# Unlocking the Future

## Realising the value and supporting the uptake of ATMPs in the EU

European Alliance
for Transformative
Therapies

#MEPsforATMPs

# Executive Summary

**Advanced Therapy Medicinal Products** (ATMPs) **represent a transformative shift in medicine**. Unlike medicines that manage symptoms, ATMPs, including cell and gene therapies, address the root causes of diseases, including gene and cell therapies, offer the potential for long-lasting or even permanent benefits with just a single administration. This transformative approach not only improves patient outcomes but also reduces the long-term burden on patients and healthcare systems.

ATMPs are identified in the Draghi Report[1] as **emblematic of the EU's potential to lead in cutting-edge medical innovation**. Despite being the first region to adopt an ATMP-specific regulatory framework, the EU is now lagging behind in the global race for innovation. The Draghi report highlights the EU's growing competitiveness gap in pharmaceutical innovation and underscores the need for a sustainable and predictable market to ensure continued investment in research and development. **ATMPs are a litmus test for the EU's ability to translate scientific excellence into global competitiveness.**

ATMPs are not just medical breakthroughs. They are **integral to the EU's pharmaceutical and life sciences ecosystem.** The EU's current political ambition to boost its global standing in innovation and competitiveness provides an opportunity to address issues faced by ATMPs that stand to benefit **patients, EU healthcare systems, and societies.** Ongoing and upcoming EU policy and legislative initiatives, such as the revision of the General Pharmaceutical Legislation (GPL), the implementation of the Health Technology Assessment (HTA) and Clinical Trials Regulations, and the upcoming EU Biotech Acts offer a window of opportunity to further integrate innovation and improve patient access. As the Commission advances the implementation of the Draghi Report, complementary actions at national level will also be necessary to achieve these objectives.

> *ATMPs are not simply a scientific breakthrough or an economic development that can benefit society at large. For people living with chronic, life-long and often untreatable conditions, they represent hope to extend, restore and transform life and to remove disability. This has a tremendous impact on the patients' quality of life but also on their identity and their ability to live a full life and to reach their potential.*
>
> **AVRIL DALY, PRESIDENT OF EURORDIS**
> **PATIENT REPRESENTATIVE**

The **European Alliance for Transformative Therapies** (TRANSFORM) **is a multi-stakeholder alliance** connecting MEPs and policymakers with patient groups, medical experts, associations, scientists, researchers, industry actors, networks, and other relevant stakeholders.

TRANSFORM's recommendations aim to **create a policy ecosystem that allows all eligible patients to benefit from transformative therapies**. Addressed to EU policymakers, healthcare providers, and Member States, these recommendations call for reframing pharmaceutical expenditure as a long-term strategic investment, removing structural barriers to access for ATMPs, develop sustainable and innovative approaches to manage the costs of treatment and care, and expanding diagnosis. The diverse expertise and collaborative efforts of TRANSFORM's members underscore the importance of these recommendations for **effectively integrating ATMPs into healthcare systems and ensuring patients can fully benefit from these medical advances.**

**Immediate action is needed to address the challenges faced by ATMPs** and to ensure their successful integration into healthcare systems. The EU must be ready to develop, authorise, and provide access to these therapies, as delays could result in missed opportunities for patients, society, and healthcare systems. Building a vibrant ATMPs ecosystem is critical to sustain investment in clinical research and biomanufacturing capabilities, and to ensure that innovative treatments remain available to those who need them. The **time to act is now** to ensure that patients across the EU can benefit from these groundbreaking therapies.

[1] The Future of European Competitiveness – A Competitiveness Strategy for Europe.

# TRANSFORM policy recommendations

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| 1 | Reframe pharmaceutical expenditure in innovative therapies as a long-term strategic investment |
| 2 | Remove structural barriers to the implementation of innovative contracting schemes |
| 3 | Greater flexibility in HTA methodologies and value appraisal where uncertainty in clinical evidence is justified |
| 4 | Expand diagnosis for faster patient access and support centres of excellence for adequate delivery of care |
| 5 | Securing the future of ATMPs through a qualified workforce |
| 6 | Leverage existing national resources and infrastructure for broader ATMP utilisation |

# Realising the promise of ATMPs in the EU

**Advanced Therapy Medicinal Products (ATMPs) are a revolution in the field of science and medicine. They have the potential to rectify the underlying causes of many diseases, including rare, genetic conditions and cancers, and restore body function while also halting disease progression.**

As of 2025, 27 ATMPs have been approved by the European Medicines Agency (EMA).[2] Yet, barriers persist in many EU Member States which directly impacts access to these scientific breakthroughs for eligible patients. ATMPs are often administered with a single dosage and provide benefits that are long-lasting, often for several years or potentially permanently. EU health systems are not yet ready to adequately evaluate and absorb these medicines, leading to missed opportunities for patients, society at large, and healthcare systems. The public sector, who plays an important role in the ATMP ecosystem, also face challenges hindering their development.

