CRYOPDP

JUN 2024

Care Beyond Measure: Unleashing Patient-Centric Breakthroughs in Healthcare

How is Patient-Centricity driving the evolution of Life Sciences?

PATIENT CENTRICITY
WHAT ROLE DOES IT PLAY IN SHAPING THE FUTURE OF LIFE SCIENCES?

LEO PHARMA:
THE PATIENT AT THE CENTRE OF EVERYTHING WE DO

CELL AND GENE THERAPIES
ARE SET TO REVOLUTIONIZE HEALTHCARE: HERE'S HOW

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Contents

Preface

In recent years, "patient centricity" has become the cornerstone of the life science industry. This is particularly applicable now, as the industry spends more of its research endeavors developing personalized medicines - like cell and gene therapies - against conditions that were previously thought to be incurable.

Over the last decade, several cell and gene therapies have gained approval following fantastic outcomes in patients with some cancers and rare diseases. These therapies have the power to truly revolutionize the future of medicine -- as they have the potential to cure many chronic and rare diseases. As a result, research into these therapies has gained increased momentum.

This momentum spills across adjacent industries, including the logistics industry, which must also prepare itself for the delivery of these life-changing medications. Successfully delivering cell and gene therapies vein-to-vein requires reliable logistical support with safe, efficient, temperature-controlled transportation. Because cell and gene therapies are largely required by patients that present with severe illnesses, any delays in delivery could have massive consequences. With these therapies, there is no room for error.

At CRYOPDP, we have been helping the life science industry create a healthier tomorrow. And we take this responsibility seriously. For years, we have transported drugs to public and private organizations, supported the smooth running of clinical trials, and delivered packages of life-saving medication straight to the patient's or caregiver's home.

This exclusive ebook builds on the latest developments in patient centricity and cell and gene therapies to paint a picture of how the life science and logistics industry is innovating to address the unmet needs of patients and stakeholders in the life sciences industry.

Patient Centricity

What role does it play in shaping the future of Life Sciences?

CEDRIC PICAUD
CRYOPDP CEO

The life sciences industry has one clear goal: to improve (and where applicable, save) patients' lives by developing innovative and effective drug therapies. Although the goal has remained the same, the approach is changing for the better -- from disease-centricity to patient-centricity. But what does this mean? Read along to find out.

To date, there is no clear definition of patient centricity within the life sciences. Depending on who you ask, the terms patient engagement or patient-focused are used as synonyms for patient centricity.[1] Regardless of the term used, at the heart of the matter, patient centricity refers to engaging and incorporating patients and their perspectives at every stage throughout the organization -- from research and development to logistics and drug administration.

Because patient-centricity empowers patients and facilitates better (self) care, it looks different for every life science company. That's because every company has slightly different missions and values. They're also creating different services and products. For this reason, keeping the patient at the center of care cannot be an undertaking to simply "tick the box" -- it will not work.

To truly become patient-centric, life science companies must understand and connect with patients throughout their healthcare journey -- from the first visit to their doctor, their diagnosis, the delivery of drugs to their home/ pharmacy, the administration of these drugs, through to end-of-life care. The life science industry must then accommodate accordingly: by creating a high-quality patient-centric healthcare ecosystem.

But how is the life science industry responding to this change? How are companies shifting gears to become more patient centric?

First, patients are demanding accurate and accessible health information. In response to this, the life science industry is developing digital tools and content to provide patients with better information that is available at their fingertips. The traditional strategies of reaching the patient through only the physician are no longer enough. That method is completely outdated in today's digital world.

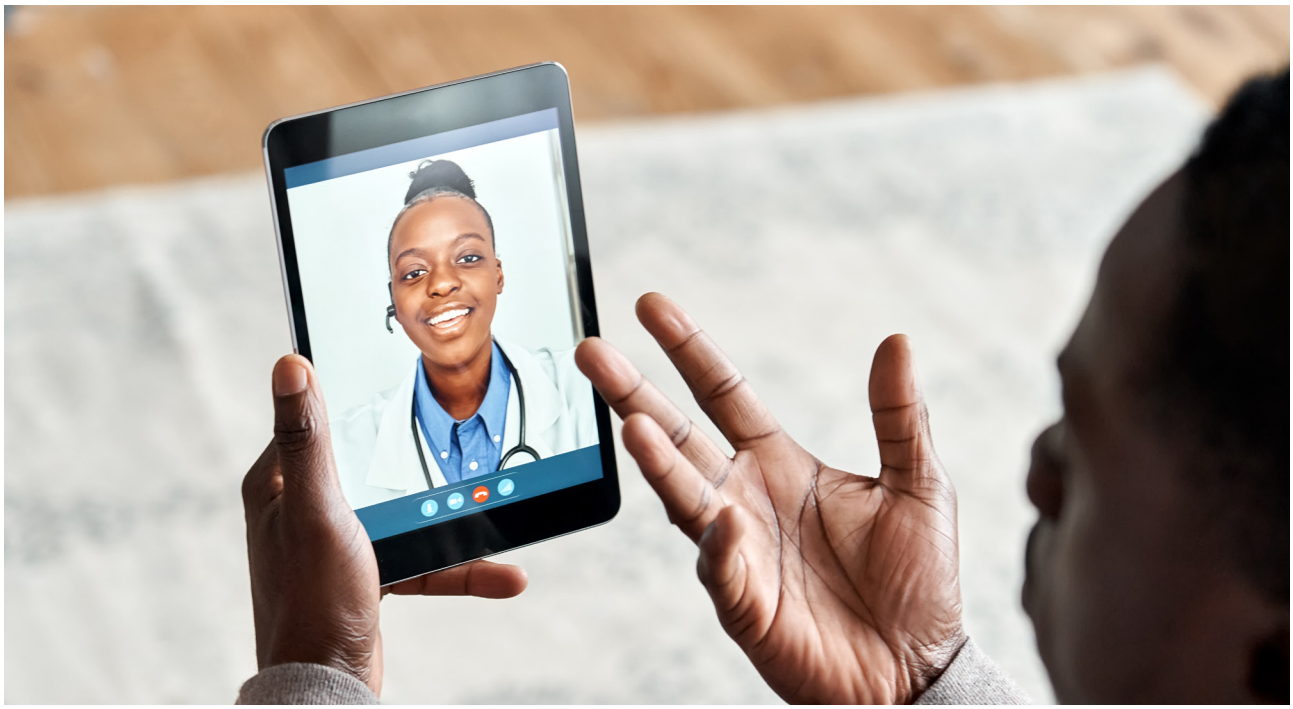
Life science companies of today must go digital to ensure they don't lose relevance in the industry. As a result, omnichannel approaches are being developed so patients can be met exactly where they are (whether in the clinic, on a website, or even on social media channels like Instagram, TikTok, and Facebook). Based on these interactions, patient (and caregiver) insights are gathered to map patients at every stage of their healthcare journey (from diagnosis to end-of-life care). This activity enables life science companies to identify gaps where patients require further support -- whether in terms of disease awareness, drug adherence, multicultural marketing, or something else.

Second, patients want to be heard so they can have better healthcare experiences. In response, life science brands are strengthening collaborations with patient advocacy groups and including patients on pharmaceutical advisory boards. For example, a whitepaper by Deloitte highlights how a small biotech company focused on a rare condition, found that while the company itself was focused on white blood cell count, patients wanted to "stop itching at night so they can sleep better."

Novo Nordisk also recently established patient advisory boards called DEEP (Disease Experience Expert People) to give patients (and advocates) the center stage. As a result, patients can now able to give their input for the products that life science companies are developing.[2] Similarly, Pfizer works with various advocacy organizations to learn from patients' experiences with a condition or treatment, discuss side effects or side effect management, get patient feedback, connect with patients, and more. In 2019, they developed a network, called the Pfizer Oncology Patient Centric Ecosystem (POPCE) to further embed patients' insights and experiences into the life-saving work that they do.[3] This leads to better patient care and longer-term customer loyalty.

"...patients want to be heard so they can have better healthcare experiences."

Third, patients want to be represented by the brands serving them. The life science industry is now launching campaigns and working with ambassadors that patients can resonate with and trust. For example, both Johnson and Johnson (J&J) and ViiV Healthcare



have debuted HIV campaigns 'Positively Fearless' and 'Me in You, You in Me', respectively. The campaign ambassadors recruited include those from the LGBTQ+ community. These campaigns aim to encourage conversation around HIV prevention and the stigma surrounding it. They also aim to educate, destigmatize, and give a voice to groups that are otherwise easily overlooked.

