therapy Catapult; 2022 [16/6/2022]. Available from: https://ct.catapult.org.uk/news-media/general-news/cgt-catapult-works-closely-nhs-through-accelerated-access-collaborative.
42. Department of Health and Aged Care. Health Technology Assessment Policy and Methods Review. Terms of Reference. Canberra, ACT: Australian Government; 2023.
43. Whittal A, Nicod E, Drummond M, Facey K. Examining the impact of different country processes for appraising rare disease treatments: a case study analysis. International journal of technology assessment in health care. 2021;37(1).
44. Canadian Agency for Drugs and Technologies. Guidelines for the Economic Evaluation of Health Technologies: Canada. 4th ed. Ottawa: Canadian Agency for Drugs and Technologies in Health,; 2017.

45. Institute for Clinical and Economic Effectiveness. Advancing Health Technology Assessment Methods that Support Health Equity. Boston: ICER; 2023.

46. National Institute for Health and Care Excellence. Review of methods, processes and topic selection for health technology evaluation programmes: conclusions and final update.
Appendix: Discussion and rationale for conclusions – methods London: NICE; 2022 [Available from: https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation.

47. Australian Genomics. Our project areas. Victoria: Australian Genomics; 2022 [Available from: https://www.australiangenomics.org.au/our-project-areas/.

48. Australian Genomics. New GHFM grants deliver $46.5 million for genomic research 2022 [Available from: https://www.australiangenomics.org.au/new-ghfm-grants-deliver-46-5-million-for-genomic-research/.

49. Rare Voices Australia. Rare Voices Australia and Research. Victoria: Rare Voices Australia; 2022 [15/6/2022]. Available from: https://rarevoices.org.au/research/.

50. International Rare Diseases Research Consortium. POLICIES AND GUIDELINES: International Rare Diseases Research Consortium; 2020 [28/03/2023]. Available from: https://irdirc.orincludeg/wp-content/uploads/2020/05/IRDiRC-Policies-and-Guidelines-May-2020.pdf.

51. Somanadhan S, Nicholson E, Dorris E, Brinkley A, Kennan A, Treacy E, et al. Rare Disease Research Partnership (RAinDRoP): a collaborative approach to identify research priorities for rare diseases in Ireland. HRB Open Res. 2020;3:13-.

52. UCD School of Nursing Midwifery and Health Systems. Rare Diseases Research Partnership (RAINDROP). Dublin, Ireland: University College Dublin; 2023 [Available from: https://www.ucd.ie/nmhs/research/researchdomains/holistichealthandwellbeingacrossthelifecontinuum/rarediseasesresearchpartnershipraindrop/.

53. Khosla N, Valdez R. A compilation of national plans, policies and government actions for rare diseases in 23 countries. Intractable & Rare Diseases Research. 2018;7(4):213-22.

54. Lambert D MR, Jackie T, O'Connell SM, O'Sullivan G, Lynch SA, Traeacy EP. The Irish National Rare Disease Office (NRDO): A national step towards improving access to health and care services for individuals and families living with Rare Diseases. International Journal of Integrated Care. 2017;17(5).

55. Parliament of Australia. Rare Diseases 2022 [Available from: https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/Newdrugs/Report/section?id=committees%2Freportrep%2F024755%2F77601.

56. Prest A, Lapham K, Grainger D. Horizon Scanning Strengthening Australia's approach to horizon scanning for new therapies Sydney, NSW: Biointelect; 2022.

57. National Health Service. Rare Disease Advisory Group Terms of Reference. 2020.

58. Rare Voices Australia. Rare Disease Registry Audit: Key Findings and Project Update 2022 [Available from: https://rarevoices.org.au/rare-disease-registry-audit-key-findings-and-project-update/.

59. Australian Bureau of Statistics. Multi-Agency Data Integration Project (MADIP) 2022 [Available from: https://www.abs.gov.au/about/data-services/data-integration/integrated-data/multi-agency-data-integration-project-madip.

60. Medicines Australia. Strategic Agreement 2022-2027. Building a Future for Earlier Access to New Medicines. 2022.

61. National Health Centre for Advancing Translation Services. Rare Diseases Registry Program (RaDaR) 2022 [Available from: https://ncats.nih.gov/radar#:~:text=NCATS%20launched%20the%20Rare%20Diseases,a%20specific%20diagnosis%20or%20condition.

62. National Organisation for Rare Diseases (NORD). IAMRARE Registry Program 2021 [Available from: https://rarediseases.org/iamrare-registry-program/.

63. Genomics England. 100,000 Genomes Project 2022 [14/6/2022]. Available from: https://www.genomicsengland.co.uk/initiatives/100000-genomes-project.