This situation clearly highlights the need to rethink how these medicines are perceived and how policies support their development and uptake. It is crucial that healthcare systems are equipped to recognise the value of ATMPs and integrate them effectively into clinical practice. This will ensure that patients, clinicians, industry, governments, and society can fully benefit from these medical advances.

The European Alliance for Transformative Medicines (TRANSFORM) sets here below its vision for how this can be achieved. Through this position paper, TRANSFORM shares its recommendations to build a policy ecosystem that will allow all eligible patients to benefit from these revolutionary therapies. It is critical that EU health systems are ready for ATMPs, as these therapies are currently being investigated to treat an increasing number of diseases, which will impact a potentially much larger patient population.

## A growing competitive gap in the EU

The Draghi report[3] identifies **ATMPs as emblematic of the EU's potential to lead in cutting-edge medical innovation**. It frames them as a litmus test for the EU's ability to translate scientific excellence into global competitiveness. The report highlights the EU's growing competitiveness gap in the pharmaceutical market, including for innovative therapies such as ATMPs. The creation of a sustainable and predictable market is critical to ensure continued funding streams into research and pipeline development. In the EU ATMPs do not yet have an established market and are struggling to maintain investors' interests due to their limited application and availability. **Failing to create a viable economic model for ATMPs, could deter manufacturers from launching their products in the EU, reduce investment in clinical research and drive clinical trials to other world regions.** A loss of clinical research in the EU would not only translate into a loss of opportunities for patients and research, but also hinder the upscaling and maintaining of medical infrastructure, such as laboratories and medical centres, to support the development, delivery and monitoring of innovative medicines.

**The Draghi report identifies significant challenges** impeding the EU's progress in this field: lower and more fragmented public and private R&D investment in the EU and a weaker supporting environment, and a slow

[2] EMA CAT Quarterly Highlights and Approved ATMPs (May 2025). Available here.
[3] The Future of European Competitiveness – A Competitiveness Strategy for Europe.

and complex EU regulatory framework with varied approval timelines and more limited access to structured scientific advice. Patient treatment with ATMPs require cutting-edge infrastructures and trained healthcare professionals. Significant differences persist across Member States' healthcare systems, particularly in their capacity and willingness to invest in innovation. The fact that ATMPs must undergo 27 distinct national pricing and reimbursement procedures and a limited use of cross-border healthcare pathways are adding to the complexity of securing patients' access.

**The EU's current political ambition to boost its global standing in innovation and competitiveness gives an opportunity to revisit, streamline and address issues in the ATMPs EU and national frameworks.** Ongoing and upcoming EU policy and legislative initiatives, such as the revision of the GPL, the implementation of the HTA and clinical trials legislations, and the forthcoming Biotech Act offer a window of opportunity to address challenges faced by ATMPs and future-proof the EU regulatory framework for integrating innovation and improving access to patients

# Delivering sustainable innovation: ATMPs' unique value proposition for healthcare systems and patients

ATMPs represent a new class of medicines that target on the root cause of disease, offering long-term or potentially curative benefits rather than symptom management. They help to restore function and reduce long-term treatment burden. **They can provide significant value whether used as first-line interventions or as second- or later-line options for patients with limited alternatives**. Several EU-approved ATMPs have already demonstrated measurable improvements over traditional treatments across oncology, haematology, and rare diseases.

By integrating these therapies into clinical practice, health systems can **unlock their full value** by improving patient outcomes, productivity, and long-term health system sustainability. Achieving this will require both the **evolution of Member States' health systems and infrastructures** and **a paradigm shift** in how the value of ATMPs is assessed **from expenditure to investment**.

