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EUCOPE White Paper on Innovative Payment Models for ATMP Access

A White Paper prepared by EUCOPE's Cell & Gene Therapy Working Group

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European Confederation of Pharmaceutical Entrepreneurs AISBL

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Innovative Payment Models for ATMP Access

Executive Summary

Advanced Therapy Medicinal Products (ATMPs), encompassing gene, cell and tissue-engineered therapies, represent a major advance in biomedical innovation. Some ATMPs are designed as single-administration interventions delivering durable or potentially curative outcomes, while others provide long-term therapeutic effects for chronic, high-burden conditions. Alongside their clinical value, ATMPs can also generate wider societal and economic benefits for healthcare systems, patients, caregivers, and the European Union's (EU's) biotechnology ecosystem.

Across the EU, however, authorised ATMPs continue to face uneven and often delayed reimbursement, with some products being withdrawn from the market for access-related reasons. A primary driver of this lies in the fact that the unique characteristics of ATMPs not always fit with existing reimbursement, budgeting and accounting frameworks. For some ATMPs, expenditure may be concentrated at or around administration, while clinical and economic benefits are realised over several years, and evidence regarding the durability of benefit may continue to develop after market entry.

Traditional reimbursement arrangements may remain appropriate for some ATMPs, while others may require alternative approaches to address uncertainty, affordability or annual budget impact. **No single reimbursement model will be suitable in every case**. Member States, therefore, need sufficient flexibility and improved guidance to select an approach that best reflects the characteristics of the therapy and the realities of the national healthcare system.

Although pricing and reimbursement remain the responsibility of individual Member States, the EU can help address common legislative, data, accounting, and operational barriers that may prevent appropriate reimbursement approaches from being implemented in practice. **Accordingly, EUCOPE recommends the following actions:**

1. **Support national implementation through existing EU coordination mechanisms.** Existing EU mechanisms should facilitate structured exchange between Member States on implementation challenges, national experience and good practices, while preserving flexibility for product- and country-specific agreements.

2. **Ensure the implementation of the European Health Data Space (EHDS) supports outcomes-linked reimbursement approaches.** The implementation of the EHDS should support consistent minimum core outcome datasets, interoperable real-world data sources and early alignment between developers, regulators, health technology assessment (HTA) bodies, and payers.

3. **Promote clearer and more consistent interpretation and application of EU budgeting and accounting principles**. EU-level guidance should be improved to help clarify how existing public budgeting and accounting frameworks apply to multi-year and outcomes-linked reimbursement agreements and identify where national interpretations create avoidable barriers

4. **Improve the operational usability and predictability of existing EU cross-border healthcare mechanisms.** Existing EU cross-border healthcare pathways should provide greater clarity and predictability for patients requiring treatment across the EU, including on authorisation processes, responsibilities, and necessary ancillary costs.

I. The transformative potential of ATMPs

Advanced therapy medicinal products (ATMPs) are a class of innovative medical products that encompass gene therapies, somatic cell therapies, tissue-engineered products and combined ATMPs.[1] They represent a therapeutic paradigm in which biological and genetic technologies are used to modify, restore, or replace defective cellular or genetic functions. Some ATMPs are designed as single-administration interventions that may provide durable or even potentially curative outcomes, while others are being developed to modify the course of chronic conditions by slowing disease progression, reducing complications, or decreasing reliance on concomitant therapies. The impact of ATMPs can therefore be understood across several dimensions: (1) they can generate substantial clinical value for patients with conditions that currently lack effective treatment options; (2) by altering disease trajectories, ATMPs not only reduce the need for repeated interventions, hospitalisation, and long-term medication use but also reduce caregiver burden; (3) the development of ATMPs contributes to broader societal and economic benefits through scientific advancement, high-value employment, and strengthening of the European Union's (EU's) biotechnology ecosystem.[2]

For the EU, ATMPs also represent an important strategic opportunity to reinforce its position within the global biotechnology landscape by stimulating industrial growth and innovation, especially as international competition in this area intensifies. These broader impacts are increasingly recognised in policy discussions around innovation, strategic autonomy and health system sustainability. The Draghi Report on EU's Future on Competitiveness is one example where ATMPs are explicitly identified as strategic assets at the EU's disposal to improve long-term competitiveness.[3] The proposed European Biotech Act (Part I) similarly introduces several measures targeting ATMPs, recognising that scientific innovation alone is insufficient unless supported by an enabling regulatory and policy environment that facilitates development, manufacturing and timely patient access.[4] Together, these initiatives highlight the importance of policies that support innovation translation and infrastructure development within the European Union.