Fourth, mandates from regulatory authorities are also moving towards patient-centricity. Regulatory authorities now expect life science companies to incorporate patient perspectives into the product development and approval process. The FDA, for example, issued final guidance in late 2020 recommending that pharmaceutical research includes people with different demographic characteristics (like sex, age, ethnicity, age, language, etc.) and non-demographic characteristics (such as comorbidities, patients with organ dysfunction, etc.) in clinical trials. [4] Finally, patients demand better solutions with integrated personalized approaches and precision medicine. This coupled with a significant drop in blockbuster drugs and an acceleration of personalized treatments and precision medicines (further driven by FDA approval) elevates the patient's voice within the life science industry. According to the Personalized Medicine Coalition, the U.S. Food and Drug Administration (FDA) has approved 17 personalized medicines in the year 2021 alone. Personalized medicines have accounted for more than a third of new drug approvals over the last four to five years.

These are just some of the ways in which patient centricity is shaping the future of the pharmaceutical industry and the clinical trial sector. **No matter how you look at it, the future of the life science industry focuses on patient centricity and patient empowerment.** These changes have repercussions for other industries, like the technology industry, the pharmaceutical industry, and the logistics industry, which share responsibilities with the life science and pharma industries in their plans of making medicine more patient-centric.

"According to the Personalized Medicine Coalition, the U.S. Food and Drug Administration (FDA) has approved 17 personalized medicines in the year 2021 alone."

Novel gene therapies for lung diseases

MARIANA VIEGAS
Senior Research Assistant at Gene Medicine Group
(Oxford University)

CRYOPDP had the opportunity to speak with Mariana Viegas about the advancements in gene therapy.

Mariana Viegas is a Senior Research Assistant for the Gene Medicine Group of the University of Oxford and in this interview, she explores the developments of her group for treating lung diseases. **Readers can listen to the full episode on our podcast - Unfreeze your Science.**

Listen on YouTube

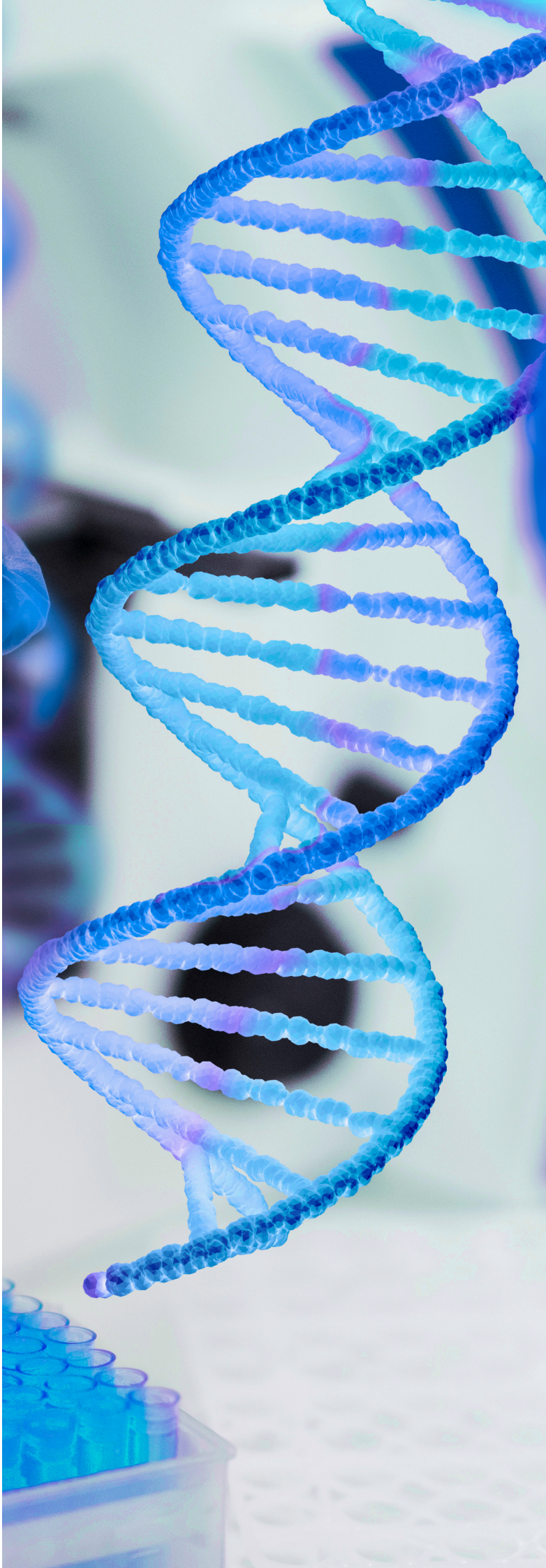
Listen on Spotify

What is gene therapy?

Gene therapy is the use of genetic material to treat or prevent diseases. A typical example where gene therapy can be useful is when someone has a disease caused by a mutation in a gene that leads to that gene not being functional. Then, introducing, a normal copy of that gene into the cells of the patient could decrease symptoms or even cure the disease.

How do you deliver the genetic material into target cells?

We take advantage of viruses' natural ability to enter our cells. We use lentivirus, which has been genetically engineered to remove all the unwanted parts - the parts that cause disease and the parts that help them make more viruses. So, instead of carrying the viral genetic material, which could make us sick, the virus carries genetic material that is therapeutic for treating genetic diseases. A great feature of these lentiviral vectors is that we can add different proteins to the envelope to target different tissues, a process called pseudotyping. We use 2 proteins called F and HN that can bind to receptors in the target lung cells and allow the virus to enter the cells. In this way, we can deliver the therapeutic genetic cargo into the lungs of patients. Another great feature of lentiviral vectors is that the genetic cargo they carry is integrated into the genome of the cell. This means that the therapy can provide a prolonged therapeutic benefit and that there is a potential for a cure that will last for the patient's lifetime.



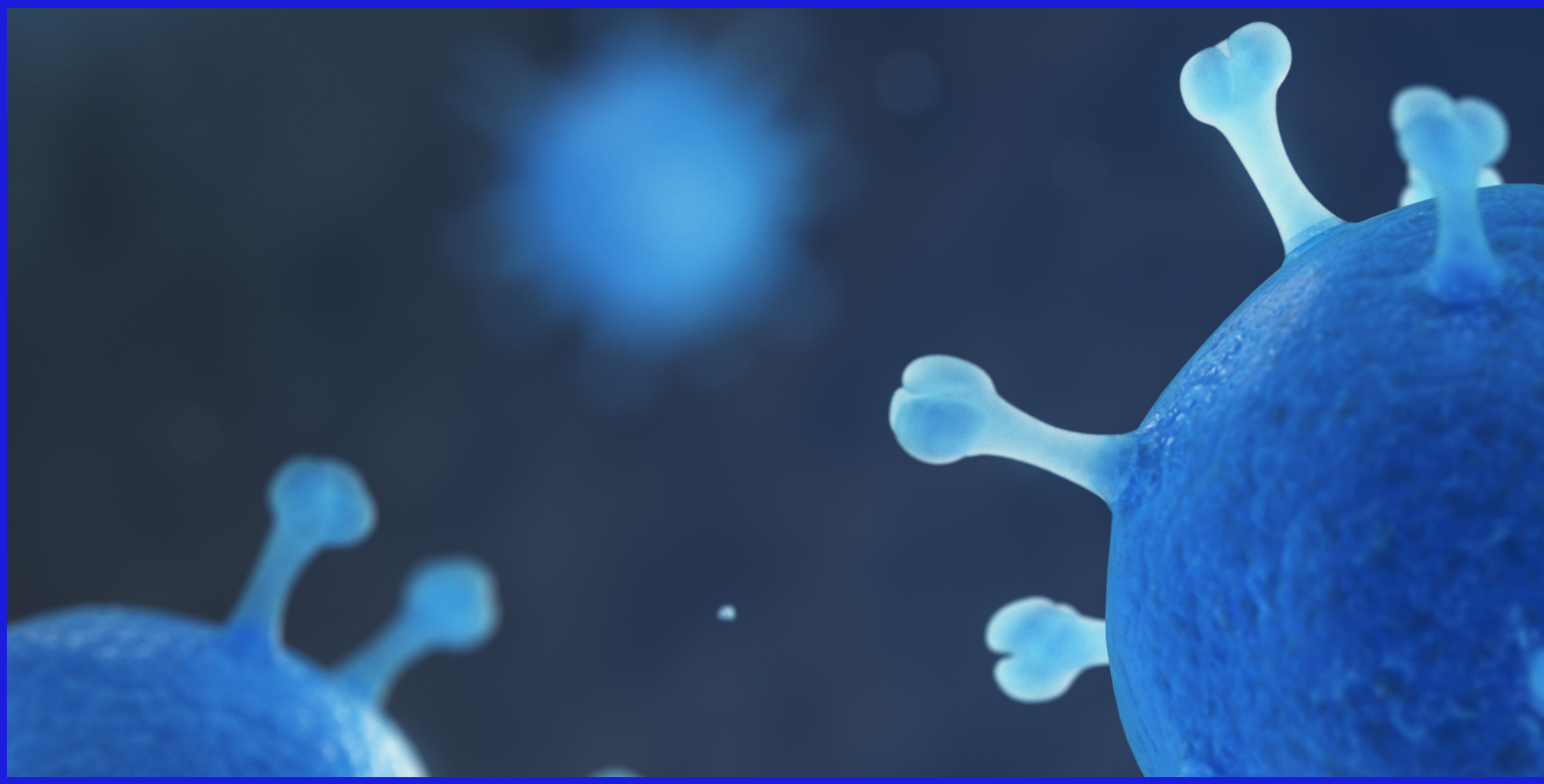
Could you provide some specific examples showcasing the application of these modified lentiviruses in treating lung diseases?