64. UKBiobank. Improved diagnosis of rare diseases using shared common disease genetic architectures 2021 [14/6/2022]. Available from: https://www.ukbiobank.ac.uk/enable-your-research/approved-research/improved-diagnosis-of-rare-diseases-using-shared-common-disease-genetic-architectures#:~:text=Using%20UK%20Biobank%20data%20provides,will%20provide%20annual%20progress%20updates.

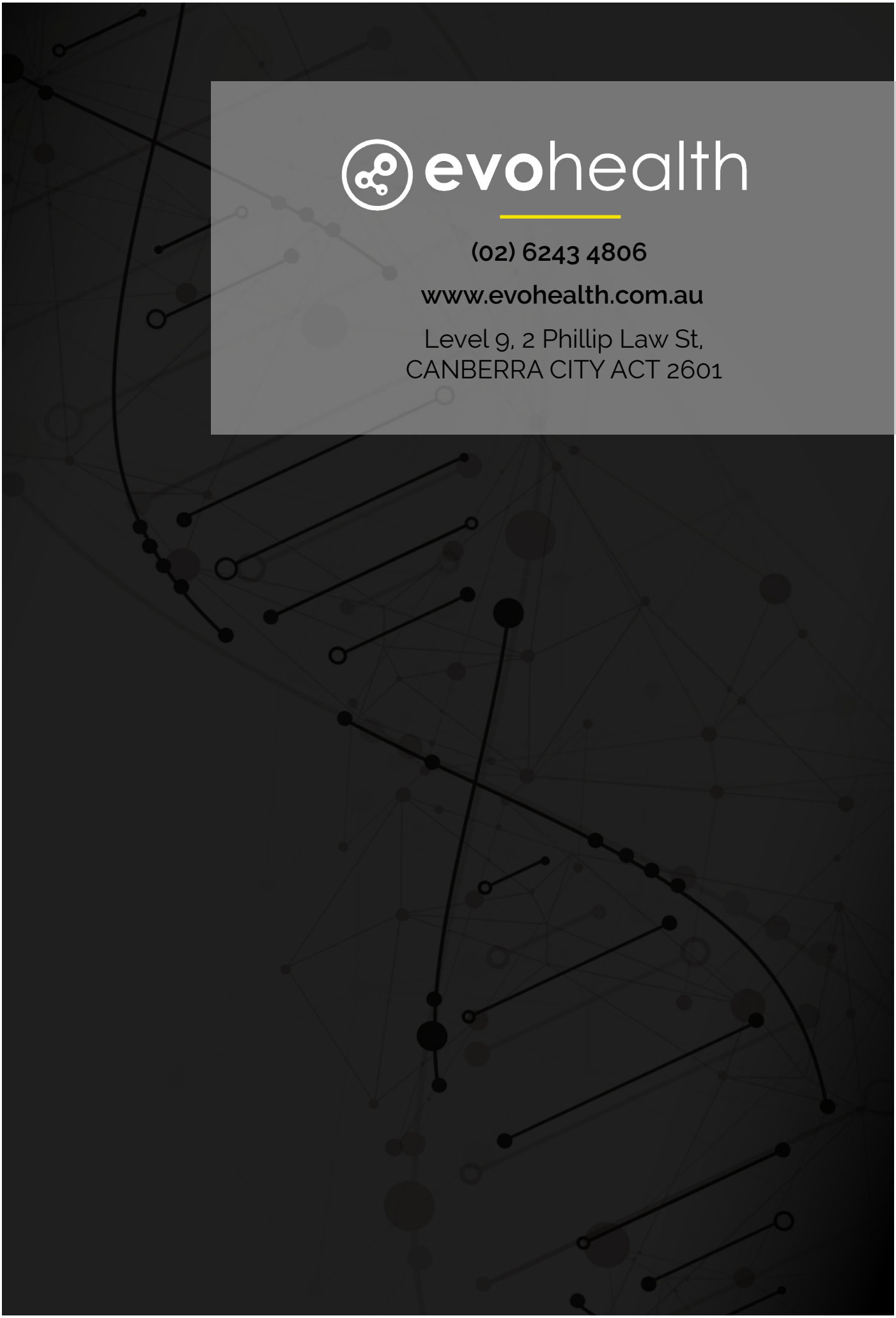
65. AusBiotech. Regenerative Medicine Advisory Group 2022 [Available from: https://www.ausbiotech.org/

about-us/regenerative-medicine-advisory-group.

