NOVOTECH
The Asia Pacific CRO

# Accelerating Genetic Therapy Clinical Trials in Asia-Pacific

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## Introduction and Executive Summary

A growing number of biotechnology companies, both in the West and in Asia, are specializing in gene therapies and other regenerative treatments boosted by the approval of the first genetic therapy agent (tisagenlecleusel) by the FDA in 2017.

Between 2015 and 2019, the number of industry-sponsored genetic therapy trials more than quadrupled (CAGR + 43%), with the Asia-Pacific region being involved in about 40% of all trials (ex-Japan).

Since 2001, over 300 sites in Asia-Pacific have been involved in 335 different genetic therapy trials. This report aims at highlighting the main considerations for biotechnology companies when planning for genetic therapy clinical trials, and why Asia-Pacific is a key destination to conduct such trials.

Gene therapies have unique properties and potentially very severe side effects. Clinical trial sponsors must therefore ensure that they select experienced sites, investigators and partners.

Australia has established practical and predictable processes and timelines for genetic therapy clinical trials making it an ideal location for initiation of a clinical trial.

# 1. Landscape of genetic therapy clinical trials

Since the first gene transfer trial was approved back in 1989, the clinical development of gene therapies has accelerated dramatically. We have observed an acceleration of research and development efforts in this field since 2015.
Genetic therapy is a technique that seeks to manipulate a patient's genes to treat an illness[1]. Gene therapies can be commonly classified in three main categories:

- CAR T-Cells, where T Lymphocytes are modified with a retroviral vector to target cancer cells.
- Oncolytic viruses, such as lentiviral vectors and adeno-associated virus (AAV) which are designed to trigger oncolytic pathways.
- Other gene repair strategies and genome editing techniques, such as the CRISPR/Cas9 technology.

Most genetic therapy candidates are focused in oncology, and more specifically haematological malignancies such as acute leukemias and multiple myeloma. Chimeric antigen receptor (CAR) T-cells therapies are increasingly used across a broad variety of haematological and solid tumour indications. Compared with traditional therapies, clinical responses using gene therapies can be highly variable but can lead to more durable clinical progress or sometimes full remission.[2]

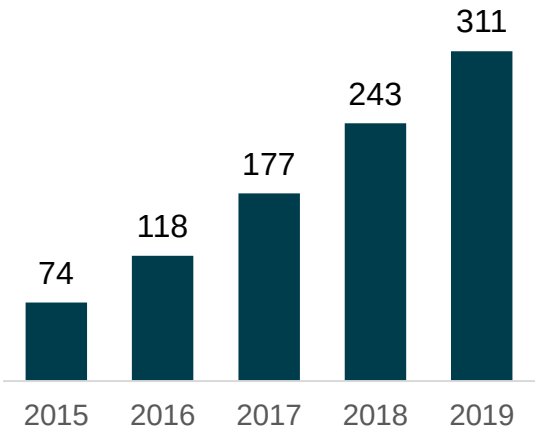
A growing number of biotechnology companies, both in the West and in Asia, are specializing in gene therapies and other regenerative treatments boosted by the approval of the first genetic therapy agent (tisagenlecleusel) by the FDA in 2017, followed by another agent (axicabtagene ciloleucel) shortly after the same year.[2] Between 2015 and 2019, the number of Industry-sponsored genetic therapy trials more than quadrupled (CAGR + 43%), with the Asia-Pacific region being involved in about 40% of all trials (ex-Japan). China was the most frequently involved country, fuelled by local innovation from Chinese sponsors. Australia and South Korea, which are known to be preferred clinical trial locations for western biotechnology companies, are ranked second and third respectively thanks to their significant pool of specialized sites and investigators (Graph 1 and 2). [3]

Many sites across Asia-Pacific have developed a strong track-record in managing clinical trials with gene therapies. Since 2001, over 300 sites in Asia-Pacific have been involved in 335 different genetic therapy trials (Figure 1).