Cystic Fibrosis

For example, we've been focusing on Cystic Fibrosis. Cystic Fibrosis is caused by mutations in the CFTR gene, which codes for the CFTR protein. This protein controls the transport of chloride ions in and out of cells. Mutations in the CFTR gene may cause the CFTR protein to be defective or not even produced at all, which can lead to mucus accumulation in the airways. This makes it difficult to breathe freely and also results in an increased risk of infection.

Because we know that this disease is caused by a lack of a normal CFTR gene, introducing a normal copy of this gene should provide a cure for these patients. We performed studies with our modified lentiviral vectors, where we delivered a reporter gene to mice, and we demonstrated that a single dose could last a mouse's lifetime, about two years.

We've also used special lung cells grown at an air-liquid interface to mimic the cells exposed to air in the lungs. When we treated cells from cystic fibrosis patients with our lentiviral vector, we saw a restoration of CFTR function. We have also recently done toxicology studies which showed the treatment to be safe and supported the approval of a clinical trial in humans. Our therapy for Cystic Fibrosis has been taken on by a pharmaceutical company, and we expect clinical trials to start soon, which we're all quite excited about.



Surfactant Protein Deficiency

Another example and one of our current main focuses is to treat a very rare disease in newborn babies called Surfactant Protein Deficiency. Lung surfactant is a layer composed of lipids and proteins that coats the inside of the lungs, making them slippery and allowing the lungs to inflate easily without collapsing. Mutations in the genes that code for Surfactant Proteins mean newborns don't produce enough surfactant, which can result in fatal respiratory distress. These babies are intubated at birth and often don't survive more than a few months.

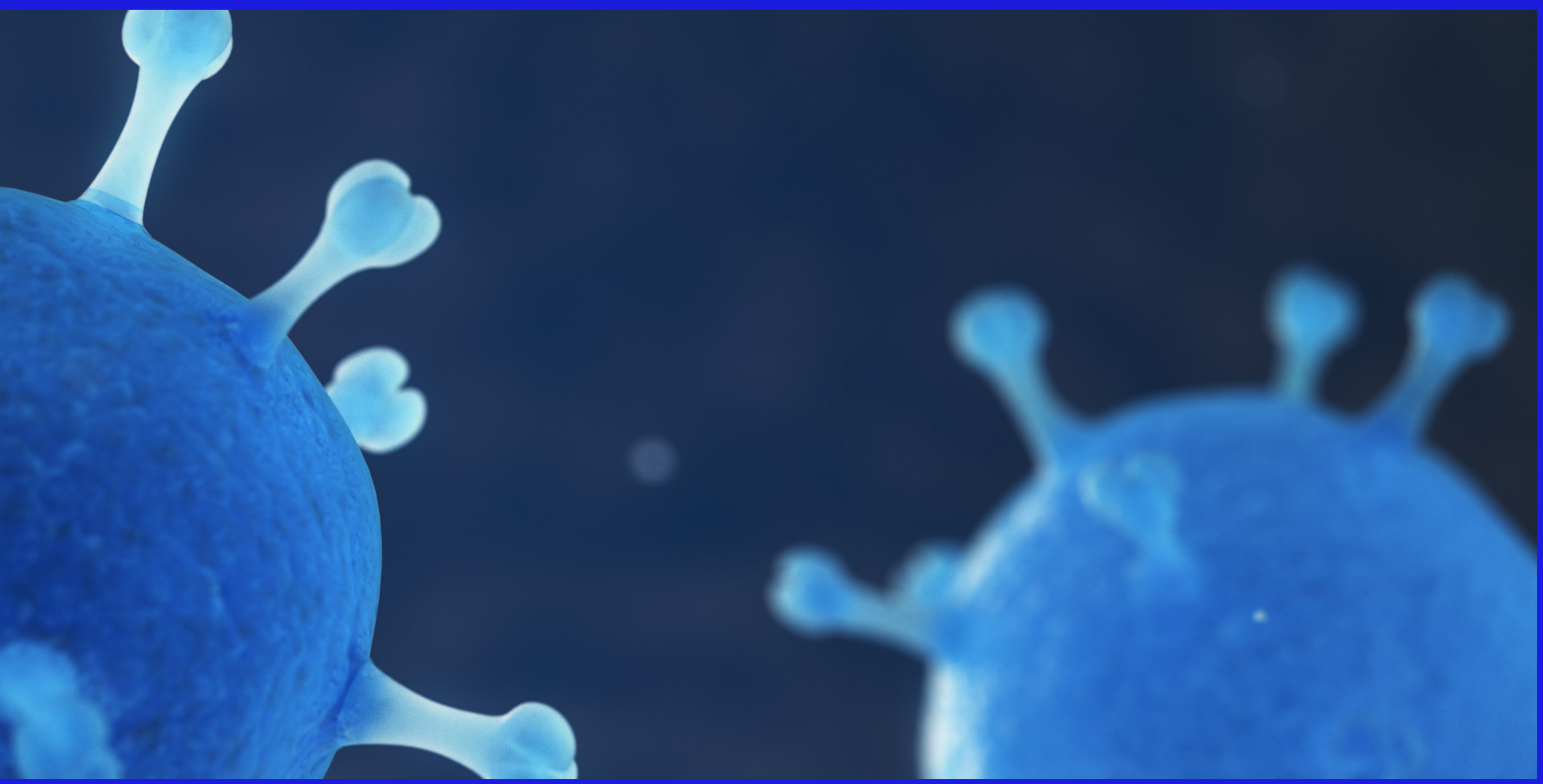
To treat this disease, we have developed a modified lentivirus to deliver a functional copy of surfactant protein genes into target lung cells. We used a mouse model that was genetically engineered to ensure that under normal conditions, the Surfactant Protein gene is expressed and the mouse is completely healthy, but under certain conditions, the surfactant protein gene is no longer expressed, and so the disease is induced, with symptoms very similar to what we observed in babies with this condition.
Survival of these mice once the disease is induced is very short, only a few days. However, when we give our modified lentivirus to these mice to deliver a functional copy of the surfactant protein gene, we see that most mice survive for significantly longer. These are quite promising results, and we're working towards a new treatment for this terrible condition.

What do you think about the future of gene therapy research?

Gene therapy has a lot of potential for treating currently untreatable diseases. The work I mentioned today is only a fraction of what is possible with gene therapy, with lots of exciting new avenues of work and potential new ways to tackle diseases in the coming future.

Listen the podcast episode **here**

Discover more about the Gene Medicine group work **here**

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Cell and Gene Therapies are set to Revolutionize Healthcare: Here's How

Breaking Barriers in Healthcare:
The Paradigm Shift of Cell and Gene Therapies

RICHARD ROSSI
EXPERIENCED COLD CHAIN PROFESSIONAL IN CONTROLLED TEMPERATURE STORAGE AND DISTRIBUTION

The first chemotherapy drugs were discovered by mistake -- during World War II -- when humans were accidentally exposed to mustard gas. At that time, the only other treatments for cancer were radiotherapy and surgery. But these weren't necessarily promising for the treatment of all forms of cancer, especially cancers that had progressed.

Scientists were recruited to study the symptoms of people that were exposed to copious amounts of mustard gas. Based on their research, mustard gas agents were transformed into chemotherapy drugs used for the treatment of cancers. Chemotherapy is still the standard first line of cancer therapy for many people with cancer. Because chemotherapy doesn't only target cancer cells, they are associated with many side effects including diarrhea and hair loss.

But with a focus on patient centricity, the life science industry as we know it is changing.

Over the last couple of years, we have seen personalized medicine take the center stage. One particular class of products, called Advanced Therapeutic Medicinal Products (or ATMPs, for short), is gaining a lot of interest from scientists, doctors, researchers, investors, and patients, alike. Put simply, these therapies utilize cells, tissues, and/or gene approaches to develop products that can repair, generate, or replace faulty cells that cause diseases.
ATMPs, including cell and gene therapies (CGTs), have emerged as a groundbreaking solution, offering long-term symptom relief and even complete cures for patients who were previously considered incurable. These therapies have the potential to shift the paradigm in chronic and rare diseases, transitioning from mere disease management to achieving full recoveries. What was once a distant aspiration for scientists is now becoming a tangible reality, as various CGTs receive approvals based on promising results from clinical trials.