II. A rapidly expanding but fragile innovation landscape

Once considered experimental, ATMPs are now an established regulatory class of medicines under EU law,[5] with 31 products having received a positive EMA opinion as of December 2025, compared with fewer than ten a decade ago; and the development pipeline remains active, with the EMA's Committee for Advanced Therapies (CAT) continuing to review a substantial number of ongoing procedures.[6]

Initially concentrated in rare genetic disorders, ATMP development is broadening to include non-rare indications in oncology, neurology, cardiovascular disease, and regenerative medicine. This expansion increases the potential patient population and may amplify the

[1] European Medicines Agency (EMA), "Advanced therapy medicinal products: Overview." https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview
[2] Grace Marsden, Adrian Towse, Steven D. Pearson, Bill Dreitlein, and Chris Henshall, Gene Therapy: Understanding the Science, Assessing the Evidence, and Paying for Value, Institute for Clinical and Economic Review (March 2017). https://icer.org/wp-content/uploads/2020/11/ICER-Gene-Therapy-White-Paper-030317.pdf
[3] Mario Draghi, The Future of European Competitiveness: In-depth Analysis and Recommendations, European Commission (September 2024). https://commission.europa.eu/document/download/ec1409c1-d4b4-4882-8bdd-3519f86bbb92_en?filename=The%20future%20of%20European%20competitiveness_%20In-depth%20analysis%20and%20recommendations_0.pdf
[4] European Commission, Proposal for a Regulation of the European Parliament and of the Council on establishing a framework of measures for strengthening the Union's biotechnology and biomanufacturing sectors, particularly in the area of health, and amending Regulations (EC) No 178/2002, (EC) No 1394/2007, (EU) No 536/2014, (EU) 2019/6, (EU) 2024/795 and (EU) 2024/1938 (European Biotech Act), COM(2025) 1022 final (16 December 2025). https://health.ec.europa.eu/document/download/ec1475b7-e3f9-409e-b927-fc7e69306a8c_en?filename=biotech_reg-com2025-1022_act_en.pdf
[5] Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 ('ATMP Regulation)
[6] European Medicines Agency (EMA), Committee for Advanced Therapies (CAT), "CAT quarterly highlights and approved ATMPs – December 2025," EMA/CAT/380337/2025 (2 December 2025). https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-december-2025_en.pdf

impact and benefit of these therapies on healthcare systems.[7] A large share of ATMP development continues to focus on rare diseases, reflecting both the underlying genetic mechanisms addressed by many gene and cell therapies and the significant unmet need among people living with a rare disease (PLWRD).

This trajectory is expected to continue as the global ATMP pipeline expands across multiple therapeutic areas and larger patient populations. More than 1,200 cell, gene and tissue engineering clinical trials are currently ongoing worldwide, including more than 150 Phase III studies, underlining the urgency of ensuring that reimbursement and healthcare systems evolve at the same pace as scientific innovation.[8]

Given their transformative potential and the serious conditions, they are intended to treat, regulatory authorities have introduced mechanisms to facilitate the timely development and approval of these therapies. Within the EU, several regulatory pathways aim to accelerate patient access to promising treatments, such as the PRIME (PRIority MEdicines) scheme which provides early and enhanced regulatory support to medicines that may offer major therapeutic advantages,[9] reflecting a broader regulatory willingness to accommodate the specific development challenges associated with ATMPs.

Yet the evolution of the ATMP landscape has not been without challenges. A number of authorised products have subsequently left the EU market or faced limited uptake across Member States, largely due to commercial and health system factors, including pricing and reimbursement constraints, manufacturing complexity, and limited scalability of production, rather than safety concerns. It is also worth noting that some of the challenges become more pronounced as patient populations become smaller and therapies more individualised. At the narrowest end of the population continuum, conventional evidence generation, dedicated registry infrastructure and statistically powered outcome assessment may not always be feasible or proportionate.