[1] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy [Accessed Jan 15th 2020]
[2] Ginn SL, Amaya AK et a. Genetic therapy clinical trials worldwide to 2017: An update. J Gene Med. 2018;e3015
[3] GlobalData

**Graph 1.** Number of industry-sponsored genetic therapy trials initiated globally each year
(2015 – 2019)

*CAGR 4years = +43%*




**Graph 2.** 2020 Breakdown of site location in Asia-Pacific ex-Japan for open Industry-sponsored genetic therapy trials [as of Jan 2020]

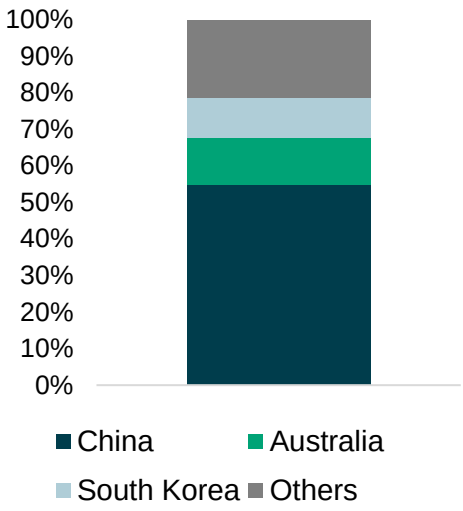
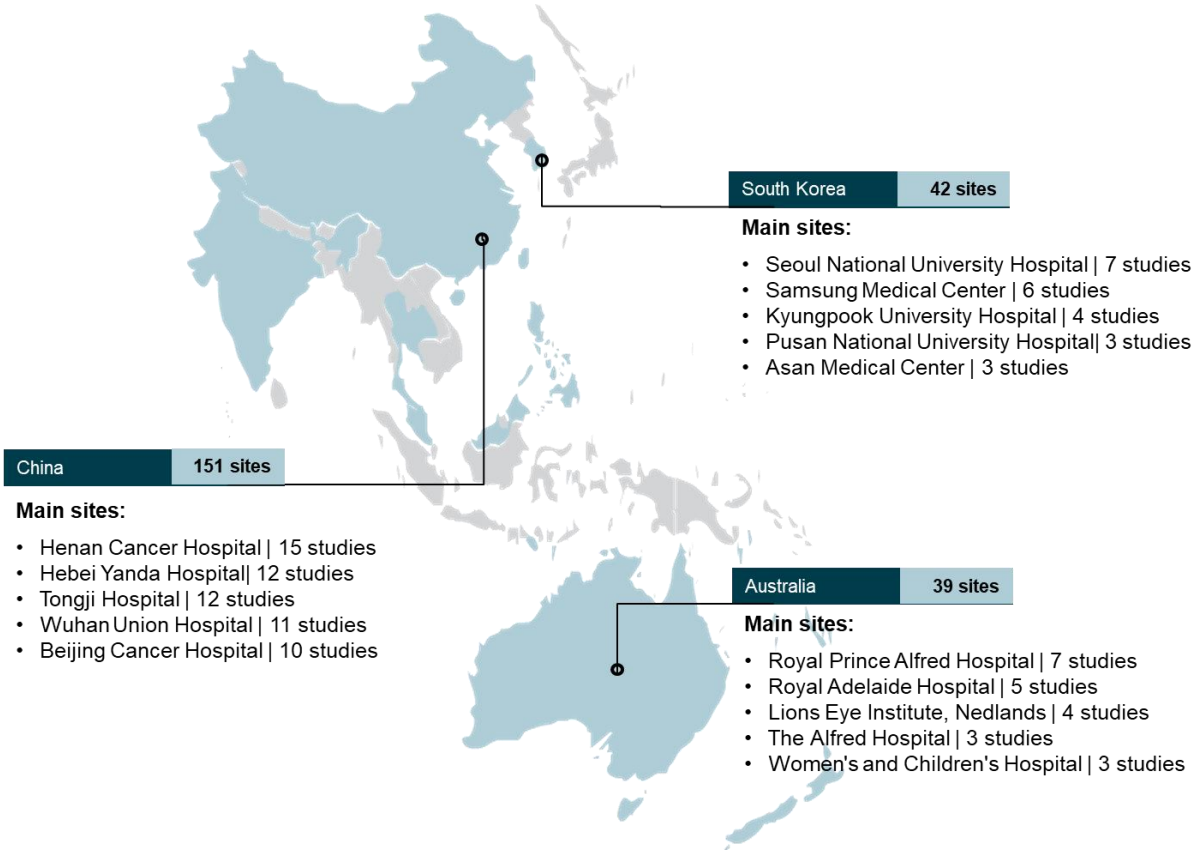