66. Therapeutic Goods Administration (TGA). Advisory Committee on Biologicals (ACB) Canberra, Australia2022 [9/6/2022]. Available from: https://www.tga.gov.au/committee/advisory-committee-biologicals-acb.
67. British Infection Association (BIA). Cell and Gene Therapy Advisory Committee (CGTAC) 2022 [9/6/2022]. Available from: https://www.bioindustry.org/bia-membership/advisory-committees/cell-gene-therapy-advisory-committee.html.
68. Food and Drug Adminstration. Cellular, Tissue, and Gene Therapies Advisory Committee Washington: U.S. FDA; 2019 [20/7/2022]. Available from: https://www.fda.gov/advisory-committees/blood-vaccines-and-other-biologics/cellular-tissue-and-gene-therapies-advisory-committee.
69. Pharmaceutical Benefits Scheme (PBS). Pharmaceutical Benefits Advisory Committee (PBAC) Membership 2021 [Available from: https://www.pbs.gov.au/pbs/industry/listing/participants/pbac.
70. Medical Services Advisory Committee. MSAC Membership 2022 [Available from: http://www.msac.gov.au/internet/msac/publishing.nsf/Content/msac-membership.
71. Department of Health and Social Care. Independent Report Gene Therapy Advisory Committee (GTAC) annual report 2010: UK Government; 2012 [20/6/2022]. Available from: https://www.gov.uk/government/publications/gene-therapy-advisory-committee-gtac-17th-annual-report.
72. Woltmann J. Reviewing The Effectiveness of UK Drug Horizon Scanning Efforts & The Production of NICE Commentary Along Therapeutic Specialties. Value in Health. 2017;20(9):A694-A5.
73. National Institute for Health and Care Excellence (NICE). NICE topic selection process for technology appraisals (TA) and highly specialised technologies (HST) 2022 [Available from: https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/topic-selection-flowchart.pdf.
74. Australian Health Ministers' Advisory Council. Newborn Bloodspot Screening. National Policy Framework. In: Department of Health, editor. Canberra, ACT: Department of Health.; 2017.
75. The Advanced Therapy Treatment Centres (ATTC) Network. Advanced Therapy Treatment Centres 2020 [9/6/2022]. Available from: https://www.theattcnetwork.co.uk/resources.
76. Pharmaceutical Benefits Advisory Committee (PBAC). Review of the base-case discount rate in the PBAC Guidelines. Public Summary document. Canberra, ACT: Australian Government; 2022.
77. Jørgensen J, Kefalas P. The use of innovative payment mechanisms for gene therapies in Europe and the USA. Regenerative Medicine. 2021;16(4):405-22.
78. Institute for Clinical and Economic Review. Adapted Value Assessment Methods for High-Impact "Single and Short-Term Therapies" (SSTs): Institute for Clinical and Economic Review; 2019 [28/03/2023]. Available from: https://icer.org/wp-content/uploads/2020/10/ICER_SST_FinalAdaptations_111219.pdf.
79. Department of Health and Aged Care. 2020-25 National Health Reform Agreement (NHRA). Canberra; 2020.
80. NSW Government. NSW Immune Effector Cell Thrapy service plan (2023-28). In: Health, editor. NSW: Strategic Reform and Planning Branch; 2022.
81. Department of Health and Aged Care. Newborn Bloodspot Screening. Canberra: Australian Government; 2017 [20/7/2022]. Available from: https://www.health.gov.au/initiatives-and-programs/newborn-bloodspot-screening#:~:text=The%20Australian%20Health%20Ministers%20Advisory%20Council%20%28AHMAC%29%20endorsed,be%20added%20or%20removed%20from%20the%20NBS%20programs.
82. Rare Impact. Improving patient access to gene and cell therapies for rare diseases in Europe. France.: EURORDIS. Rare Diseases Europe.; 2020.
83. Australian Government Department of Health and Aged Care. Clinical Trials Activity Initiative 2022 [Available from: https://www.health.gov.au/initiatives-and-programs/clinical-trials-activity-initiative.
84. Australian Clincial Trials Alliance. National platform for health and medical research 2021 [Available from: https://clinicaltrialsalliance.org.au/latest-news/national-one-stop-shop/.
85. Australian Commission on Safety and Quality in Health Care. The National One Stop Shop - a national platform for health-related human research Australia: Australian Commission on Safety and Quality in Health Care; 2023 [28/03/2023]. Available from: https://www.safetyandquality.gov.au/national-one-stop-shop-national-platform-health-related-human-research.
86. Murdoch Children's Research Institute (MCRI). Australian Friedreich Ataxia Stem Cell and Gene Therapy Consortium 2022 [Available from: https://www.mcri.edu.au/research/projects/FAConsortium.
87. Nemeh F, Buchbinder R, Hawley CM, Nelson MR, Waterkeyn JG, Reid CM. Activities supporting the growth of

Clinical Trial Networks in Australia. Trials. 2022;23(1):81.