These experiences highlight the importance of addressing the structural, legislative, reimbursement and market-access conditions that determine whether innovative therapies can be sustainably developed, launched, reimbursed and maintained across Member States.[10] **Importantly, barriers increasingly extend beyond reimbursement to manufacturing scalability, specialised treatment-centre capacity, workforce readiness, long-term evidence generation, and the operational complexity associated with delivering highly personalised therapies.**

III. ATMPs and current financing reimbursement systems

ATMPs can be tailored with great precision to specific treatment conditions and often target difficult or otherwise impossible to treat indications that mostly address genetic defects and rare diseases. They follow a complex lifecycle (see Annex I) but can deliver value well beyond the traditional clinical benefit, including reduced treatment burden, improved quality of life, avoidance of lifelong therapy, durable clinical effects and, in some cases, the potential for cure. They also provide broader economic and societal benefits, such as reduced caregiver burden, productivity gains and scientific spillovers.

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[7] Straits Research, "Advanced Therapy Medicinal Products (ATMP) Market Size, Report, 2034" https://straitsresearch.com/report/advanced-therapy-medicinal-products-market

[8] Alliance for Regenerative Medicine (ARM), Q4 2025 Cell & Gene Therapy Sector Data (2026), "Ongoing Clinical Trials by Phase and Therapeutic Approach", p. 1. https://alliancerm.org/wp-content/uploads/2026/01/ARM-Q4-2025-CGT-Sector-Data.pdf?utm_source=chatgpt.com

[9] European Medicines Agency (EMA), "Legal framework: Advanced therapies." https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview/legal-framework-advanced-therapies

[10] Katherine Leong and Richard Macaulay, "OP73 Navigating the Advanced Therapy Medicinal Products (ATMPs) Conundrum: Insights From ATMPs Withdrawn in the European Market," International Journal of Technology Assessment in Health Care (2024)." https://www.cambridge.org/core/services/aop-cambridge-core/content/view/96CD2016765DA7C2217679AEA240D825/S0266462324001326a.pdf/op73-navigating-the-advanced-therapy-medicinal-products-atmps-conundrum-insights-from-atmps-withdrawn-in-the-european-market.pdf

However, the way this value is realised over time may present challenges in value assessment, reimbursement rules and public budgeting approaches. Many ATMPs require significant upfront expenditure at the point of administration, while the clinical and economic benefits emerge gradually over years. This requires a financing offset, particularly where upfront investment coincides with uncertainty regarding the durability of long-term clinical benefit. Depending on the characteristics of the individual ATMP, different reimbursement approaches may therefore be appropriate to address uncertainty, affordability or annual budget impact. Health financing systems in the EU were largely designed around conventional medicines requiring continuous or repeated treatment rather than therapies characterised by a single or limited number of administrations combined with long-term clinical benefit. While traditional reimbursement approaches may remain appropriate for certain ATMPs, others may benefit from alternative methods that better address the specific access and financing challenges presented by the therapy. Healthcare systems should have sufficient flexibility to select the most appropriate solution according to the characteristics of each individual ATMP.[11]

Uncertainty about long-term clinical outcomes can complicate reimbursement decisions. Although clinical trials may demonstrate strong short-term effectiveness, evidence regarding durability of response may still be evolving at the time of market entry. In addition, the small patient populations associated with many ATMPs can make it difficult to generate large datasets for traditional health technology assessment frameworks. These challenges have prompted growing interest in developing reimbursement approaches that better align payment structures with the specific access and financing challenges presented by ATMPs while reflecting the realities of different national healthcare systems. The challenge is therefore not the availability of innovative payment models, but ensuring that legislation, reimbursement rules, public budgeting rules and accounting principles provide sufficient flexibility to enable their practical implementation where appropriate.

IV. Innovative payment approaches

As more ATMPs enter clinical practice, Member States are increasingly exploring a broader range of reimbursement and funding approaches alongside traditional agreements.

