BioSpectrum
the business of Bio & Health Sciences
ASIA EDITION

Addressing Accessibility and Affordability of Cell & Gene Therapies

01 April 2024 | Analysis | By Ayesha Siddiqui

Cell and gene therapies (CGT) are one of the hottest sectors in the pharmaceutical industry. Quite a few companies in the field are making remarkable advancements toward potentially curative treatments for challenging diseases using groundbreaking science. Despite a steady stream of regulatory approvals and promising growth prospects, the high manufacturing costs associated with these therapies often render them inaccessible to the majority of patients. To address this issue, companies are actively striving to streamline and optimise the highly intricate and labour-intensive process of cell and gene therapy manufacturing. Let's explore further.

The most sought-after and hot sector in the pharmaceutical industry, which has witnessed an outpouring of billions and record-breaking approvals in recent times, is cell and gene therapy. Last year, the United States Food and Drug Administration (US FDA) approved seven cell and gene therapy products, including the world's first approved CRISPR gene editing therapy, Casgevy, two cell therapy products, and the first oral faecal microbiota product, Vowst.

Globally, 30 gene therapies have been approved (including genetically modified cell therapies). The cell and gene therapy sector has expanded tremendously, with the number of drugs in development growing nearly six-fold from 511 development-stage candidates in 2013 to just over 3,000 in 2023, according to Citeline's Pharmaprojects.

By 2025, the FDA aims to review and approve 10-20 gene and cell therapies annually. With an increasing number of products obtaining regulatory approval in the coming years, the market size for CGT is projected to reach $94 billion by 2030, according to Precedence Research. Oncology is anticipated to maintain its lead as the primary indication and area of significant advancement for cell and gene therapies, projected to account for 44 per cent of the CGT market by 2029. Other therapeutic areas poised to derive benefits from CGT include neurodegenerative, autoimmune, and cardiovascular diseases.

Asian Scenario

The Asia Pacific region has been leading in the field of cell and gene therapies, with several countries investing significantly in research and development. China, in particular, has emerged as an important market for CGTs, particularly CAR-T therapies, surpassing the USA in the number of clinical trials conducted. The industry is considered a strategic priority by the government, with CAR T-cell therapy clinical trials in China accounting for over 50 per cent of registered CGT studies worldwide. Currently, there are over 200 ongoing CAR-T trials in China covering a wide range of targets and indications, from

haematology-oncology to solid tumours, according to reports from Nature.

Yescarta, developed by Fosun Kite, and relma-cel, from JW Therapeutics, stand as China's first regulatory-approved CAR T-cell therapies, heralding a new era for the industry. A notable achievement is cilta-cel, developed by Legend Biotech, which has successfully gained FDA approval, marking its global recognition.

With lower R&D development costs than in advanced markets, China is becoming an attractive market for the development of CGT, and therefore may emerge as a strong competitor of overseas-made CGT, notes a GlobalData report. Adding to this momentum, Bayer AG announced the global expansion of its life science incubator network, Bayer Co. Lab, to Shanghai, China. At the new site in China, Bayer will collaborate with Shanghai Pharmaceuticals to focus on oncology and CGT innovations.

While India lags behind China in the production of cell and gene therapies, a wave of new biotech startups is emerging to address this challenge. Immuneel Therapeutics and ImmunoACT are currently developing CAR-T cell therapies. ImmunoACT's NexCAR19 therapy received approval from India's Central Drug Standards Control Organisation (CDSCO) for treating relapsed or refractory B-cell lymphomas and leukaemia. This approval positions ImmunoACT to lead India's indigenous CAR-T cell therapy efforts, with NexCAR19 undergoing Phase II trials for other lymphomas and leukaemia types. Similarly, Immuneel Therapeutics' IMN-003A CAR-T is in Phase II trials for B-cell lymphomas and leukaemia. The successful completion of these trials holds promise in meeting the critical need for effective cancer therapies in India. Recently, German biotech firm Miltenyi Biotec launched operations in India, planning to establish a centre in Hyderabad.

Singapore is emerging as a top destination for CGT manufacturing, with numerous companies unveiling plans to set up facilities in the country. SCG Cell Therapy is among those, announcing the establishment of a manufacturing facility and R&D centre in Singapore. Concurrently, Biosyngen inaugurated a new cell therapy GMP facility in Singapore, further bolstering the city-state's position in the field. Adding to this momentum, the Advanced Cell Therapy and Research Institute Singapore (ACTRIS) recently opened a new 2,000 sqm cell therapy facility to address the growing clinical demand for CGT treatments in Singapore. Thermo Fisher Scientific has also contributed to Singapore's CGT landscape, launching a Cell Therapy Collaboration Center Program aimed at advancing cell therapy initiatives across the Asia-Pacific region.