> *To support faster and more streamlined uptake of ATMPs, the EU can play a key role in addressing systemic fragmentation and enabling cross-border coordination.*
>
> **ANGELOS ATHANASOPOULOS, EAHAD, TRANSFORM MEMBER CLINICIANS' REPRESENTATIVE**

To ensure that ATMPs are delivered to patients in a timely manner so that they can take fully advantage of the health benefits they offer, TRANSFORM recommends Member States to:

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| 1 | **Reframe pharmaceutical expenditure in innovative therapies as a long-term strategic investment** |
| 2 | **Remove structural barriers to the implementation of innovative contracting schemes** |
| 3 | **Allow greater flexibility in HTA methodologies and value appraisal where uncertainty in clinical evidence is justified** |

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## Reframe pharmaceutical expenditure in innovative therapies as a long-term strategic investment

**TRANSFORM calls on Member States to reframe pharmaceutical expenditure as a long-term strategic investment rather than an immediate cost. Member States should recognise the value of medical innovation for sustainable health systems. This should include broadening health outcomes indicators used to assess long-term economic impact.**

In addition to improving patients' health outcomes, ATMPs can offer broader benefits to strained healthcare systems and society.

### FRAMING HEALTH EXPENDITURE AS LONG-TERM INVESTMENT: THE ECONOMIC CASE FOR INVESTING IN RARE DISEASE TREATMENT

People living with rare diseases incur an average annual healthcare cost of €121,900, which is six times higher than that of those without a rare condition. This figure includes medical and non-medical costs (such as supportive care and caregiving) as indirect costs such as loss of productivity and income. However, this figure does not include the cost in the loss of quality of life that comes with living with a rare disease. Collectively, rare diseases cost Europe €249.3 billion annually, surpassing even the cost of cardiovascular diseases. Thus, looking at the broad economic repercussions of diseases such as rare diseases, it can be concluded that their long-term value outweighs their immediate cost on healthcare systems and society.

*Source Charles River Associates, The Economic Cost of Living with a Rare Disease Across Europe, 2024)*

By establishing early and accurate screening programmes to identify patients, healthcare systems can avoid long-term care for patients suffering from chronic and debilitating diseases. Ensuring ATMPs are delivered in a timely manner to patients, whether as a first-line or later-line treatment, can reduce long-term healthcare and societal costs, making a targeted investment in ATMPs both impactful and cost-effective. As evidence surrounding ATMPs continues to grow, it is increasingly clear that these therapies offer substantial patient and societal benefits. Consequently, the costs associated with innovative therapies such as ATMPs should be reframed as long-term investments in health and society, rather than immediate expenditures. By improving patient outcomes and reducing disease burden, **ATMPs can generate long-term savings for healthcare systems[4] while strengthening Europe's life sciences competitiveness by driving demand, expertise, and investment that fuel and sustain innovation across the ecosystem.**

### FRAMING HEALTH EXPENDITURE AS LONG-TERM INVESTMENT: THE ECONOMIC CASE FOR INVESTING IN RARE DISEASE TREATMENT

An example on how ATMPs broader financial impact can be assessed, can be found in Italy where in March 2025, the Italian Ministry of Health introduced a pilot measurement system for Spinal Muscular Atrophy (SMA), a group of rare neuromuscular disorders that cause muscle weakness and atrophy due to the loss of motor neurons. This proposed system measures and monitors the savings in both direct and indirect costs achieved using Advanced Therapy Medicinal Products (ATMPs) in this disease area, by employing an economic model based on real-world data. This system gathers data that will feed methods for accounting for healthcare spending on the purchase of ATMPs, capable of capturing the opportunities arising from the specific cost-benefit profile of treatment based on these therapies. This

[4] Ingrid Maes, Hafida Boufraioua, Walter Van Dyck, Lies Schoonaert. (2019). Innovative funding solutions for paradigm changing advanced therapy medicinal products (ATMP) in Belgium - Multi-stakeholder consensus on gene therapy funding solutions. https://www.inovigate.com/media/filer_public/e8/9c/e89ca2b0-1dcf-48fb-9afc-9e911ddcef84/innovative_funding_solutions_-_short_version_without_appendix_vs09.pdf

example could be replicated by other Member States to adequately capture the value ATMPs bring to patients, healthcare systems and broader society.