This shift reflects the rapid expansion and increasing diversity of the ATMP pipeline, moving from a limited number of high-impact therapies to a growing portfolio of products targeting both rare and more prevalent diseases. As this landscape develops, more structured and systematic reimbursement approaches will be needed instead of ad hoc, case-by-case solutions. Without them, implementation risks becoming fragmented and administratively burdensome, potentially slowing uptake and delaying patient access.

The choice of reimbursement approach should be driven by the specific access and financing challenges presented by each ATMP. Relevant considerations may include the therapy's clinical profile, the nature and degree of outcome uncertainty, the size of the eligible patient population, and the budgetary, accounting and administrative realities of the healthcare system concerned; these are outlined in more detail below. A clearly defined and operationally workable toolbox of reimbursement options is therefore needed, enabling manufacturers and payers to identify the approach that best reflects the characteristics of the therapy and the circumstances of the individual health system.

Traditional reimbursement arrangements may remain appropriate for some ATMPs. Where specific access or financing challenges arise, alternative approaches may be better suited to help address high upfront costs, uncertainty about long-term clinical benefit, or both.

[11] Association of the British Pharmaceutical Industry (ABPI), Establishing payment models that support timely access to ATMPs (September 2021, version 2). https://www.abpi.org.uk/media/0ldleloy/abpi-payment-models-position-paper_-2september2021-final-v2.pdf

The table below present a high-level overview of the most common archetypes of both traditional and more innovative reimbursement and funding approaches that may support ATMP access. In practice, individual agreements may combine features of different approaches, while their accounting and budgetary treatment will depend on the contractual design and applicable national rules.

Table 1: Innovative reimbursement and funding approaches for ATMPs

Traditional reimbursement agreements			
Approach	*Core principle*	*Potential advantages*	*Key challenges*
Standard reimbursement	The agreed price is reimbursed through the usual national arrangements, without a specific financial or outcome-linked agreement.	Familiar and comparatively straightforward to administer. May remain appropriate for some ATMPs where the available evidence and budget impact do not warrant a more complex arrangement.	For one-shot therapies, expenditure may be concentrated at or around administration, while benefits are realised over a longer period. The payer also bears the financial risk associated with uncertainty regarding the durability of benefit.
Fixed spread-payment arrangement	The total reimbursement amount and payment schedule are agreed at treatment initiation, with payment distributed over several periods, often annually (annuity payment model). Future payments are not contingent on subsequent clinical outcomes.	Improves affordability through spreading cash flow over time and facilitates financial planning. Where national accounting and public budgeting rules permit, it may also reduce annual budget impact.	Requires long-term contracts and clear rules on payment responsibility; can raise accounting and public finance questions.
Outcomes-based (OB) reimbursement agreements			
Approach	*Core principle*	*Potential advantages*	*Key challenges*
Payment-at-result model	A maximum price and a series of outcome-linked payments are agreed when treatment is initiated. An initial instalment may be paid at administration, while each subsequent payment becomes due only after the corresponding clinical outcome has been verified. If the outcome is not achieved, the payment obligation for that instalment does not arise, and no payment is made.	Aligns reimbursement with demonstrated clinical value; reduces annual budget pressure; transfers a significant share of treatment failure risk to the manufacturer; contractual certainty; may improve the alignment between value creation and expenditure recognition over time; enables the national health service to purchase only what generates real value.	Requires clearly defined outcome milestones, robust data collection systems, long-term follow-up, strong contractual certainty on when each payment becomes due. Its budgetary and accounting treatment will continue to depend on national rules.
Adaptive annual outcome-based	A maximum reimbursement amount and annual assessment framework are agreed upfront, but each year	Links annual reimbursement to the continued delivery of clinical benefit and may align payments with the	Requires outcomes that can be assessed consistently each year and a clear methodology for