**Figure 1**. Overview map of Asia-Pacific sites involved in genetic therapy trials *[Source GlobalData]*



# 2. Considerations for clinical trials

The US FDA, EMA and Australian TGA have all individually released guidance to biotechnology sponsors looking to engage in genetic therapy clinical trials. [4, 5, 6] These requirements define what is and isn't a genetic modified organism, the rules that apply for sponsors, and recommendations for clinical monitoring and treatment follow-up. All three regulatory bodies insist on the need for long-term clinical follow-up of patients. Gene therapies have unique properties and clinical effect. This results in very specific treatment length, durability of response as well as side effects when compared with traditional treatments.

Adverse events can appear long after the therapy is administered, so it is critical the sites involved are experienced in using these therapies. Specific storage, preparation and administration of genetic therapies can also require specialised facilities and expertise. The implication for biotechnology companies is the need to seek clinical partners and sites with the ability to adapt to the specific requirements of genetic therapy trials. Furthermore, the study protocol must be adapted to allow for such long-term clinical follow-up requirements. Some of the information collected as part of the long-term clinical follow-up can include but is not limited to:

- Development of new or recurrent cancer
- Development of infections
- Other immunogenicity reactions

It is important to note the long-term follow-up plan must depend on the nature of the therapy and its propensity to modify the host genome.

## Considerations in Australia

Australia has become a preferred location for biotechnology companies to run their clinical trials. Sponsors often look to Australia for its high-quality clinical environment, straightforward regulatory process and attractive R&D refund scheme.

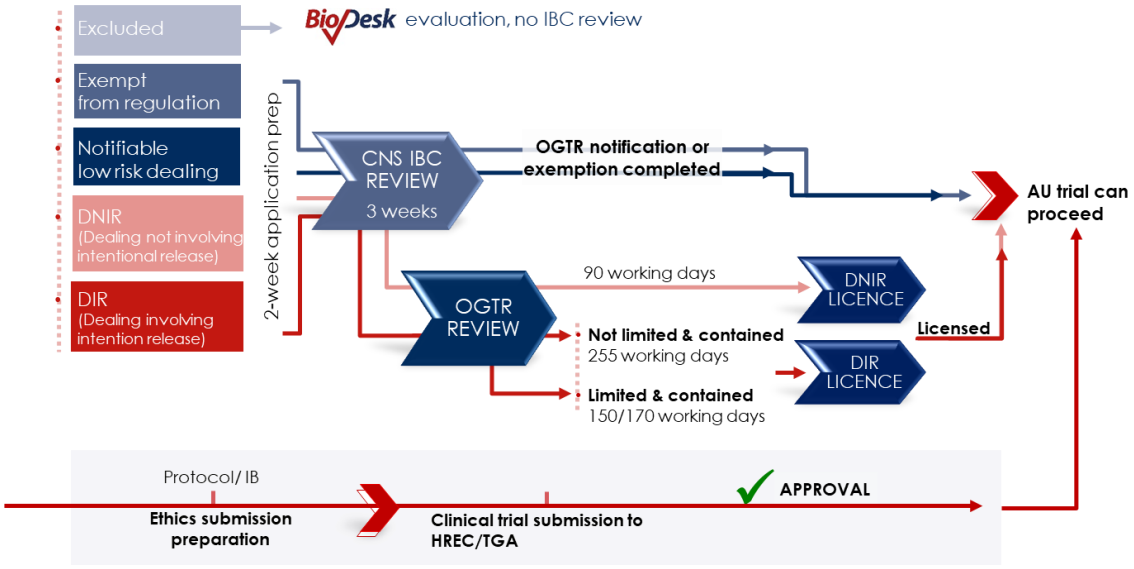
For gene therapies, Australia has established practical and predictable process and timelines for genetic therapy clinical trials which is part of the growing interest from biotechnology companies for this location. The Office of Gene Technology Regulator (OGTR) governs the use of gene therapies in Australia, including clinical trials.