But with a focus on patient-centricity, the life science industry as we know it is changing

A Case for CGTs: Diffuse Large B-Cell Lymphoma

What is Diffuse Large B-Cell Lymphoma?

Diffuse Large B-Cell Lymphoma (DLBCL) is a type of cancer affecting the lymphatic system. It is characterized by its aggressive nature and rapid growth in the lymph nodes, liver, bone marrow, spleen, and other organs. DLBCL arises from the production of abnormal B lymphocytes, which normally play a crucial role in combating infections. However, in DLBCL, these abnormal cells fail to fully mature and accumulate in the lymph nodes and other organs, compromising the patient's ability to fight infections effectively.

Regardless of the chosen medical approach, DLBCL treatment is often intense and requires

frequent hospital visits over a short period. Coping with the diagnosis and treatment of this cancer can be challenging for patients, leaving them feeling fatigued and drained, particularly during and after treatment.

Standard treatment for Diffuse Large B-Cell Lymphoma

Standard treatment for Diffuse Large B-Cell Lymphoma (DLBCL) is determined by various factors, such as the location and stage of the cancer, as well as the patient's symptoms. The treatment goal can range from aiming for a cure to controlling the symptoms and the progression of the cancer for as long as possible.

The standard therapy typically involves a combination of chemotherapy and immunotherapy. Chemotherapy is used to destroy cancer cells, while immunotherapy involves the use of antibodies that attach to cancer cells, marking them for destruction by the immune system. However, a drawback of these standard treatments is that they are not targeted and can also affect healthy cells, resulting in side effects like hair loss.

How CGTs are changing the game?

Cell and gene therapies (CGTs) are revolutionizing the approach to DLBCL treatment. In some cases, patients may undergo high-dose chemotherapy followed by a stem cell transplant. Autologous transplants involve using the patient's own stem cells collected prior to the procedure, while allogeneic transplants use stem cells from a donor. Stem cell transplantation can potentially

" Coping with the diagnosis and treatment of this cancer can be challenging for patients, leaving them feeling fatigued and drained, particularly during and after treatment."

address the underlying issue by replacing problematic cells and offering a potential cure.

Another innovative therapy gaining prominence is CAR-T therapy, which is a personalized form of immune-cell-based treatment. CAR-T therapy involves modifying a patient's own immune cells to recognize and target cancer cells more effectively. This tailored approach has shown promising results in DLBCL and other types of cancer, providing new hope for patients.

"Clinical studies evaluating the effectiveness of Breyanzi have shown significant clinical benefits."

CGTs are transforming the treatment landscape for DLBCL, offering targeted and potentially curative approaches that hold great promise for patients.

Gene therapy, specifically CAR-T therapy, has become available to patients with certain types of lymphoma. One notable example is Breyanzi, a CAR-T therapy that received approval from the U.S. FDA and the European Medicines Agency (EMA) in 2022 for the treatment of large B-cell lymphoma, including DLBCL.

To create each dose of Breyanzi, the patient's blood is extracted, and T-cells, a type of white blood cell crucial for the immune system, are collected. These T-cells are then modified in a laboratory to express chimeric antigen receptors (CARs) that allow them to recognize and bind to proteins on cancerous B-cells. This modification flags the cancer cells for elimination.

Clinical studies evaluating the effectiveness of Breyanzi have shown significant clinical benefits. Patients treated with Breyanzi demonstrated meaningful disease control, event-free survival, complete responses to therapy, and progression-free survival, especially in comparison to patients who experienced relapse within 12 months after standard

first-line therapy. A high percentage of patients **(86%)** achieved either a complete or partial response, with **66%** achieving a complete response.

While there are potential risks of side effects associated with Breyanzi therapy, the therapy has received approval because the benefits outweigh the risks. A single treatment with Breyanzi offers patients a more favorable prognosis compared to standard combination therapy with chemotherapy and immunotherapy.

In summary, Breyanzi has shown improved survival rates and, in some cases, the potential for curing patients. Its success has rapidly established CAR-T therapies as a valuable treatment option for patients with certain types of lymphoma.

Cell and gene therapies (CGTs) are shaping the future of oncology, bringing about a significant transformation in the field. The emergence of personalized medicine has challenged the traditionalone-size-fits-allapproach in healthcare, emphasizing the need for better health outcomes and patient-centric strategies. Consequently, CGTs have garnered substantial funding and support, revolutionizing the treatment landscape.

The potential of CGTs is evident in the FDA's approval of over 20 cell and gene therapy products. These innovative therapies have been authorized for the treatment of various chronic conditions, including cancers, mucogingival conditions, retinal dystrophy, and spinal muscular atrophy. This remarkable progress highlights the shift from disease management to seeking genuine, long-term cures facilitated by CGTs.

However, despite the promising prospects, several challenges lie ahead. The implementation of cell and gene therapies faces obstacles related to ethics, regulations, costs, and logistics. These factors could impede the translation of life-saving therapeutics from the research bench to the patient's bedside. Overcoming these hurdles is crucial to unlock the transformative potential of CGTs and extend their benefits to millions of individuals suffering from incurable chronic and rare diseases, thereby enhancing their quality of life.

In conclusion, CGTs represent the future of medicine, offering hope and transformative potential in treating conditions that previously had no effective treatments. While there are obstacles to overcome, the continued development and integration of cell and gene therapies have the potential to revolutionize the life science and pharmaceutical industries, paving the way for better outcomes and improved quality of life for patients. life-saving therapeutics from the bench to the bedside.

Regulating Cell and Gene Therapies

Ensuring Safety and Efficacy

Being biological agents, cell and gene therapies (C&GT) require high standards of regulation. From bench to bedside, the overarching need for these therapies is to improve the lives of patients and tackle currently hard to treat (or impossible to treat) diseases. Tight regulations in the use and manufacture of these medicines are paramount to not only ensuring their safe use, but also allows for the planning and development of next generation therapeutics [1]. Biological agents such as cells and nucleic acids have a unique set of challenges with regards to regulation. For example, cell therapies in which cells are introduced (or re-introduced) into a patient are required to act on the site of interest, for example a tumour. However, it is possible that these cell states could shift and become inefficient or displaced in vivo, leading to off-target side effects [2]. With regards to gene therapy, therapies could be miss delivered to healthy tissue or indeed the wrong chromosome in the case of gene editing [3][4]. Indeed, the gene editing tool CRISPR/Cas9 which is praised for revolutionising gene therapy has much noted off-target effects in the range of >50% [5]. Due to these highly complex issues, patients who have received Cell or gene therapies require stringent follow up monitoring, this can be for as long as 15 years but is vital to ensure safety as well as improving current practices [1].

Currently, C&GT are regulated regionally with the FDA[6] and NIH regulating in the USA and in the EU under Advanced Therapy Medicinal Products (ATMP) Regulation (Directive 2001/83/

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EC, as amended by Regulation [EC] 1394/2007) [7]. Concentrating on EU regulation, these therapies are subclassified into four clusters: 1) gene therapy, 2) somatic cell therapy, 3) tissue-engineered therapies, and 4) combined advanced therapies. ATMPs are evaluated centrally, with a single licence valid across all EU nations, by the Committee for Advanced Therapies (CAT) of the European Medicines Agency [8]. The regulatory pathway chosen will depend on the properties of a product and the patient population it is intended to treat. The regulatory framework offers many regulatory procedures for moving ATMPs from clinical trials to market authorization.

An exemplar therapy which falls under these regulations utilises both gene therapy and cell delivery and is known as Chimeric antigen receptor T cell therapy [9][10]. Chimeric antigen receptor T cell therapy is the use of genetically engineered single chained antigen-recognition domain (extracellular) combined with 1 or more T cell domains (intracellular) [11][12]. The use of gene therapy techniques allows for the chimeric antigen receptor (CAR) to be introduced into T cells, rewriting the cells genetic code to make it target specific new antigens, a technique employed for the treatment of various cancers. The T cells used can be either allogeneic and autogenous meaning they can come from either healthy donors or the patient themselves respectively [13]. Lentiviral or retroviral vectors are the most commonly used for the delivery of CAR scripts into T cells, which leads to the permanent modification of the T cells genome to therapeutic advantages [14].

