Boosting Attractiveness of the EU for ATMP Developers

Advanced Therapy Medicinal Products (ATMPs) represent a paradigm shift in healthcare by offering new way to help patients, addressing the root causes of diseases and potentially curing patients.

By giving the possibility of a one-time treatment, these innovative products result in an added value for patients, their families, healthcare systems and society.

In recent years, there have been many scientific breakthroughs, leading to an increasing number of ATMPs being developed and brought to patients, including the potential for use in more prevalent conditions.

Over 15 years ago, the EU was a pioneer in the field of ATMPs in terms of their development, authorisation, and regulation, promoting patient access to these life-changing therapies.[1]

Despite its head start and strong scientific outputs, the EU is now facing a declining attractiveness for ATMP development as other regions – mainly the US and Asia – are consolidating their leadership in the sector.

As a key driver of health innovation, the field is of strategic importance to the EU's competitiveness, open strategic autonomy, and resilience.[2]

[1] 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

[2] COM(2024) 137 final

To regain its leadership in the development and deployment of breakthrough therapies, the EU must build on the historic momentum and ensure legislation focus on accelerating the translation of science into therapies for a wider patient.

With this paper, EuropaBio puts forward recommendations to improve the EU's attractiveness for ATMPs developers by:

- Realising the EU potential for ATMP R&D by ensuring sufficient funding for innovation and a supportive legislative framework for biotech innovators of all sizes.
- Improving the EU clinical trials ecosystem by addressing existing challenges to streamline and speed up trials to incentivise ATMPs creation and development.
- Recognising the unique value proposition of ATMPs and work towards the sustainable integration of ATMPs into healthcare systems across the EU, embracing flexible and inclusive approaches to HTA, pricing & reimbursement to enable faster and easier access for European patients.

Realising the EU's Potential as an ATMP R&D and Industrial Hub

The EU's role as a pivotal hub for ATMP innovation has been increasingly challenged due to its decline of R&D activities compared to other regions. Despite historical strengths, the EU has not been as successful in bringing innovation to market and is falling behind the US and increasingly Asia in the number of developers, clinical trials, investments, and available therapies.[3] Ambitious and resolute actions by policymakers can reverse those trends and fully realise the EU's potential.

In 2023, investments into R&D for ATMPs was nine times higher in North America compared to Europe.[4] The EU has fewer ATMP developers which translate into less ATMP clinical trials started in the EU (341) than in the US (974) and Asia (784).[5]

Ultimately, compared to the US, in the EU there are less approved ATMP and fewer remaining on the market.[6,7] This is not only affecting the EU's competitiveness but also EU patients who risk having delayed or no access to these breakthrough therapies.

Mario Draghi's report on the future European competitiveness confirmed Europe's lower R&D spending compared to the US and emphasised the need to support biotech innovation.[8] Slow, complex, and unpredictable regulatory frameworks are negatively impacting the competitiveness and attractiveness of the EU as an innovation hub for biotech, including for ATMPs and orphan medicines. The report highlights the need for further investments into and support for health biotech which is critical to the EU's competitiveness and resilience.

[3] Charles River Associates (2024), Impact of the GPL on Europe's innovation ecosystem and biotechnology companies, pp. 25-26. Available here.
[4] Ibid., pp. 27
[5] The Sector Snapshot: August 2024 - Alliance for Regenerative Medicine (alliancerm.org)
6] CAT quarterly highlights and approved ATMPs Nov 2023 - Jan 2024 (europa.eu)
[7] Current FDA Approved Cell & Gene Therapies – Mirus Bio.
[8] Mario Draghi, The future of European competitiveness, Part B In-depth analysis and recommendations (September 2024), pp. 187-204. Available here.

Health biotech innovation is fuelled by a supportive investment landscape that rely on predictable intellectual property (IP) and regulatory incentives frameworks. The proposed revision of the GPL will significantly impact the environment in which the biotech industry operates and the predictability and stability of Europe's incentives regime that has successfully supported the development of these transformative therapies. The GPL should include a strong and predictable framework for biotech innovation and be complemented by actions to improve access to finance to support the growth of a thriving ATMP industrial sector.[9]

Comparison of numbers of clinical trials across continents

341	974	784
clinical trials in the EU	clinical trials in the US	clinical trials in Asia

[9] ARM-EFPIA-EuropaBio-EUCOPE-ISCT-joint-paper-on-Hospital-Exemption-Scheme-July-2023.pdf

EuropaBio Recommendations:

- Within the revision of the GPL, ensure that baseline protections for innovative medicines remain strong and predictable. To guarantee a strong R&D biotech sector, the EU should introduce a Regulatory Data Protection (RDP) baseline above the status quo of 8 years together with an Orphan Market Exclusivity (OME) period of at least 10 years. The limit of the validity of the Orphan Designation (OD) must also be removed.
- Within the revision of the GPL, maintain HE only in exceptional circumstances and introduce a clear definition of '*non-routine*' to ensure the HE scheme is harmonised across the EU.
- Work toward consolidating investment funds and opening new investment opportunities, including by completing the Capitals Market Union and making greater use of EU funding (e.g., from the European Investment Bank or European Innovation Fund), as leverage to maximise private investments, especially in higher risk R&D and to help smaller companies.
- Ensure that EU public-private partnerships are made more accessible to smaller companies and foster cooperation between academia, industry, and regulators to facilitate the translation of innovation to market.

Improving the EU Clinical Trials Ecosystem

Increasing EU attractiveness will require improving the EU clinical trial ecosystem to streamline and speed-up trial launch.[10] Developers face challenges in patient recruitment due to the small and heterogenous populations normally targeted by ATMPs, complex regulatory requirements, and need for specialised facilities and trained healthcare professionals. The development of an appropriate framework where single-arm studies have a role in the development of ATMP could partly compensate for the issue of small patient populations.