payment model	creates a new contingent reimbursement obligation only while the treatment continues to deliver the agreed benefit. Consequently, the final reimbursement amount, duration and cumulative payments remain unknown at treatment initiation.	annual cost of the chronic therapy being replaced by the ATMP in question. By creating reimbursement obligations only while clinical benefit continues, the model can simultaneously address long-term outcome uncertainty, affordability and annual budget impact.	calculating annual payments. Wherever possible, outcomes should be derived from routine clinical practice or existing healthcare data to minimise administrative burden.
Upfront payment with outcome-linked rebates or refunds	Full payment, or a substantial part of it, is made at treatment initiation. Subsequent rebates, clawbacks, or refunds may then apply if the agreed clinical outcomes are not achieved.	Relatively straightforward to implement; enables risk-sharing between payer and manufacturer; may align net reimbursement with realised clinical benefit.	The payer typically needs to finance and recognise the full cost upfront, hence annual budget pressure may persist; a substantial part of the risk initially remains with the healthcare system; rebate and refund processes may be operationally complex.

No single model will universally be optimal. The starting point should therefore not be the reimbursement model itself, but the specific access and financing challenges presented by the individual ATMP. Different payment models target different challenges: some mitigate uncertainty regarding long-term clinical outcomes, while others improve immediate affordability by smoothing annual budget impacts or facilitating sustainable financing over time. Certain payment models may introduce complexity that could be avoided through simpler arrangements – successfully implementing innovative reimbursement approaches requires identifying the underlying challenge before selecting of the most appropriate reimbursement approach. Such assessment should consider several dimensions:

- **Degree and type of clinical uncertainty**: Therapies with well-established, durable benefits may fit annuity models, depending on budget impact, while those with greater uncertainties may require outcome-linked or hybrid structures, or other forms of evidence generation or re-appraisal of value.
- **Size and distribution of patient population:** For small, rare disease populations, or for smaller Member States, year-to-year budget volatility can be high, making risk-pooling or payer reinsurance models potentially more appropriate approaches. For very small or highly individualised cohorts, however, dedicated registry infrastructure and conventional statistical outcome tracking may not be feasible. Reimbursement arrangements should allow for proportionate, fit-for-purpose approaches to evidence collection and outcome verification.
- **Budget impact and predictability**: When a therapy's clinical outcomes are relatively certain, but upfront costs are high, spreading payments can help manage budget pressures. By contrast, subscription models may work better when the patient population is more stable or predictable, allowing payers to set a fixed budget in advance.
- **Data infrastructure**: Outcome-based or hybrid models rely on standardised, interoperable and objectively verifiable (real-world) evidence. Depending on the size

of the population and the characteristics of the therapy, outcome verification may draw on routine claims data, treatment-centre records, disease registries, longitudinal patient data or other routinely collected healthcare data. The feasibility of these approaches will increasingly depend on the effective implementation of the European Health Data Space (EHDS). and the interoperability of relevant data sources.

- **Manufacturer profile and financial resilience**: Smaller companies may struggle with long-term deferred or conditional payments; opting for an innovative model should also reflect liquidity constraints and revenue predictability.

Ensuring that providers, payers and delivery organisations can work within models that are acceptable, feasible, flexible and predictable is therefore essential for these approaches to function effectively. Overall, EU Member States are moving towards more flexible and sophisticated payment mechanisms, but progress remains uneven, with differing levels of readiness, infrastructure, and policy constraints across Member States.

V. Enabling sustainable access: EUCOPE policy priorities

Even where innovative reimbursement approaches are appropriate, experience across Member States shows that their implementation succeeds only when the surrounding access pathway is workable in practice. Annual budgeting constraints, the feasibility of outcomes measurement, and the readiness of care pathways can determine whether an innovative agreement becomes a scalable solution or remains a one-off exception. For this reason, innovative reimbursement approaches should be considered as one option within a broader access toolkit and selected according to the specific access and financing challenges presented by each individual ATMP. While reimbursement decisions remain a national competence, EU-level action can make a meaningful contribution by creating the legislative, regulatory and operational conditions that support Member States in implementing the most appropriate reimbursement approaches, while learning from one another's experience.

EUCOPE therefore recommends to:

1. Optimise existing EU coordination mechanisms to support Member States in the practical adoption of appropriate reimbursement options for ATMPs.