*Source: Position Paper of #VITA – Value of Innovation of Advanced Therapies (April 2025)*

## 2 Remove structural barriers to the implementation of innovative contracting schemes

**TRANSFORM calls for removing structural barriers to innovative payment schemes, including by updating the current EU accounting rules to allow for annuity payments.**

### THINKING OUTSIDE THE BOX: INNOVATIVE PAYMENT MODELS AND SCHEMES FOR A GENE THERAPY TARGETING A RARE BLEEDING DISORDER

Following EMA licensing of a gene therapy for a rare bleeding disorder in 2023, seven countries (Austria, Denmark, Germany, Italy, Spain, Switzerland, and UK) took innovative approaches to manage access to the therapy. For example, Austria used a newly created supra-national fund for high priced and specialised medicines so that the cost associated with the therapy would not impact health budgets; Denmark reimbursed the therapy on a performance-based model whereby costs are annually incurred by the payer, if the therapy proves effective in the long-term. A digital platform was established to report on the effectiveness of the product. In Germany, a gene therapy was made available to patients through the first national, success-based reimbursement agreement with the National Association of Statutory Health Insurance Fund that includes a pay-for-performance element.

This example shows that Member States can develop innovative access schemes that are tailored to their national framework and needs. TRANSFORM encourages Member States to share these examples and best practices so that they can be replicated and benefit patients for broader access to ATMPs. Also, given that ATMPs differ in terms of mechanism of action, patient populations and diseases treated, data available or that can be collected, and healthcare delivery needs, there is no 'one size fits all' model.

*Sources: Austria, Denmark and France*

Updating the EU accounting rules would enable Member States to make greater use of innovative payment schemes and better integrate ATMPs into the healthcare systems. Under current EU accounting rules, the full cost of a medicine must be recorded upfront, even if payments are spread out over years to reduce the immediate impact on healthcare systems. The delayed payments are treated as debt increasing the country's recorded liabilities. This approach creates a budget impact, counteracting the original goal of reducing it. Therefore, **the Commission should issue guidelines on the interpretation of EU accounting rules, enabling more Member States to treat medical innovation such as ATMP as intangible component of gross fixed assets and implement multi-year payments without full upfront accounting.**

## 3 Greater flexibility in HTA methodologies and value appraisal where uncertainty in clinical evidence is justified

**TRANSFORM calls for:**

- **Ensuring the implementation the EU HTA regulation does not lead to duplication or delays in the value assessment process at the national level.**

- **The use of flexible methodologies in the Joint Clinical Assessments (JCAs) to recognise ATMPs' unique development challenges and their limitations for evidence generation.**
- **The meaningful inclusion of stakeholders, such as patients, caregivers and clinicians, to bring real-life and lived-in experiences to value assessment processes, which is especially critical when clinical evidence is limited.**
- **A broader approach to value definition for innovation, going beyond unmet medical need and taking into account long-term benefits to patients, healthcare systems and society.**

## Implementing the EU HTA regulation so that it does not lead to duplication or delays in the value assessment process at the national level

The fragmentation in national practices, methodologies and data requirements for HTA and pricing and reimbursement processes means that ATMP sponsors must develop different application dossiers for each Member State, slowing the time to patient and increasing complexity for this process. The HTA Regulation, which came into application in January 2025, promised to streamline the HTA process for Member States by providing harmonised EU-level joint clinical assessments to support Member States in their value assessment process. **TRANSFORM members are concerned that the JCA methodologies as applied by Member States may not streamline the process as intended. Instead, they could lead to additional burden by compounding the different Member States requirements.** An example is the acceptability of surrogate endpoints.[5] Developers will have to demonstrate a correlation with the final endpoint to be accepted for JCA, however each Member Sate may decide whether they accept the surrogate endpoint. To ensure the HTA Regulation delivers on its goal of faster and more consistent access, the EU should promote clear, predictable guidance on evidence requirements and foster early dialogue between developers and assessors to align expectations across Member States.

## The use of flexible methodologies in the Joint Clinical Assessments (JCAs) to recognise ATMPs' unique development challenges and their limitations for evidence generation

**TRANSFORM recommends that the Member States Coordination Groups on HTA recognises the specificities of ATMPs, while also ensuring that the process does not increase bureaucratic burden and further delays patient access.**