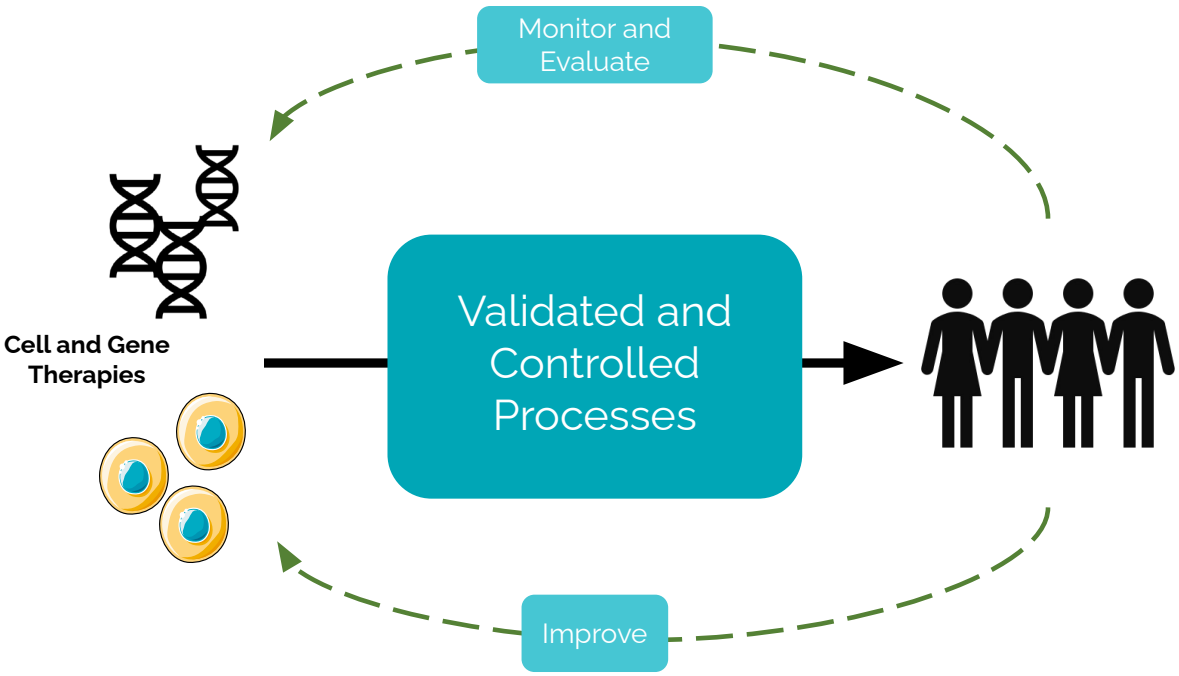
CAR-T cell therapies are currently classed as advanced therapy medicinal products under EU regulations. Autologous or allogeneic CAR-T cells, among other treatments, are categorised as gene therapy medicinal products under the umbrella term of ATMPs. Two CAR-T cell treatments, Yescarta™[15] and Kymriah™[16] currently have approved use in patients and are used for paediatric and adult patients respectively, sharing a common specific target of CD19 positive cells and is used in the treatment of B cell precursor acute lymphoblastic leukima (Kymriah™) and large B cell lymphoma (Yescarta™) [17] [18]. Both drugs finished their marketing

"CAR-T cell therapies are currently classed as advanced therapy medicinal products under EU regulations."

authorisation processes in 2018 under the prioritised medications PRIority MEdicines (PRIME) scheme, a system put in place in 2016 which provides regulatory support for medicines with the potential to significantly improve the lives and outlook of patients [19]. Since the majority of ATMPs that advance to authorisation or at least clinical trials are made from autologous mononuclear cells, starting material is typically obtained by apheresis facilities run by hospitals or blood banks [20,21]. From this arises an atypical situation where a product begins under one set of regulations (EU Tissues and Cells Directives) before moving to another set of regulations (ATMP Regulation), and in which a hospital serves as a service provider to industry[22,23]. The EU Tissues and Cells Directives underwent a review that is to be adopted in 2022 to revise the framework for blood, tissues, and cells. The new framework aims to allow for flexibility to better align scientific developments and discovery and thus increase commercialisation and globalisation of these technologies. Furthermore, a key focus was to remove superfluous legislation from technical provision allowing for standards to be updated more quickly. Alignment of these two frameworks will allow for contemporaneous rather than sequential operations, thus will facilitate the rapid emergence of C&GT use and development [24].

"Furthermore, a key focus was to remove superfluous legislation from technical provision allowing for standards to be updated more quickly."

Due to their anticipated high prices and complexity, access to ATMPs, including cellular therapies, will likely present a unique challenge for patients, medical professionals,



and national health systems [25] [26].

Real-world data is a key component of the European Medicines Agency big data strategy, and major work is being done to get the infrastructure ready to support this shift. As regulators become more knowledgeable and as science and medicine advance, accelerated processes like PRIME will continue to evolve. The focus of efforts to unify interpretations across the EU will probably continue to be on the interaction between European medicinal product rules and frameworks for genetically modified organisms. As manufacturing processes become more automated, risk and unpredictability should be reduced. Decentralized or "bedside" manufacturing may also become more prevalent, but it will still require high level regulatory permission and control.

In order to allay regulators' concerns about graft versus host disease, cell rejection, and the dangers of gene editing, therapies. like allogeneic CAR-T treatments will also need to be supported by a lot of data. Health-related personal data under the General Data Protection Regulation (GDPR) may see modifications to better enable secondary use of data acquired to support investigative and regulatory objectives.

In conclusion, the regulatory landscape of cell and gene therapy is rapidly evolving. More data is needed in order to better inform regulatory practices and to improve and grow the use of C&GT for all. As of August 2022, the clinical trial landscape of these therapies is vast with 42567[27] **and 5364**[28] **registered trials for cell and gene therapy respectively, showcasing the great potential of these revolutionary treatment strategies that could be tapped into with correct and efficient regulatory structure.** [28]

"As manufacturing processes become more automated, risk and unpredictability should be reduced. Decentralized or "bedside" manufacturing may also become more prevalent, but it will still require high level regulatory permission and control."

Global Cell and Gene Therapy Market & Trends

By

IMAPAC
Imagine Your Impact

Explore all APAC Cell & Gene Therapy companies and their pipeline & manufacturing capabilities in Imapac Market Intelligence Tracker available on our website. For details about conferences and events related to Cell & Gene Therapy, reach out to us:

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About IMAPAC

IMAPAC started by providing quality conference and networking opportunities for businesses in the life science industry. As it expanded its portfolio to include market research reports, webcasts, and digital solutions, it has become the go-to solution for business intelligence and networking activities in the life science industry.

What is the Company Mission Statement?

We are on an unrelenting mission to help life science businesses around the world generate tangible growth through our cause-driven business conferences. Our conferences are designed to break down barriers, inspire creativity, and drive positive change. We believe that conferences should offer more than just contacts; they should provide inspirational ideas and contribute to society as well.

Our Impact on the Life Science Industry

Over the past 3 to 5 years, IMAPAC has launched multiple new projects and expanded into new geographies. In 2017, IMAPAC launched the Logistics portfolio with conferences in Singapore and Korea, and now we are expanding into Japan. In 2018, we successfully launched the Biologics World Nordics event catering to the Scandinavian market, marking our first event in Northern Europe. IMAPAC has also relocated the Biologics Manufacturing Asia event from China to Singapore, making it the flagship show for the industry in Singapore with over 40 exhibitors and 500 attendees. In 2019, we entered the Japanese market with the launch of Biologics Manufacturing Japan.

Additionally, in 2019 we launched our market research division, producing bespoke market intelligence reports on different segments of the Life Science industry. We have also introduced LeadGen 360 digital solutions to assist biopharma and life science companies in brand awareness, generating high-quality leads, and conducting top-notch product launches.

IMAPAC continues to evolve and provide comprehensive solutions for the life science industry, including conferences, market research reports, webcasts, and digital marketing services.

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Cell and gene therapies (CGT) are poised to cause a major disruption in the biopharma sector. With more than 900 businesses focusing on advanced therapies worldwide and over 1000 cell and gene therapy clinical studies currently underway, the sector is expected to witness a surge in approvals, with up to 20 therapies potentially receiving approval annually starting from 2025. This trend is projected to continue growing over time.

The industry is utilizing numerous cutting-edge cell and gene therapies to treat severe diseases like cancer as well as rare diseases. Among the available treatments is LUXTURNA, a curative gene therapy for an inherited retinal condition that causes blindness. This therapy represents a significant advancement in medicine and was the first curative gene therapy to receive approval.

"In terms of geographical trends, there has been a decrease in developers in Europe and an increase in the United States and Asia Pacific regions"

In terms of geographical trends, there has been a decrease in developers in Europe and an increase in the United States and Asia Pacific regions, indicating a shift in focus. North America holds a dominant position in the global cell and gene therapy market, driven by a high prevalence of genetic diseases and increased research and development (R&D) activity. In North America alone, more than 200 companies operate in the CGT market. Additionally, favorable regulatory policies and guidelines in the United States further support market growth. Industry giants are capitalizing on these opportunities by focusing on the US market to launch their CGT products.