Member States should identify and address the national legislative, administrative, reimbursement, budgeting and accounting barriers that may restrict the implementation of appropriate reimbursement approaches for ATMPs. **Existing EU coordination mechanisms can meaningfully support national authorities in this process by facilitating structured exchange on national experience implementation challenges and good practices**. These may include regulatory coordination through the EMA, HTA cooperation structures, system-level learning through the European Commission Expert Group Health Systems Performance Assessment (HSPA), and pricing and reimbursement exchange via the National Competent Authorities on Pricing and Reimbursement (NCAPR). Such cooperation should support Member States in adapting their systems while preserving the flexibility required for product- and country-specific agreements.

2. Ensure the implementation of the European Health Data Space (EHDS) supports consistent EU data standards to enable innovative payment approaches for ATMPs

Outcomes-linked arrangements and post-launch evidence development depend on access to reliable (real-world) data. However, data capture remains fragmented across Member States, and existing systems vary in quality, coverage, and interoperability, limiting their operational usability for follow-up. **The implementation of the EHDS should be leveraged to support consistent minimum core outcome datasets for ATMPs where post-launch evidence is needed. Implementation should equally promote interoperability between national registries, routine claims data, treatment-centre**

data systems and other relevant real-world data sources. This includes supporting the consistent capture and cross-border comparability of outcome data across Member States to enable more reliable evidence generation for regulatory and reimbursement decision-making. Early alignment between developers, regulatory authorities, Health Technology Assessment (HTA) bodies, and payers on clinically meaningful endpoints, follow-up requirements, and appropriate data sources should also be supported. Data and monitoring expectations should remain proportionate to the size and characteristics of the population concerned. For very small or highly individualised cohorts, for example, the absence of a dedicated registry should not in itself prevent an outcomes-linked arrangement where reliable follow-up can be achieved through alternative, fit-for-purpose data sources.

3. Promote a more consistent interpretation of existing EU legislation, reimbursement rules, public budgeting and accounting principles

EU-level guidance should be improved to support coordination among Member States on how existing European System of Accounts (ESA 2010) rules are interpreted in relation to multi-year and outcomes-linked payment models for innovative therapies such as ATMPs. Under current EU accounting standards, including ESA 2010 – which provides the statistical framework for reporting government expenditure in the EU – public spending is generally recorded on an accrual basis. In practice, however, the interaction between statistical reporting requirements and national budgetary rules or fiscal planning frameworks may influence how Member States assess the budgetary impact of certain innovative payment models. This can affect their perceived feasibility, even where they are designed to smooth expenditure over time or better align payment with realised clinical outcomes. Improved EU-level coordination should help identify where national budgetary or public accounting interpretations create barriers. Ensuring these frameworks are applied flexibly prevents them from unnecessarily restricting Member States that wish to implement appropriate, long-term reimbursement approaches for ATMPs. **Particular emphasis should be placed on addressing accounting and public budgeting considerations early during the design phase of innovative reimbursement agreements**, rather than allowing them to become administrative barriers during final implementation.

4. Improve the operational usability and predictability of existing EU cross-border healthcare mechanisms

Establishing treatment capacity for ATMPs in every national health system may not always be feasible; cross-border pathways therefore are essential to ensure patient access. However, the EU's existing cross-border care arrangements and reimbursement rules were not necessarily designed to accommodate the complexity of ATMPs delivery, often concentrated in a limited number of specialised centres. An additional barrier may also arise for highly individualised therapies where a patient must undergo a new national assessment and coverage process even where the same underlying platform technology and evidence have already supported treatment in another Member State.[12] Improving clarity and predictability of patient pathways under existing EU cross-border healthcare mechanisms, including the Cross-Border Healthcare Directive and the S2 authorisation route under the EU Social Security Coordination framework, can help ensure access to appropriate centres. Optimising these frameworks should focus on **reducing administrative complexity, increasing transparency regarding authorisation criteria, timelines and administrative requirements of the S2 route, ensuring that National Contact Points are sufficient resources and equipped to guide patients and clinicians through ATMP-specific pathways, and providing clearer guidance on**

[12] This topic is addressed in greater detail in a forthcoming EUCOPE position paper on cross-border access to highly specialised therapies.

eligibility, authorisation, and allocation of clinical and financial responsibilities across the treatment pathway. EU-level cooperation should therefore also explore how greater reliance on shared evidence and coordinated assessment could support faster national decisions for these therapies, while respecting Member State competence. The interaction between existing cross-border healthcare mechanisms should also provide greater clarity regarding the treatment of necessary ancillary costs associated with ATMP delivery and support more consistent implementation across Member States.