As therapies move toward ever more personalised treatment, ATMP development faces major hurdles as they target conditions with lower prevalence, higher disease burden and severity, and scarce availability of meaningful comparative treatments. Many conditions targeted by ATMPs are childhood-onset genetic conditions where the use of placebo or delayed treatment may be inappropriate. In this context, **ATMP developers face ethical and practical challenges in conducting randomised clinical trials, which considered as the golden standard of clinical evidence generation.** Because ATMP trials often rely on small, single-arm designs and surrogate endpoints, they cannot always generate the type or volume of data traditionally required by regulatory and reimbursement systems, highlighting a mismatch between current evidence expectations and the realities of ATMP development.[6]. In the most severe cases, failure at the HTA stage can block patient access if payers decide against reimbursement. Even where reimbursement is granted, the absence of an adapted HTA framework can lead to delays or sub-optimal decisions driven by high levels of perceived uncertainty.[7]

EU regulatory pathways have already considered these specificities and provided early regulatory support and innovative approaches, such as the PRIME scheme,[8] a dedicated scientific committee within the EMA, conditional market access under exceptional circumstances, and the introduction of regulatory sandboxes in the revision of the General Pharmaceutical Legislation. However, **national HTA and pricing and**

[5] A surrogate endpoint is a biological or clinical marker used in HTA to predict a treatment's real health benefit, such as survival or recovery, when long-term outcomes are not yet available.
[6] Iglesias-Lopez C. et al. Methodological Characteristics of Clinical Trials Supporting the Marketing Authorisation of Advanced Therapies in the EU. Front. Pharmacol., 29 November 2021. https://doi.org/10.3389/fphar.2021.773712
[7] OD Expert Group. (2023). AN EU HTA FIT FOR RARE DISEASEs. https://od-expertgroup.eu/277-2/
[8] PRIME is a scheme run by the European Medicines Agency (EMA) to enhance support for the development of medicines that target an unmet medical need. This voluntary scheme is based on enhanced interaction and early dialogue with developers of promising medicines, to optimise development plans and speed up evaluation so these medicines can reach patients earlier.

**reimbursement agencies face challenges in adequately assessing the value these therapies bring**, as many HTA processes were designed to evaluate pharmaceuticals developed for chronic conditions with costs spread over a long period of time and volume discounting. While some national HTA bodies allow greater flexibility in evaluating innovative therapies, there is a risk that JCAs could adopt a more stringent approach, potentially limiting patient access. The EU HTA Regulation is an opportunity to **ensure that JCA methodologies fully reflect the specificities of ATMPs and make greater use of real-world evidence** to support their value assessment, ensuring that patient access to transformative therapies is not hindered by regulatory barriers.

## The meaningful inclusion of stakeholders, such as patients, caregivers and clinicians, to bring real-life and lived-in experiences to value assessment processes, which is especially critical when clinical evidence is limited

ATMPs may be the first and sole treatment for a particular disease, as is often the case in many ATMPs used in rare diseases. Member State may lack the adequate expertise, both in terms of a value assessment and clinical use, to fully evaluate the holistic value of the therapy. Stakeholders, including patients and healthcare professionals, can provide informative insights into the clinical manifestation of the disease, treatment requirements, impact on the quality of life, current treatment standards and healthcare resource utilisation. Tjey can also offer a unique perspective of the lived experience of patients and caregivers, as well as the expected benefits from these therapies. Therefore, **TRANSFORM also calls for the inclusion of stakeholders in value assessment processes to more accurately the value ATMPs can bring.** TRANSFORM appreciates the fact that the JCA endeavours to ensure these voices are included, yet, crucial conversations remain regarding the Conflict-of-Interest rules when it pertains to the selection of experts.

## A more holistic approach to value definition for innovation, going beyond unmet need and taking into account long-term benefits to patients, healthcare systems and society

The current regulatory framework tends to focus primarily on immediate impacts in areas of unmet medical need, often rewarding innovation based on short-term results. However, for future advancements - especially in the case of therapies like ATMPs - this approach may overlook the broader, long-term value they bring to patients, caregivers, and healthcare systems.

As such, in the upcoming revision of the General Pharmaceutical Legislation, the definition of unmet medical need should be broadened to accommodate not only the immediate, but also the evolving needs of diverse patient groups. This would allow for a more flexible, forward-looking framework that recognises the full potential of innovative therapies, encouraging continued investment and research in areas that may not yet be fully understood but offer substantial long-term benefits.

### DEMONSTRATING THE VALUE OF ATMPS

TRANSFORM members reports insights on the patients' lived experiences, the disease's impact on their quality of life, combined with information on the long-term economic burden of the current standard of care compared to novel therapies, can support HTA bodies and payers in their decision-making process by demonstrating the added value of ATMPs.