EuropaBio is concerned about the workability and complexity of the Clinical Trials Regulation (CTR) compared to other regions.

Issues with differences between Member States, challenging response timelines, potentially longer review timelines as well as a clinical trial submission portal that is not fit for purpose are hurdles for developers.

The interplay of the CTR with the Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR) for trials including devices and diagnostics is also creating challenges.

EU GMO requirements remain a regular hurdle for developers that delay development and increase costs with national interpretation of the legislations resulting in highly fragmented procedures across the EU (e.g., the classification, requirements and timings for GMO applications and approvals). Although the revision of the GPL brings forward improvements, it is essential to ensure an efficient and streamlined process to handle the increasing number of ATMPs in development and keep pace with scientific progress.

[10] The launch of trials with the period to approval trials, set up study, and recruit patients is over 200 days in EU countries compared to 159 days in the US. See here.

Finally, EuropaBio is concerned about the sustainability of the EU's clinical trial environment due to the rising costs and lengths of clinical development and lower and less predictable incentives, including orphan designation, proposed in the GPL.[11] This will make it more challenging to secure financing for clinical development, even as ATMP developers heavily rely on RDP to maintain a competitive edge.[12]

EuropaBio Recommendations:

- The ACT EU initiative, which supports clinical trials, should *give specific consideration to ATMPs* by delivering recommendations and recognising ad hoc funding.
- In the upcoming review of the MDR/IVDR framework, clarify the interplay between legislations in the context of clinical trials and, if necessary, propose new measures to address challenges experienced by sponsors.
- As announced in the EU Biotech and Biomanufacturing Initiative, *review the Clinical Trials Regulation* to create an EU environment capable of supporting large-scale and multi-country CTs, including by improving the coordination between ethic committees and streamlining approval timelines for CTs to reduce burden on authorities and sponsors.
- Following an evaluation, *adopt a science-based approach* for the assessment of medicines containing or consisting of GMOs with the aim of simplifying and accelerating procedures.

[11] SME_Report_ATMP.pdf (europabio.org)
[12] Charles River Associates (2024), Impact of the GPL on Europe's innovation ecosystem and biotechnology companies, pp 42. Available here.

Recognising the Value Proposition of ATMPs

Even if science is rapidly advancing, it will only matter if it reaches patients. Value assessment frameworks are tools to measure the value of health interventions and treatments. The resulting assessment can help support pricing and reimbursement decisions and determine whether the treatment should be funded by the healthcare system. The integration of ATMPs into healthcare systems remain a primary challenge in Europe.

In Europe, these assessments are often conducted by Health Technology Assessment (HTA) bodies. Many of these frameworks were developed to assess conventional small molecule and biologic medicines for highly prevalent diseases and do not fully capture the transformative value of potentially curative ATMPs.

The reliance on randomised clinical trials, even in cases where such trials are not feasible, under the methodologies being developed under the HTA Regulation underline the challenges to overcome to improve patient access to ATMPs. Greater coordination and collaboration between stakeholders are needed to develop harmonised evidence requirements that can facilitate patient access to ATMPs, including the use of real-world data and evidence (RWD/E) to fill knowledge gaps, as well as recognise the high value of ATMPs in terms of societal benefits, clinical benefits, and reduction in burden of treatment.

Sustainable integration of ATMPs into healthcare systems is complex and can lead to challenges that are unique to a particular healthcare system, or highly nuanced depending on the characteristics of disease and treatment. This will require a variety of approaches that allow sufficient flexibility to adapt to the individual needs of Member States.

In specific cases, this could include the use of innovative payment models, such as outcome-based models, that are gaining broader acceptance as effective solutions for distributing the risk of uncertainty between payers and manufacturers. These models can improve health systems' readiness to ATMPs by accommodating the upfront cost of these therapies.

Accelerating the integration of ATMPs into healthcare systems will also require investments into the necessary infrastructure for the manufacturing and administration of these therapies, as well as the availability of highly specialised industrial and healthcare workforces. Cross-border healthcare could improve the accessibility of ATMPs, especially when they are used to treat ultra-rare diseases in only a few highly specialised centres. However, the current EU cross-border healthcare framework is placing significant hurdles for the application to ATMPs, and there is an urgent need for improvements to ensure it becomes an effective access solution for European patients.

EuropaBio Recommendations:

- Foster greater coordination and dialogue between public authorities, patients, developers, and healthcare professionals to identify solutions to accelerate the integration of ATMPs into healthcare systems. Facilitate coordination at EU level and between stakeholders to address shortages of skilled workforce and healthcare professionals, to ensure sufficient future capacity within healthcare systems for the use of ATMPs for all eligible patients.
- Adopt *flexible HTA methodology/processes* that are fit for purpose for ATMPs, and more specifically that:

1. Are based on a comprehensive evaluation of benefits: the metrics used to evaluate the benefit of medicines should consider a wider range of factors, including societal implications, level of innovation, and disease-specific measures, as well as the profound impact of potentially curative medicines.
2. Apply a pragmatic approach to the assessment of the available evidence: any assessment in this regard should consider the challenges of conducting research in populations with rare diseases and/or the unique characteristics of ATMPs and associated clinical trial design limitations, allowing more flexible approaches to permissible data.
3. Take into account a balanced set of perspectives: all relevant stakeholders, including medical experts, patients, and carers, as well as specific technical committees for specialised technologies, should be able to participate in a clear and transparent process that represents a meaningful contribution to HTA considerations.

- Foster the *exchange of best practices* on innovative payment models for ATMPs, supported by EU guidance on accounting rules not hindering payment over time.
- Take actions to improve the *EU cross-border healthcare framework* and ensure it works for patients in line with EuropaBio's recommendations.