Conclusion

ATMPs have moved from scientific promise to routine clinical reality, with long-term benefits that can extend well beyond the clinical sphere. Yet access to these transformative therapies remains uneven across the EU. The key challenge is not a lack of potential solutions, but the gap between the characteristics of many ATMPs and the way health systems are organised to value, budget, contract, and operationalise access. Innovative reimbursement approaches can help address specific access and financing challenges as one element within a broader implementation toolkit, if legislation, reimbursement rules, public budgeting rules, and accounting principles enable their practical application. The main question therefore shifts from how to pay for a high-cost medicine towards how to finance a health and economic investment whose value will be realised over many years. Greater predictability in reimbursement frameworks would not only support timely and sustainable patient access but also provide developers with clearer and more reliable commercialisation pathways for ATMPs across the EU. Healthcare systems require flexible mechanisms that appropriately balance cutting-edge innovation with affordability and long-term fiscal sustainability. In turn, this will reduce regional access disparities, strengthen the EU's global competitiveness for life-sciences investment, and accelerate patient access to life-changing therapies. EUCOPE therefore calls for coordinated EU and national action focused on removing implementation barriers and strengthening the operational readiness of healthcare systems to integrate transformative therapies as part of the EU's broader competitiveness and innovation agenda. The policy debate has largely identified the challenges. The priority now is implementation.

Annex I – The ATMP Development and Delivery Lifecycle

- **Clinical development** is often shaped by small patient populations and limited conventional evidence generation, often necessitating adaptive trial designs and continued post-authorisation data collection to monitor safety and effectiveness. Health technology assessment (HTA) bodies and reimbursement authorities often require robust clinical evidence comparable to that expected for more common diseases. However, generating such evidence can be significantly more challenging in these particular cases, and long-term outcomes may take many years to observe. As a result, developers may face prolonged clinical development timelines, higher trial costs, and increased uncertainty.

- **Manufacturing processes** are frequently complex and resource intensive. For example, therapies based on autologous cells may require the collection of biological material from an individual patient, transport to a specialised facility for genetic modification or expansion, and subsequent return of the final product for administration to that same patient. Maintaining product quality and identity throughout this process requires strict chain-of-custody and chain-of-identity procedures, as well as highly controlled manufacturing environments and specialised technical expertise.

- **Logistical challenges** bring further complexities. Many ATMPs rely on biological materials with limited shelf lives and strict temperature requirements, meaning that storage, transportation, and handling must be carefully coordinated. The supply chain must ensure continuous monitoring of temperature, location, and traceability in order to preserve product integrity. In contrast to conventional medicines that are distributed in large volumes through established pharmaceutical supply chains, ATMPs often involve small, patient-specific shipments requiring highly specialised logistics infrastructure.

- **Regulatory requirements** can vary across Member States, increasing intricacies and timelines. Greater regulatory convergence and early scientific dialogue are therefore critical to support efficient scale-up while maintaining product quality and safety.
    - In this context, **delays due to the variations in GMO Regulation** across Member States – particularly pronounced for multi-country trials and decentralised or point-of-care manufacturing – have left to a less competitive and less attractive environment to realise multicentre clinical trials with investigational advance therapies in the EU. In this respect, EUCOPE considers measures within the revision of the EU General Pharmaceutical Legislation and the recently proposed EU Biotech Act I to signal a positive shift towards reducing duplications and inefficiencies, in particular with the introduction of a risk-proportionate exemption from environmental risk assessments for specific categories or ATMPs containing or consisting of genetically modified organisms that present no or negligible risks proposed by the latter.
    - **Ethical debates and inconsistent ethical standards** across countries also create regulatory differences. These variations complicate approval processes and limit cross-border clinical trials, restraining adoption by creating uncertainty and delaying therapy availability in some regions.