Australia also aims to become a hub for these therapies. AusBiotech and Medicines Australia are driving the Cell and Gene Catalyst initiative to accelerate development and commercialisation in Australia, with a focus on strengthening the ecosystem and collaborating with industry leaders. The country also launched Australia's National Cell and Gene Manufacturing Blueprint, outlining a strategic approach to establish the country as a regional leader. The blueprint emphasises infrastructure and workforce development to bolster manufacturing capabilities and capacity.

Addressing Prohibitive Costs

Cell and gene therapies offer hope for life-threatening debilitating conditions, but access remains out of reach for the patients who need it the most. Scaling CGT operations is critical to meet the growing demand for treatment. 20 per cent of cancer patients who are eligible for CAR-T therapies pass away while waiting for a manufacturing slot.

"We have to challenge the status quo, because therapies can't just be approvable – they need to be accessible too. More therapies approved do not automatically translate into increases in the number of patients treated. Today, it is estimated that less than 3 per cent of patients who could benefit from CAR-T therapies (to name just one category) have been able to access them," said **Jason C. Foster, CEO, Ori Biotech.**

Ori Biotech, based in London and New Jersey, has developed a proprietary, full-stack manufacturing platform that closes, automates and standardises CGT manufacturing. Ori is set to commercially launch its platform this year.

Manufacturing poses the biggest obstacle in the field of gene therapy. According to SK Pharmteco, the expenses for manufacturing and cost of goods can range from $500,000 to $1 million for gene therapy, excluding research and clinical trial expenses, ultimately burdening patients with hefty costs. The approval of CSL Behring's Hemgenix, the first FDA-approved gene therapy for haemophilia B, marked a significant milestone but also set a record for its price tag — an eye-popping $3.5 million for a single treatment, making it the world's most expensive drug. Similarly, Bluebird's Zynteglo, carries a list price of $2.8 million, further escalating drug pricing. Analysis by the Institute for Clinical and Economic Review suggests that gene therapy's average cost falls between $1 million and $2 million per dose, highlighting the financial challenges associated with accessing these innovative treatments.

The manufacturing process for CGTs is not only daunting, time-consuming, and laborious, but there is also a significant shortage of skilled personnel to handle the sophisticated processes required. According to BioPlan Associates' 20th Annual

Report and Survey of Biopharmaceutical Manufacturing, 51.3 per cent of the industry is facing critical shortages in manufacturing staff, more than doubling from just 21.2 per cent in the past three years. This substantial increase underscores the severity of the staffing shortages within the cell and gene therapy contract manufacturing industry.

“One of the manufacturing bottlenecks faced by cell and gene therapy startups as they scale up production is difficulty in hiring and retaining manufacturing talent who can navigate the certification process, and eventually translate to GMP manufacturing. The global competition for highly qualified manufacturing talent is evident. The biopharma industry has long grappled with this challenge, and it’s more challenging for startups to attract experienced talent and train new hands in the biotech sector compared to multinational companies. Data from Cytiva’s 2023 Global Biopharma Resilience Index shows that only 24 per cent of biopharma executives are positive about having access to manufacturing talent capable of working in GMP environments in the Asia Pacific,” said **Krishna Karnati, Commercial General Manager, Genomic Medicine, APAC, Cytiva.**

Contract Development and Manufacturing Organisations (CDMOs) are also not fully equipped to handle CGT manufacturing. According to Top1000bio.com database of global biologics facilities, only a handful of the CDMOs can produce either late-stage clinical, or commercial-scale therapies.

“Other bottlenecks include the manufacturing facilities themselves – designing or upgrading these so they can accommodate large-scale production of cell and gene therapies that adhere to regulatory standards, guarantee product quality, and support adaptable production processes – and securing cell lines with the required purity, viability, and genetic stability,” said **Thomas Carlsen, CEO of the Novo Nordisk Foundation Cellerator, Denmark.**

The Novo Nordisk Foundation Cellerator – a facility for the further development and manufacture of cell therapies for use in clinical trials, and a hub within the Nordic cell therapy ecosystem – is being developed to address all these challenges. For example, the company is working to secure cell lines at an early stage and construct a facility that is specifically designed for the large-scale production of high-quality cell therapies.