Therefore, TRANSFORM supports the involvement of stakeholders such as patients and clinicians in the ATMP's value assessment processes to provide invaluable insights and support the evaluation of ATMPs.

# Revolutionising patient access: Innovating healthcare systems for the future

Following the national pricing and reimbursement process, ATMPs enter national healthcare systems where they must be integrated into patient care pathways. TRANSFORM has identified a series of hurdles preventing streamlined patient access and suggests some solutions to tackle these challenges to enable faster uptake of ATMPs at national level.

## 4 Expand diagnosis for faster patient access and support centres of excellence for adequate delivery of care

**TRANSFORM calls on the European Commission to support Member States and existing expert networks in expanding newborn screening (NBS), early diagnosis and referral programmes to fully benefit from innovative therapies, such as ATMPs.** Great disparities exist in the EU in terms of the number of screening services offered to newborns. Expanding these practices adequately will ensure that diagnosed patients will have a greater chance at accessing life-saving therapies like ATMPs before the onset of or progression of symptoms, giving a greater chance at optimal quality of life and increasing the long-term value of the therapy offered. In addition, such expansion of screening services supported by registries on long-term outcome will also deliver much needed data and information to further study these conditions so that adequate treatment and care practices can be developed.[9] It will be critical that such expansion in testing is integrated within the patient care pathway and that patients with no treatment options are offered support services to care for the symptoms and improve quality of life.

**TRANSFORM calls for the establishment of a minimum set of newborn testing to be applied in all Member States and fostering harmonisation by leveraging the European Reference Networks. This minimum number should include tests for diseases for which an approved treatment is available.**

> *Early administration of gene therapy for patients with a particular type of severe combined immunodeficiency can have a significant impact on a baby's health, meaning a life free of regular treatment.*
>
> MARTINE PERGENT, IPOPI, TRANSFORM STEERING GROUP MEMBER

[9] European Confederation of Pharmaceutical Entrepreneurs AISBL (EUCOPE). (2025). The Future of Healthcare: Advancing Screening and Testing in Oncology, ATMPs, and rare diseases. Available here.

In this context, existing expert networks, such as European Reference Networks (ERNs) and other clinical networks, are already tasked with developing guidelines and best practices for diagnosis in the target disease areas covered by ATMPs.

**TRANSFORM advocates for further strengthen these networks, including with financial support, and continues integrating their work into national healthcare systems, as already done by some EU-funded projects.**

> *The national health system is slow in adapting to this new class of products. Due to the limited number of patients, including paediatric populations and rare diseases, there is a necessity to create centres of excellent to deliver the best care.*
>
> GIOVANNI MIGLIACCIO, EPTRI, TRANSFORM BOARD MEMBER REPRESENTATIVE OF ACADEMIA

## 5 Securing the future of ATMPs through a qualified workforce

**TRANSFORM encourages the EU and Member States to take a coordinated approach to strengthen the EU workforce for ATMP delivery.** The delivery of ATMPs relies on trained healthcare professionals with an understanding of both the disease and the medical technology to know when to optimally use these medicines. This expertise is cultivated throughout the clinical development of these medicines. It is therefore **important for ATMP development and delivery that the EU continues to invest in medical upskilling from researchers and technicians to clinicians and regulatory experts.** Without the necessary workforce, ATMPs cannot be developed or delivered to patients. The EU could benefit from a mutually reinforcing system, whereby more expertise strengthens the overall healthcare system and could contribute to more innovation, treatment, economic growth, and strategic autonomy. Investing in skills and healthcare workforce capacity will also be key to ensure that the EU remains attractive for clinical innovation. In recent years, the EU has experienced a decline in clinical trials for ATMPs compared to other world regions. Clinical trial activity is twice as high in the US and almost three times as high in China than in the EU. The number of ATMP trials conducted in the US and Asia-Pacific region grew by 70% and 67%, respectively from 2014-2021, while Europe remained stagnant.[10] While this decline is influence by multiple factors – such as regulatory complexity and difficulties in conducting multi-country clinical trials – the shortage of skilled workforce is part of the equation. If this trend continues, Europe risks losing critical scientific expertise and skilled talent to regions with more dynamic clinical and regulatory environments.