- Finally, **delivery** further adds to the complexity of these therapies. Many ATMPs require specialised hospital infrastructure, such as cryogenic storage, advanced laboratory facilities, and trained multidisciplinary teams capable of administering complex procedures and monitoring patients over extended periods. As a result, treatment is frequently concentrated in specialised centres with the expertise and infrastructure needed to safely deliver these therapies.

Annex II – Innovative Payment Models: Selected Case Studies Across Europe

***Italy has been one of the earliest adopters of outcomes-based payment agreements for ATMPs**, supported by the Italian Medicines Agency's AIFA registry platform, established in 2005. These arrangements enable systematic outcome tracking and allow reimbursement to be linked to predefined clinical milestones.[13] However, existing public-budgeting and accounting arrangements have constrained the use of genuine multi-year approaches, as expenditure associated with staged payments may need to be recognised within the year in which the therapy is administered. **Italy is now exploring the next evolution of financing for one-shot advanced therapies, including multi-year budgeting, dedicated funding arrangements and payment-at-result mechanisms**. Under a proposal currently under discussion, an initial payment would be made when the therapy is administered, while each subsequent payment would become due only once the corresponding clinical outcome had been contractually verified. Where an outcome is not confirmed, the related payment obligation would not arise, and the payment would not be made. The risk associated with therapeutic performance beyond the initial payment would therefore remain with the manufacturer rather than being pre-funded in full by the payer. This differs from traditional payment-by-result arrangements, under which payment is generally made upfront and later adjusted through rebates or clawbacks. The proposed payment-at-result approach would instead allow expenditure to be recognised across the financial years in which the individual payment obligations arise. It is particularly relevant to one-shot therapies, where expenditure is concentrated at administration while clinical benefit is realised and verified over several years. The broader Italian debate therefore illustrates a potential shift from treating these therapies solely as single-year pharmaceutical expenditure towards considering them as a predictable, multi-year health investment.*

***Spain** has implemented a related approach that combines outcomes-based reimbursement with payment caps and national outcome registries. In this model, outcomes are monitored through the national Valtermed registry system. Payments are typically divided into stages: an initial payment when treatment is administered, followed by a subsequent payment at a later milestone if the patient maintains a defined clinical response. This model integrates real-world data collection into reimbursement arrangements and enables ongoing evaluation of therapeutic effectiveness at a national level.*

***Denmark** has also implemented staged payments in which instalments are made over time, and where the treatment does not demonstrate the expected clinical effect, subsequent payments may be discontinued. This model is designed to address affordability challenges associated with therapies that provide long-term benefits but require substantial upfront expenditure.*

*More recently, **Germany** has introduced a **national success-based reimbursement model** linked to a gene therapy for haemophilia B. In 2025, the therapy became available under an agreement with the statutory health insurance association (GKV-Spitzenverband). This arrangement links reimbursement to the clinical success of the therapy at the individual patient level. The model addresses a central challenge associated with one-time gene therapies: uncertainty about their long-term effectiveness. Under this agreement, reimbursement is contingent on treatment performance, ensuring that payments reflect the therapeutic outcomes achieved by the patient. The model has been described as the first national performance-based reimbursement agreement of its kind in Germany.[14]*

*Innovative payment arrangements are also being piloted outside the EU alone, where in the **United Kingdom**, through the Voluntary Scheme for Branded Medicines Pricing, Access and Growth (VPAG), NHS England has committed to testing alternative payment models for high-cost innovative medicines. The first pilot programme focuses on a gene therapy for haemophilia and incorporates an outcomes-based reimbursement structure. The pilot aims to assess how such payment models function in the NHS context and to identify implementation challenges, including data collection, outcome monitoring, and contractual arrangements.*

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[13] Entela Xoxi, Karen M. Facey, and Americo Cicchetti, "The Evolution of AIFA Registries to Support Managed Entry Agreements for Orphan Medicinal Products in Italy," Frontiers in Pharmacology 12:699466 (2021). https://doi.org/10.3389/fphar.2021.699466

[14] CSL Behring, "Innovative Gentherapie in Deutschland verfügbar" (2 May 2023). https://www.cslbehring.de/news/2023/pm-launch-gentherapie-de