Currently, the US FDA has approved several cellular and gene therapy products for marketing. Six of these therapies are CAR-T cell therapies used to treat specific haematological cancers. The table next page provides a list of the approved therapies in the US.

More than 1,000 cell and gene therapies are currently under development, and it is expected that up to 70 of these treatments will receive approval in the United States by the year 2030. The US is projected to offer a growing number of innovative cell and gene therapies in the coming years.

APAC – The Fast-Growing Market for CGT

The Asia-Pacific (APAC) region has emerged as a fast-growing market for cell and gene therapy. Since the early 2000s, Asian countries have posed significant challenges and opportunities in this field. With its large population, Asia has always been an attractive market for pharmaceutical companies. Many companies are now recognizing Asia's progress in cell and gene therapy, driven by its active involvement in research, its suitability as a site for clinical trials, and its regulatory distinctions from Western countries. Substantial investments in research and clinical translation in Asian countries have contributed to the region's prominence. IMAPAC research reveals that there are thousands of regenerative medicine and advanced therapy trials taking place across Asia, making it a major center for growth in the field.

The cell and gene therapy market in Asia is currently experiencing a compound annual growth rate of over 40%, surpassing the growth rate in other parts of the world by about 4%. This growth is supported by government initiatives, academic and research institutes, and investment communities that promote the development of the cell and gene sector in Asia. There are more than 250 cell and gene therapy developers in the Asia-Pacific region. The table below provides the number of companies engaged in CGT development.

Proper name	Trade name	Manufacturer	Drug class	
idecabtagene vicleucel	ABECMA	Celgene Corporation, a Bristol-Myers Squibb Company	CAR T-cell therapy	Read more
nadofaragene firadenovec-vncg	ADSTILADRIN	Ferring Pharmaceuticals A/S	Gene therapy	Read more
HPC, Cord Blood	ALLOCORD	SSM Cardinal Glennon Children's Medical Center	Cell therapy	Read more
lifileucel	AMTAGVI	Iovance Biotherapeutics, Inc.	Cell therapy	Read more
fidanacogene elaparvovec-dzkt	BEQVEZ	Pfizer, Inc.	Gene therapy	Read more
lisocabtagene maraleucel	BREYANZI	Juno Therapeutics, Inc., a Bristol-Myers Squibb Company	CAR T-cell therapy	Read more
ciltacabtagene autoleucel	CARVYKTI	Janssen Biotech, Inc.	CAR T-cell therapy	Read more
exagamglogene autotemcel (exa-cel)	CASGEVY	Vertex Pharmaceuticals Incorporated	Cell and Gene therapy	Read more
HPC, Cord Blood	Clevecord	Cleveland Cord Blood Center	Cell therapy	Read more
HPC, Cord Blood	Ducord	Duke University School of Medicine	Cell therapy	Read more
delandistrogene moxeparvovec-rokl	ELEVIDYS	Sarepta Therapeutics, Inc.	Gene therapy	Read more
Allogeneic Cultured Keratinocytes and Fibroblasts in Bovine Collagen	GINTUIT	Organogenesis Incorporated	Cell therapy	Read more
HPC, Cord Blood	HEMACORD	New York Blood Center, Inc	Cell therapy	Read more
etranacogene dezaparvovec-drlb	HEMGENIX	CSL Behring LLC	Gene therapy	Read more
HPC, Cord Blood	None	Clinimmune Labs, University of Colorado Cord Blood Bank	Cell therapy	Read more
HPC, Cord Blood	None	MD Anderson Cord Blood Bank	Cell therapy	Read more
HPC, Cord Blood	None	LifeSouth Community Blood Centers, Inc.	Cell therapy	Read more
HPC, Cord Blood	None	Bloodworks	Cell therapy	Read more
talimogene laherparepvec	IMLYGIC	BioVex Inc., a wholly owned subsidiary of Amgen, Inc.	Oncolytic viral therapy	Read more
tisagenlecleucel	KYMRIAH	Novartis Pharmaceuticals Corporation	CAR T-cell therapy	Read more
donislecel-jujn	LANTIDRA	CellTrans Inc.	Cell therapy	Read more
Azficel-T	LAVIV	Fibrocell Technologies, Inc.	Cell therapy	Read more
atidarsagene autotemcel	LENMELDY	Orchard Therapeutics (Europe) Limited	Cell therapy	Read more
voretigene neparvovec-rzyl	LUXTURNA	Spark Therapeutics, Inc.	Gene therapy	Read more
lovotibeglogene autotemcel (lovo-cel)	LYFGENIA	bluebird bio, Inc.	Cell and gene therapy	Read more
Autologous Cultured Chondrocytes on a Porcine Collagen Membrane	MACI	Vericel Corporation	Cell therapy	Read more
omidubicel-onlv	OMISIRGE	Gamida Cell Ltd.	Cell therapy	Read more
sipuleucel-T	PROVENGE	Dendreon Corporation	Cell therapy	Read more
allogeneic processed thymus tissue–agdc	RETHYMIC	Enzyvant Therapeutics GmbH	Allogeneic processed tissue	Read more
valoctocogene roxaparvovec-rvox	ROCTAVIAN	BioMarin Pharmaceutical Inc.	Gene therapy	Read more
elivaldogene autotemcel	SKYSONA	bluebird bio, Inc.	Cell and gene therapy	Read more
allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat	STRATAGRAFT	Stratatech Corporation	Cell therapy	Read more
brexucabtagene autoleucel	TECARTUS	Kite Pharmaceuticals, Inc.	CAR T-cell therapy	Read more
beremagene geperpavec	VYJUVEK	Krystal Biotech, Inc.	Gene therapy	Read more
axicabtagene ciloleucel	YESCARTA	Kite Pharma Inc.	CAR T-cell therapy	Read more
betibeglogene autotemcel	ZYNTEGLO	bluebird bio Inc.	Cell and gene therapy	Read more
onasemnogene abeparvovec	ZOLGENSMA	Novartis Gene Therapies, Inc.	Gene therapy	Read more

Table: Approved Cell and Gene Therapies in the US

*Source: FDA (link **here**), accessed 15/05/2024*

Cell & Gene Therapy Developers Number of Companies

Biopharma: 225
Research & Academic : 29
Pharmaceutical: 14

South Korea with the highest number of cell therapy products approved is now set pave way in the gene therapy area. The South Korean government has taken a comprehensive approach to promoting gene and cell therapy. In 2019, Congress enacted the "Act on the Safety and Support of Advanced Regenerative Medical and Advanced Biopharmaceuticals". This statute allows for the conditional approval of pharmaceuticals for commercial scale after they have passed phase two clinical studies. This Act was enacted in August 2020.

China is another market leading in the cell & gene therapies development. China had licensed Gendicine for the treatment of head and neck squamous cell carcinoma by replacing mutant copies of the p53 tumour suppressor gene with normal copies fourteen years before the FDA approved its first gene therapy product. The CRISPR Cas9 genome editing tool is currently key development in gene therapy.

As of March 2022, the Japanese government intends to create a 10 trillion-yen ($86.5 billion) university fund to encourage research, as well as a start-up ecosystem that combines entrepreneurs, universities, funding, and public institutions.

Five major regions to look-out for are South-Korea, China, Japan, Australia and Taiwan. Below figure shows the presence of cell and gene therapy company across APAC countries.