The Choose Europe for Life Sciences Strategy introduces proposals to create centres of excellence for ATMPs. This should be complemented by the future **EU Biotech Acts and supported by increased funding for education and research, regulatory simplification, and an environment that allows the EU to attract global talent.**

## 6 Leverage existing national resources and infrastructure for broader ATMP utilisation

**TRANSFORM encourages Member States to support the integration of ATMPs within their healthcare systems by leveraging existing infrastructure, investing in new ones, considering the use of Hub and**

[10] EFPIA, Europe's share of global medicines R&D shrinks by a quarter in 20 years – as sector's declining trends continue. Available here.

**Spoke models for the effective delivery of some ATMPs and facilitating cross-border access to lifesaving ATMPs.**

ATMPs are cutting-edge medicines that rely on specialised infrastructure and expertise at every stage of their lifecycle, from research, development, and manufacturing to clinical delivery and long-term follow-up. Building and maintaining this network of hospitals, laboratories, and skilled professionals requires sustained investment to ensure Europe has the capacity to deliver these therapies

The Hub and Spoke model is particularly useful for some ATMP as it enables the use of existing medical expertise and infrastructure, specialised laboratories and other medical equipment, while minimising patient travel to the treatment centre. This model involves a 'Hub,' typically an expert medical centre to deliver the ATMP, and a 'Spoke,' a hospital or medical centre near the patient's home that regularly monitors the patient and maintains close contact with the Hub to provide data on the treatment outcome. This model facilitates patient follow up after ATMP administration, without requiring long-distance travel and leads to less burden for patients and caregivers, lower out-of-pocket expenditure, less time lost from work or school, and minimal disruption to daily activities. It also encourages better compliance with follow up medical visits. A Hub and Spoke model also facilitates data collection for long-term monitoring of ATMP safety and efficacy. This is one example of effective and alternative thinking which can make ATMPs more available. It may not be replicable for all ATMPs, but represents the paradigm shift needed to ensure that patients and healthcare systems can benefit from ATMPs.

## MAXIMISING THE USE OF LIMITED RESOURCES AND FACILITATING PATIENT ACCESS: INNOVATIVE MODELS FOR ATMP DELIVERY

The Hub and Spoke model can optimise the devliery of gene and cell therapies by maximising the use of resources. This approach can improve access, patient convenience, and resource efficiency, but its success depends on clear criteria for hub and spoke designation, adequate funding and infrastructure, and strong coordination among hospitals. Academic hospitals will play a central role in ensuring compliance with quality and manufacturing standards, while effective communication between hub and spoke centres is essential to maintain patient safety and continuity of care.

A 2022 joint paper from clinicians and patients in the haemophilia community recommended that established haemophilia centres evolve into hub-and-spoke networks for gene therapy delivery. A follow-up survey across eight Member States showed differing views on whether existing specialised centres or academic hospitals are best placed to dispense these therapies, given the costs and regulatory standards involved. The discussion highlights the need for coordinated national strategies that define roles, ensure sustainable funding, and align infrastructure to deliver ATMPs efficiently and safely.

*Sources*
*Miesbach, W., et al. (2022), Gene therapy of hemophilia: Hub centres should be haemophilia centres: A joint publication of EAHAD and EHC. Haemophilia, 28: e86-e88.* https://doi.org/10.1111/hae.14546
*Miesbach, W., et al. (2024), Administration of gene therapy for haemophilia – The hub and spoke model and its regional differences and challenges. Haemophilia, 30: 855-857?* https://doi.org/10.1111/hae.14985

France has invested in an innovative delivery model for CAR T involving centralised manufacturing with a well-coordinated distribution network between manufacturing facilities and clinical treatment centres. This model relies on robust logistics, including cold chain management and digital tracking, to ensure that the cells remain viable throughout the process. Additionally, France's national health system plays a key role in providing reimbursement and support for CAR T therapies, ensuring that patients across the country have equitable access to cutting-edge treatments. Without adequate and timely reimbursement, such integrated delivery models cannot function effectively or be scaled across Member States.

*Source: Litvinova, Y. et al. (2024), Availability and financing of CAR-T cell therapies: A cross-country comparative analysis. Health Policy, 149.* https://doi.org/10.1016/j.healthpol.2024.105153.