Unfortunately, manufacturing advancements have failed to keep pace with the rapid innovations seen in cell and gene therapies.

“The speed of innovation in the cell and gene therapy space presents a double-edged sword as developers bring academic-developed small-scale processes into commercial-scale, quality-driven manufacturing environments in highly compressed timelines. As companies try to scale production without compromising safety and efficacy, they face three intertwining issues: scarce talent pool, starting material variability and immature processes. Particularly in autologous therapies, starting material is a primary source of variability impacting manufacturing success and often heavily relies on expert personnel to tweak process parameters; yet, this process flexibility complicates the development of a robust manufacturing strategy that can scale across operators and geographies,” said **Dr Wenyan Leong, Strategy Lead, Asia Pacific and Japan, Cell Therapy Technologies, Terumo Blood and Cell Technologies.**

Terumo launched the Quantum Flex bioreactor platform, one of the first systems that enables cell therapy commercialisation from process development through manufacturing.

Though there isn't a singular solution to enhance the accessibility of CGTs, refining manufacturing processes to facilitate their large-scale production can effectively lower their costs and ensure they reach individuals in dire need of these treatments.

Digitising CGT manufacturing

By automating and standardising manufacturing processes, we can initiate large-scale production and truly industrialise CGTs. This requires the implementation of platforms designed for flexible process discovery and smooth translation to a commercial scale. Automation addresses key challenges such as the inefficiency of manual processes at scale, elevated costs, and high rates of process failure.

“Additionally, automation cuts costs by 50 per cent and enhances quality, as process failure rates plummet by 75 per cent due to reduced operator errors and minimise contamination through closed processes,” said **Fabian Gerlinghaus, Co-Founder and CEO, Cellares, USA.**

Cellares is set to launch its proprietary modular cGMP platform, the Cell Shuttle, designed for industrial-scale cell therapy manufacturing. The Cell Shuttle offers an automated manufacturing solution, slashing labour and facility size requirements by up to 90 per cent. Bristol Myers Squibb is presently utilising Cellares' Cell Shuttle platform for the automated proof-of-concept manufacturing of its CAR-T therapies.

With the current manual or semi-automated manufacturing systems, production space and the need for highly skilled operators are barriers to production capacity. Closed and automated systems address both of these bottlenecks. To that effect, Cytiva has partnered with robotics technology company Multiply Labs to design a robotic system that would automate the manual portions of cell therapy production. Lonza's platform for autologous cell therapy manufacturing, the Cocoon, is a functionally closed, automated system that is currently being used to support clinical trials in Europe and North America.

"While it is known that automated and closed processing platforms will enable scale, it has been a longstanding debate on when to adopt these sophisticated platforms. It is preferable to choose a scalable platform early in development to understand the parameters, and then scale rapidly as needed. One can scale-up or scale-out depending on their manufacturing strategy. Advanced electronic management software can help to ease scale-out strategies through integrated data reporting and protocol management across multiple devices," said Dr Leong.

While the biopharma industry has embraced technology, the primary bottleneck hindering the scale-up of cell and gene therapy (CGT) production is the absence of comprehensive 'end-to-end' solutions.

"As an industry, we are still building very large facilities full of people, using islands of automation run by and connected by people and producing data recorded by people. There is very little 'whole process' automation and limited scope for mechanisation and industrialisation, limiting productivity and constrained by the resulting high cost of goods. To achieve production scale up, we can take inspiration from other highly automated industries, and focus on developing the missing links that will enable us to use these technologies in the CGT industry and thereby achieve scale of tens of thousands of therapies a year. Those at the more commercial end of CGT are already acutely aware that step-change innovations are essential in order to provide these life-saving therapies to all of the patients that can benefit from them," said **Jason Jones, Global Business Development Lead at Cellular Origins, UK.**

Cellular Origins is working on bringing advanced robotics automation to cell therapy for the first time. Cellular Origins' platform is a configurable robotic automation solution that enables scalable, cost-effective, and space-efficient cell therapy manufacture that is designed for adaptability.

"Technology alone will not solve the issues in a vacuum. To stride forward, we need further collaboration between leaders in the space, to make sure that solutions are data-driven and grounded in excellence in biology. This huge unmet need has inspired us to partner with academics, therapeutics developers, investors to build solutions that can help bring more therapies to more people in urgent need," signs off Jason Foster.

Ayesha Siddiqui