A deeper dive into their region-wise presence:

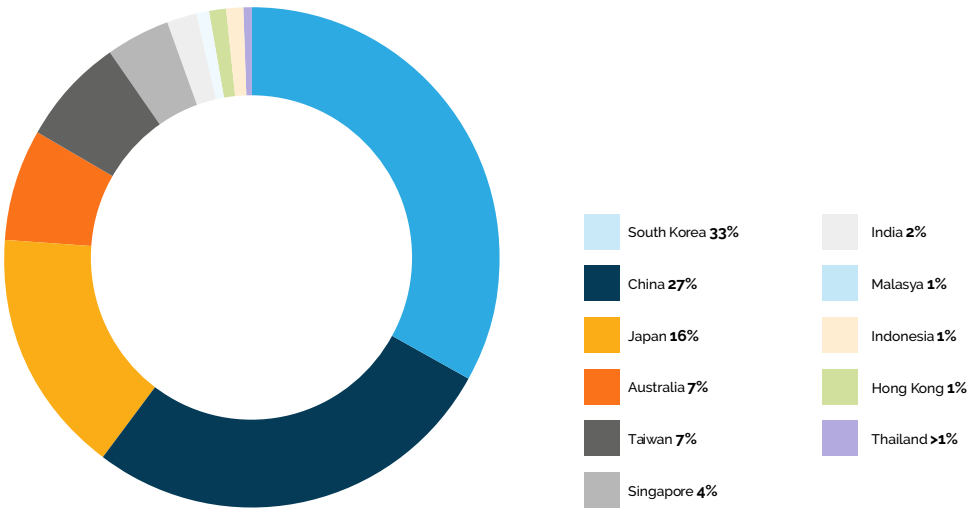


Figure: Cell & Gene Therapy Market by APAC

Breakthroughs in Cell and Gene Therapy Advancements in Europe

Despite all the developments and promises in the CGT, it could take a while for stakeholders to successfully overcome several unique European challenges before scientific discoveries in cell and gene therapy can be translated into improvements in healthcare in Europe. The adoption of CGT faces challenges such as high costs, low manufacturing yields, complex supply chain and safety and efficacy issues associated with CGT products. There are some issues that hinders the growth of a thriving CGT sector in Europe which must be addressed to hasten the development of life changing therapies. Some of these unique challenges are talent and manufacturing capacity shortfall that is further aggravated by logistical issues. For instance, in autologous cell therapy, patient's cells are extracted in the clinic, dispatched to specialized labs where the treatment is created, then transported back to the clinic to be administered, all while being subjected to time constraint and quality control. As a result, supply chains demand a high level of logistical accuracy, which is more difficult when there is no local manufacturing capability and when there is cross-border transportation, as in Europe. The procedure can be very slow for people who are dealing with advanced illness.

"Supply chains demand a high level of logistical accuracy, which is more difficult when there is no local manufacturing capability and when there is cross-border transportation, as in Europe."

More delays can be brought on by a variety of local concerns when different personnel are involved in various processes and systems. The entire supply chain flow can be affected by even a small interruption, such as a patient's apheresis appointment being delayed. In Europe, a fragmented market environment makes reimbursement a complicated and expensive process,

"It has expedited the evaluation of a number of treatments, including two cell therapies "Kymriah" by Novartis and "Yescarta" by Gilead for the treatment of aggressive B-cell lymphoma (...)"

in addition to the region's strict data protection and privacy laws. Research issue is another impediment that Europe faces in turning its strong research capabilities into market leadership. The major barrier is a lack of funding support for translational medicine. Authorities in Europe, however, are enthusiastic to fund novel therapies that focus on disease areas that are currently undertreated. As a result, the majority of the CGT therapies under development have been given orphan status by the European Medicines Agency (EMA). It has expedited the evaluation of a number of treatments, including two cell therapies "Kymariah" by Novartis and "Yescarta" by Gilead for the treatment of aggressive B-cell lymphomas and one ex vivo gene therapy "Zynteglo" by Bluebird Bio for the treatment of the the rare blood disorder beta-thalassemia. Below table lists the approved cell and gene therapies that have obtained EMA orphan status.

Medicine	Active substance	Marketing authorisation holder	Orphan designation	
Tecartus	brexucabtagene autoleucel	Kite Pharma	Treatment of mantle cell lymphoma and acute lymphoblastic laekaemia	Read more
Yescarta	xicabtagene ciloleucel	Kite Pharma	Treatment of diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma and follicular lymphoma	Read more
Luxturna	voretigene neparvovec	Novartis	Treatment of Leber's congenital amaurosis and retinitis pigmentosa	Read more
Carvykti	ciltacabtagene autoleucel	Janssen-Cilag	Treatment of multiple myeloma	Read more
Holoclar	ex vivo expanded autologous human corneal epithelial cells containing stem cells	Holostem	Corneal lesions, with associated corneal (limbal) stem cell deficiency, due to ocular burns	Read more
Strimvelis	autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence from human haematopoietic stem/progenitor (CD34+) cells	Fondazione Telethon	Treatment of severe combined immunodeficiency (SCID) due to adenosine deaminase (ADA) deficiency	Read more
Abecma	idecabtagene vicleucel	Bristol-Myers Squibb	Treatment of multiple myeloma	Read more
Zolgensma	onasemnogene abeparvovec	Novartis	Treatment of spinal muscular atrophy	Read more
Upstaza	eladocagene exuparvovec	PTC Therapeutics	Treatment of aromatic L-amino acid decarboxylase deficiency	Read more
Casgevy	exagamglogene autotemcel	Vertex Pharmaceuticals	Treatment of beta thalassaemia intermedia and major and sickle cell disease	Read more
Kymriah	tisagenlecleucel	Novartis	Treatment of B-lymphoblastic leukaemia/lymphoma	Read more
Hemgenix	etranacogene dezaparvovec	CSL Behring	Treatment of haemophilia B	Read more
Ebvallo	tabelecleucel	Pierre Fabre	Treatment of post-transplantation lymphoproliferative disorders	Read more
Roctavian	valoctocogene roxaparvovec	BioMarin	Treatment of haemophilia A	Read more
Alofisel	darvadstrocel	Takeda	Treatment of anal fistula	Read more
Libmeldy	atidarsagene autotemcel	Orchard Therapeutics	Treatment of metachromatic leukodystrophy	Read more

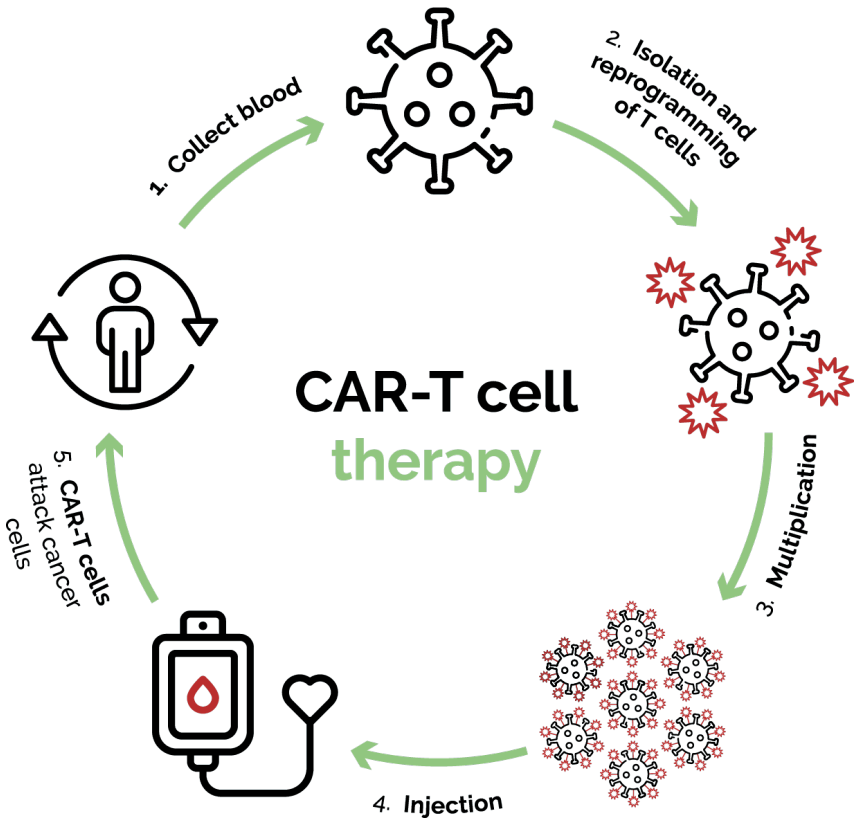
Table: Authorised advanced therapies with orphan designation in Europe.
Source: EMA (link here), accessed 5/06/2024

Viral-Vector Gene Therapies Show Great Promise

Viral-vector gene therapies have attracted significant interest from large pharmaceutical companies, as evidenced by their acquisition of several biotech startups valued at or above $1 billion in the past two years. Furthermore, global sales of viral-vector gene treatments are expected to grow at a rate of over 50% annually in the next five years, excluding the potential impact of COVID-19 vaccinations. This growth is expected to benefit a wide range of patients and have a substantial impact on the industry.

Rise of CAR-T Cell Therapies

CAR-T cell therapies have emerged as one of the most widely approved therapies in recent years. The FDA has already approved two CAR-T treatments, Yescarta and Kymriah, for oncology indications. Yescarta is approved for adults with certain forms of B-cell lymphoma, while Kymriah is approved for patients up to 25 years old with Acute Lymphoblastic Lymphoma (ALL). In addition to these approvals, three more CAR-T therapies, Tecartus in 2020, Abecma, and Breyanzi in 2021, have received regulatory approval.



The approval of CAR-T therapies has also led to an increase in mergers and acquisitions (M&A) activities within the sector. The level of investment has remained high, with 22 deals recorded in 2020. The COVID-19 pandemic has further fueled interest in cell therapy treatments, as evidenced by the surge in transactions in the first 10 months of 2021. If this trend continues, the industry is expected to witness more M&A agreements in the coming years.