To make the best use of limited expertise and ensure patients in all Member States can access lifesaving ATMPs, **TRANSFORM calls for greater use of and simplified access to existing cross-border care**

**pathways. Strengthening the Cross-Border Healthcare Directive could help reduce health inequalities by enabling patients to receive treatment in authorised centres abroad when therapies are not available nationally.**

Currently, patients seeking cross-border access to ATMPs must navigate complex legal requirements, as they need to obtain prior authorisation from their national competent authority. This process is governed by two separate pieces of EU legislation: the Social Security Regulation and the Cross-Border Healthcare Directive. However, the overlap and differences between these frameworks often create confusion for both patients and healthcare providers, making it difficult for patients to access life-saving therapies when they are unavailable in their home Member State and making existing mechanisms, such as the 'S2 form route', more difficult to use effectively.

In addition, TRANSFORM members highlight that these barriers are further exacerbated by a lack of knowledge and expertise on ATMPs among national health and reimbursement authorities. This can delay or prevent access to therapies even when they are authorised and available elsewhere in the EU.

**TRANSFORM recommends reviewing the implementation of the Cross-Border Healthcare Directive to assess whether its application supports or hinders access to innovative technologies such as ATMPs, when not available nationally. TRANSFORM also urges the Commission to clarify cross-border access and reimbursement rules to innovative therapies by specifying which legislation applies for patients seeking treatment with ATMPs abroad. The legislation should also include provisions to facilitate the access and reimbursement of treatment that is not available nationally and that may not be reimbursed due to a lack of national expertise.**

### LIMITED AND DELAYED CROSS-BORDER ACCESS TO ATMPS IN THE EU

The EU has a single gene therapy authorised for the treatment of adenosine deaminase (ADA) deficiency, a condition causing severe combined immunodeficiency (SCID), a rare disease affecting approximately 1 in 500,000 people.

This gene therapy is administered at a single centre in Milan, Italy. Due to its short shelf life, patients seeking the therapy must travel to the treatment centre to receive it. The legal mechanism allowing patients to travel cross-border to receive such treatment is through the Social Security Regulation and the so-called 'S2 form route.' However, reports[11] show that despite the availability of this treatment, only about half of the eligible patients receive it and patients must secure prior authorisation from their own Member State for treatment reimbursement. This administrative bottleneck is hindering reimbursement approval and patient access to care. In addition, this therapy is generally dosed in young children under the age of 2 and therefore requires families to travel along with the patient. The treatment itself requires a stay of 4 to 6 months near the centre, adding an increased financial and logistical burden while also depriving families of their regular income, as they are unable to work. A hospital foundation linked to this medical centre offers families support to cope with these additional burdens.

[11] Migliavacca, M. et al. Long-term and Real-world safety and efficacy of retroviral gene therapy AD deficiency. Nat Med. 2024. https://pmc.ncbi.nlm.nih.gov/articles/PMC7615698/

# About the European Alliance for Transformative Therapies (TRANSFORM)

The European Alliance for Transformative Therapies (TRANSFORM) is a multi-stakeholder alliance that connects Members of the European Parliament (MEPs) and policymakers with patient groups, medical experts and associations, scientists, researchers, industry actors, networks and other relevant stakeholders. TRANSFORM aims to foster effective dialogue and provide evidence-based policy recommendations to enable safe and timely patient access to cell and gene therapies, whilst ensuring the sustainability of healthcare systems.

TRANSFORM members include:

**CCI Europe – Childhood Cancer International Europe**

**EAHAD – European Association for Haemophilia and Allied Disorders**

**EAHP – European Association of Hospital Pharmacists**

**EFNA – European Federation of Neurological Associations**

**ESGCT – European Society of Gene and Cell Therapy**

**EUCOPE and its members: BioMarin, Bristol Myers Squibb, CSL Behring, Kite – a Gilead company, Medac, Miltenyi Biomedicine, Orchard Therapeutics, PTC Therapeutics, Regeneron, Santen and Vertex.**

**EHC – European Haemophilia Consortium**

**EPTRI – European Paediatric Translational Research Infrastructure**

**EURORDIS – Rare Diseases Europe**

**GBS-CIDP Foundation**

**IPOPI – International Patient Organisation for Primary Immunodeficiencies**

**IFCCA – International Federation of Crohn and Ulcerative Colitis Association**

**Lymphoma Coalition**

**reNEW Consortium Stem Cell Medicine**

**RI – Retina International**

**SIOP Europe – the European Society for Paediatric Oncology**

**TIF – Thalassaemia International Federation**

**WDO – World Duchenne Organization**

The European Medicines Agency (EMA), the European Haematology Association (EHA) and the European Cancer Organisation (ECO) are Observers.

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