88. Australian Clincial Trials Alliance. About ACTA Australia: Australian Clincial Trials Alliance; 2023 [28/03/2023]. Available from: https://clinicaltrialsalliance.org.au/about-acta/.
89. Centre for Biopharmaceutical Excellence. CBE Victoria, AUS: CBE; 2023 [Available from: https://cbe-ap.com.au/.
90. AusBiotech. Regenerative Medicines Consortium Programme 2022 [Available from: https://www.ausbiotech.org/programs/regenerative-medicines-catalyst-project.
91. Therapeutics Goods Administration (TGA). Clinican trials Canberra, Australia2022 [9/6/2022]. Available from: https://www.tga.gov.au/clinical-trials.
92. Australian Tax Office. Research and development tax incentive Canberra: Australian Government; 2020 [16/8/2022]. Available from: https://www.ato.gov.au/Business/Research-and-development-tax-incentive/.
93. Shaw T, Knight T, Munro R, Ickeringill T, Ladd S, McGarity S. A (further) update on the Australian Patent Box. Melbourne: Allens Linklaters; 2022 [16/8/2022]. Available from: https://www.allens.com.au/insights-news/insights/2022/02/A-further-update-on-the-Australian-Patent-Box/.
94. New South Wales (NSW) Government. Viral Vector Manufacturing Facility Stage 2 2022 [Available from: https://www.hinfra.health.nsw.gov.au/projects/project-search/viral-vector-manufacturing-facility-stage-2.
95. New South Wales (NSW) Government. Action on mRNA primes NSW to lead in combating global disease 2022 [Available from: https://www.medicalresearch.nsw.gov.au/action-on-mrna-primes-nsw-to-lead-in-combating-global-disease/.
96. New South Wales (NSW) Government. Gene and Cell Therapy Grants. NSW: NSW Government; 2022 [Available from: https://www.medicalresearch.nsw.gov.au/cell-gene-therapy/.
97. National Center for Advancing Translational Sciences. Therapeutics for Rare and Neglected Diseases (TRND) 2022 [Available from: https://ncats.nih.gov/trnd#:~:text=TRND%20program%20supports%20preclinical%20development,New%20Drug%20(IND)%20application.
98. National Health Service. NHS England announces new Innovative Medicines Fund to fast-track promising new drugs 2021 [Available from: https://www.england.nhs.uk/2021/07/nhs-england-announces-new-innovative-medicines-fund-to-fast-track-promising-new-drugs/.
99. UK Government. Cell and gene therapy: develop new treatments in the UK: UK Government; 2018 [14/6/2022]. Available from: https://www.gov.uk/government/publications/cell-and-gene-therapy-develop-new-treatments-in-the-uk/cell-and-gene-therapy-develop-new-treatments-in-the-uk.
100. CATAPULT. Cell and Gene Therapy. Cell and Gene Therapy Catapult. Annual Review 2022. Ten years of accelerating innovation in cell and gene therapies. London, UK.: CATAPULT CGT.; 2022.
101. Harrison RP, Ruck S, Medcalf N, Rafiq QA. Decentralized manufacturing of cell and gene therapies: Overcoming challenges and identifying opportunities. Cytotherapy. 2017;19(10):1140-51.
102. NIHR Innovation Observatory. NIHR Innovation Observatory United Kingdom2023 [28/03/2023]. Available from: https://www.io.nihr.ac.uk/.
103. Medicines and Healthcare products Regulatory Agency. Innovative Licensing and Access Pathway: UK Government; 2022 [8/8/2022]. Available from: https://www.gov.uk/guidance/innovative-licensing-and-access-pathway.
104. National Institute for Health and Care Excellence (NICE). Health Technology Evaluation Process, Methods and Topic Selection Review Conclusions and final update. 2022 [Available from: https://www.nice.org.uk/about/who-we-are/board/public-board-meetings/public-board-meeting-agenda-and-papers--january-2022#technology-evaluation-methods-and-process-review.
105. Zhang K, Kumar G, Skedgel C. Towards a New Understanding of Unmet Medical Need. Applied Health Economics and Health Policy. 2021;19(6):785-8.
106. Jørgensen J, Hanna E, Kefalas P. Outcomes-based reimbursement for gene therapies in practice: the experience of recently launched CAR-T cell therapies in major European countries. Journal of market access & health policy. 2020;8(1):1715536.
107. National Health Service. Innovation and Technology Payment: National Health Service, UK Government; 2021 [2/8/2022]. Available from: https://www.england.nhs.uk/aac/what-we-do/introducing-revolutionary-medicines-to-the-nhs/innovation-and-technology-payment/.
108. Benassi F, Bradshaw S. PND91-How Advanced Therapy Treatment Centers in the UK can improve market access for specialised technologies. Value in Health. 2018;21:S344.



evohealth

(02) 6243 4806

www.evohealth.com.au

Level 9, 2 Phillip Law St,
CANBERRA CITY ACT 2601