Collaborations, licensing agreements, and strategic acquisitions between large pharmaceutical corporations and companies in the cell, gene, and RNA therapy field have become common. This trend is positive as it expands the pipeline to include treatments for both rare diseases and mass market indications. The value growth of the cell and gene therapy markets is projected to accelerate until 2026, offering these therapies the opportunity to make a significant impact on a wide range of diseases.

Overall, there are strong indications that cell and gene therapies will play a significant role in the treatment landscape over the next decade, offering a diverse range of treatment alternatives.

Fresh cell lines time constraints and international shipping challenges

DR RITA LEITOGUINHO
RESEARCH CELL THERAPY SPECIALIST
AT CELL THERAPIES PTY LTD

Dr Rita Leitoguinho, Cell Therapy Specialist at Cell Therapies Pty Ltd, is subject matter expert in the development and manufacture of ground-breaking cell therapy products for the treatment of patients with cancer. Rita leads cell therapy manufacturing projects for national and international clients and manages a team of highly skilled production and quality assurance staff to deliver clients' cell therapy products to patients in clinical trials at Peter MacCallum Cancer Centre. Rita manages the Good Manufacturing Practice (GMP) process development and safety validation of these cell therapy products, ensuring they comply with Australian regulatory bodies such as Therapeutic Goods Administration (TGA). These steps are crucial to establish new and effective treatments for Australian patients.

The Cell & Gene Therapy (CGT) industry in Australia is at the forefront of many new medical breakthroughs. Due to its strategic geographical proximity to major capitals in the Asia-Pacific, International Pharmaceutical companies are partnering with Australian clinical researchers to bring personalized cancer treatments closer to the patients. As such, moving products such as a patient's blood in a safe and quick way is imperative for a successful treatment.

Although a single off-the-shelf 'allogeneic' treatment for cancer hasn't yet been formulated, immunotherapies such as T-Cell based treatments have gained notoriety of late due to their very promising effectiveness against certain types of blood cancer. The downstream success of these therapies relies heavily on obtaining high quality material in the form of leukapheresis products (filtrated white blood cells which include T-cells) from human donors. Getting high quality 'Leukopaks' can be a challenge especially in Australia where compensated donations for human blood-related products aren't permitted. As such, scientists and medical practitioners must acquire these via generous donations from healthy donor volunteers or by ordering these products from the United States, where compensation for donors has already been approved and these are therefore commercially available.

"As such, moving products such as a patient's blood in a safe and quick way is imperative for a successful treatment."

Sourcing precursor material for CGTs, and the logistics of shipping live blood products poses a challenge. Products must be shipped without losing the functionality that makes these immune cells so valuable in the first place. It generally takes 48 hours or more for human blood products to be shipped and cleared customs in Australia, relying on a very intricate logistics and transportation operation. Delayed or cancelled international flights containing such products or lack of urgency to process necessary customs declarations will occasionally render these no longer usable when they get to the patient.

One prospect that could aid mitigating Leukopak availability would be to use cryopreserved products, however, this assumes frozen products retain high viability and functionality. Tests performed on apheresis material at both ends of shipment have shown that there can be significant losses of viable cells. Though the lost of cell viability poses a challenge to the number of cells that can be used, this seems to be a small price to pay to acquire material that some countries like Australia would otherwise not be able to acquire.

Although apheresis product from healthy individuals is commercially available to purchase in the US, patient Leukopaks are much more valuable and therefore the option of cryopreservation might not be possible due to the already low

"Challenges around transport of leukapheresis affect products coming into Australia as well as products leaving Australia."

number of white blood cells.

Challenges around transport of leukapheresis affect products coming into Australia as well as products leaving Australia. Some Australian patients undergoing immunotherapy clinical trials have their leukapheresis transported to the main sponsor's manufacturing site, which can be located in Australia or as far as in the US. For these situations, cryopreservation of this material is the safest option compared to the possibility of the fresh product being lost or delayed in transit, rendering it useless.

Although cryopreservation of blood products presents a quick solution for the transport of emerging cell therapies, there is still a great appetite from the global research community requiring a sustainable shipment of blood-derived products. This includes coordination between patient/donor, sponsor, clinical site, clinician/nurses, CRO, manufacturing facility, transport/logistics company. And across the value chain, particularly for autologous cell therapies (patient-specific product), chain of identity is an imperative.

CRYOPDP as a key partner for Cell&Gene shipments

Cold-chain solutions tailor-made to each shipment

CRYOPDP is a leading temperature-controlled logistics company that has been dedicated to ensuring that critical medicines, life-saving goods, and therapies reach their intended recipients in optimal condition for a significant period of time. Our mission is to provide secure and dependable logistics services for the pharmaceutical and healthcare industries, ensuring that temperature-sensitive goods arrive at their intended destinations in pristine condition.

"Our mission is to provide secure and dependable logistics services for the pharmaceutical and healthcare industries, ensuring that temperature-sensitive goods arrive at their intended destinations in pristine condition."

CRYOPDP was founded by a group of experienced logistics professionals who recognized the specialized logistics services demand in critical industries. With a focus on pharmaceutical and healthcare logistics, CRYOPDP was created to meet the unique challenges of logistics for life-saving temperature-sensitive goods. Since then, we have grown into a global company with operations in North America, Europe, and Asia, serving customers in over 80 countries.

At CRYOPDP, we understand the imperative nature of our customers' life-saving goods and the importance of maintaining their integrity through a range of temperature-controlled solutions that span from -196°C to +25°C. With a focus on customized cold chain solutions for life-saving goods, our specialized logistics services cater to the unique needs of clients in the pharmaceutical, biologics, and medical device industries. With our state-of-the-art facilities, specialized equipment, and experienced professionals, we offer a comprehensive range of services that provide our customers and businesses with unique needs. Our facilities and equipment ensure optimal temperature control during the logistics process, guaranteeing the safety and efficacy of our clients' products.

Our services include cold chain management, temperature-controlled transportation, including deep-frozen logistics. We specialize in handling ultra-low temperatures, making us an ideal partner for the **cell and gene therapy industry,** where temperature control is critical to the success of these advanced therapies.

We are a trusted and reliable logistics partner for the cell and gene therapy industry. Our expertise in temperature-controlled logistics ensures the safe and secure transportation and delivery of these delicate and highly sensitive samples. We go beyond just transportation by providing stress-free experiences for our customers, who have the confidence that their life-saving goods are in good hands. Our commitment to compliance, sustainability, and customization makes us an industry leader in providing unparalleled services that are vital to ensuring global health and well-being. Our successful track record in temperature-controlled logistics has established us as the ideal partner for the cell and gene therapy industry.

"Our commitment to compliance, sustainability, and customization makes us an industry leader, offering customers unparalleled services"

In the healthcare logistics industry, any misstep can quickly become public knowledge, making it imperative for companies like ours to prioritize quality and compliance in their operations. At CRYOPDP, we understand the high stakes involved in handling critical and time-sensitive shipments in this industry. With a history of success in temperature-controlled logistics, our state-of-the-art facilities, experienced professionals, and specialised equipment ensure that life-saving goods are transported and delivered safely and securely.

Our commitment to compliance, sustainability, and customization makes us an industry leader, offering customers unparalleled services that are vital to ensuring global health and well-being. As a trusted partner for the cell and gene therapy industry, we have the expertise to manage the transportation of delicate and highly sensitive samples, giving our clients the confidence that their products will arrive in optimal condition.

CASE STUDY

Against the clock

cell and gene therapy shipment for a cancer patient

When our clients need our support in critical shipments, they always know they can rely on a dedicated team that guarantees rigorous transport to meet all the requirements to protect the patient's health.

THE SHIPPING CHALLENGE

A Biotech company focused on immunotherapy reached out to CRYOPDP with an emergency shipment for a cancer patient that no other carrier was able to accommodate.

The client needed to ship a cell and gene therapy for a cancer patient from Boston to St. John's Cancer Institute in Santa Monica, California, using an LN2 large dry shipper.

THE OUTCOME

This shipment was extremely time-sensitive as the treatment for the patient was scheduled for 10 am the following day. Due to the actions of our operational team, we were able to get the cell and gene therapy:

Delivered on time
to St. John's Cancer Institute
by Friday **8:00 am**

Treatment administrated
at **10:00 am** that day

Our overall mission is to **improve people's health,** and thanks to a team effort, CRYOPDP was able to fulfil the client's request to get their treatment to the patient when no other courier could, in **record time,** successfully!

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“Thinking about the *patient* is what moves and motivates us to be *better every day.*”

Cedric Picaud

CRYOPDP CEO

CRYOPDP

Enabling the Life Sciences

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