In Australia a genetic therapy clinical trial must be reviewed by an Institutional Biosafety Committee (IBC), and licenced by the OGTR. The IBC process is independent from the clinical trial regulatory approval but can be done in parallel (Figure 2). The IBC provides guidance to organisations for the identification and management of the risks associated with GMO dealings.

[4] Long term Follow-up after Administration of Human Genetic therapy Products. FDA (2018)
[5] Guideline on follow-up of patients administered with genetic therapy medicinal products. EMA (2009)
[6] Requirements under the Gene Technology Act 2000 for clinical trials in human involving GMOs. OGTR (2017)

One such IBC committee approved by OGTR is run by Novotech's regulatory division BioDesk. This IBC is the only committee that is both independent but integrated into a CRO into Australia, giving a seamless process for the setup of GMO trials.

**Figure 2.** Australia's GMO approval process




## Considerations in North Asia

In South Korea, The Ministry of Food and Drug Safety (MFDS) regulates gene therapy and cell therapy products. The submission requirements are similar to non-GMO products as well as the review timelines (30 working days). For considerations that are specific to GMOs, such as the long-term follow-up of patients, the MFDS has aligned on guidelines issued by the EMA and FDA.

In China, the NMPA (previously Chinese FDA) issued new regulation specific to cell therapy clinical practices in late 2017. Under the new regulation, the treatment of cell therapy products has been aligned with western policies to facilitate fast-track reviews and the clinical development to encourage new drug innovation.[7] The Taiwanese FDA (TFDA) also issued new regulation for cell therapies and aligned the regulatory process with practices in the US and Europe. The TFDA explicitly encourages sponsors to seek guidance from the Centre of Drug Evaluation (CDE) before submitting a formal clinical trial application.[8]

[7] Regulations on cell therapy products in China: a brief history and current status. Yijia Li, Frances Verter et al. Regen. Med. (2019) 14(8), 791-803

[8] Cell Therapy Regulation in Taiwan. Yuan-Chuan Chen, Hwei-Frang Chen and Ming-Kung Yeh. Cell Transplantation, Vol 26, pp. 483-493, 2017.

# 3. Case study

## Streamlined Solution for Cell and Gene Trials

North American Biotech drew on BioDesk expertise to accelerate approval of IV administered bacterial pro-biotic for oncology trial.

**Canadian biotech engaged global CRO**
**Global CRO unable to navigate complex requirements for the GMO product and trial stalled**
**Novotech consultants provided the fastest solution getting the trial on track**

**BioDesk got GMO study back on track**

- Trial already stalled 3 months before Novotech consultants and IBC engaged.
- As a key stakeholder to the Australian Regulator, Novotech consultants able to organize a teleconference with the Regulator within 20 minutes.
- License application written by Novotech consultants and reviewed by the CNS/Novotech IBC.
- Questions from the Regulator during review addressed directly via telephone with expert Novotech scientific consultants.
- GMO License approval obtained in the shortest timeframe possible allowing the study to start.

## Let's continue the discussion

Novotech provides regulatory and clinical consulting services to biotechnology companies through its specialized division CNS BioDesk.

BioDesk has been an OGTR accredited organization since 2006, and routinely conducts GMO clinical studies across Australia. BioDesk is the major independent IBC in Australia, which can provide central reviews nationally:

- The most experienced GMO clinical trials group in Australia.
- The first national, privately owned, commercial IBC initiated in Australia, successfully accredited by the OGTR.
- 100% approval success rate on license applications submitted to the OGTR
- Central review capabilities for multi-site trials and full GMO support.

To learn more or talk to our experts about your genetic therapy trial, visit https://novotech-cro.com/cns/gmo-solutions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