European Life Sciences:

Gateway to European Global Leadership

A three-point policy toolkit for a competitive ATMP ecosystem in Europe

European Alliance for Transformative Therapies

Introduction

ATMPs are a diverse class of highly innovative medical biotechnologies[i] with the potential to bring significant health benefits to patients while improving the sustainability of health systems. These treatments can provide long-lasting and potentially curative benefits, as they target the root cause of chronic diseases,[ii] therefore benefiting people facing considerable unmet need, including those impacted by rare, potentially life-threatening and/or chronically debilitating diseases.

In the EU, ATMPs are developed within a dynamic life sciences ecosystem.[iii] Nonetheless, they remain a high-risk investment and, because of their innovative nature, face complex regulatory, infrastructural and commercialisation challenges that make their development and launch difficult.

In view of the EU's ambition, expressed in the Draghi report, to maintain and expand its capacity to conduct research and development (R&D) and to address the competitiveness gap for pharmaceuticals, TRANSFORM puts forward the idea that ATMP development and access should become a benchmark of EU success in this ambition. **TRANSFORM believes that only a holistic, lifecycle approach can clear bottlenecks across ATMP research, development and uptake and drive EU competitiveness in the sector.**

Regulatory hurdles

Regulatory challenges remain one of the biggest hurdles faced by ATMP developers,[iv] as multiple EU legislations[v] inform the regulatory framework for ATMP R&D. The complexity of the regulatory environment developers must navigate is further compounded by the uneven transposition and implementation of EU legislation at the national level, leading to a fragmented regulatory frameworks and significant financial and administrative burden, all of which decrease the attractiveness of the EU's R&D ecosystem for conducting research.

Furthermore, regulatory challenges also impact ATMP manufacturing, owing primarily to the complexity of the good manufacturing practice (GMP) standards applied to *autologous* products, i.e., those produced from the patient's cells. In addition, the EU's lack of a fit-for-purpose and agile regulatory approach to platform technologies, such as the US Food & Drug Administration's Platform Technology Designation Program for Drug Development,[vi] further prevents the effective scale-up of ATMPs, in particular for allogeneic products, i.e., those developed from donor biological materials.

Investment, infrastructural and workforce bottlenecks

Owing to the innovative nature of ATMP R&D, startup ventures in the ATMP space require robust public funding frameworks to cushion risk, ensure access to highly specialised R&D infrastructures, and crowd in additional private risk capital. However, the EU's public funding base is insufficient and too fragmented for the requirements of the ATMP ecosystem. The health cluster under Horizon Europe totals at approximately EUR 8.2 billion; projects in this space benefit from additional national-level funding amounting to EUR 10 billion annually, or just 0.06 of the EU's GDP in 2022.[vii] In contrast, the US invested EUR 47 billion into health science programmes in 2023 alone.

Despite hosting several R&D hubs dedicated to ATMPs, **the EU has failed to support regional expertise and infrastructures against structural and systemic challenges that limit these hubs' ability to effectively translate innovation into therapeutic products.** Bureaucratic and regulatory hurdles prevent cross-border R&D collaboration in this space, while capacity and manufacturing bottlenecks further strain ATMP development.

Equally important, the EU faces significant brain drain in the life sciences sector and in healthcare delivery. The estimated EU health workforce deficit was 1.2 million in 2022.[viii] Moreover, the EU continues to lag behind third-country competitors such as the US and China in pharmaceutical R&D mployment.[ix] While employment in the sector only grew by 30% between 2000 and 2020 in the EEA, it saw an 800% growth in China over the same period.

Difficulties in the uptake of innovative therapies

Despite their promise to transform patients' lives and completely revolutionise healthcare delivery, with significant long-term benefits to the sustainability of national health systems, ATMP developers face numerous challenges in bringing their innovative products to patients. Developers face a highly fragmented landscape of pricing and reimbursement (P&R) processes, each with their own market-entry criteria, timelines, and outcomes. While there is some recognition of the need for health systems to prioritise long-term cost-effectiveness and patient/socio-economic benefit, most EU Member States still focus on short-term budget impact and immediate clinical need. Furthermore, current EU Accounting Rules prevent Member States from spreading costs incurred for a single therapy over multiple years, effectively making innovative payment models impossible. This fragmented environment leads to unsustainable or unpredictable opportunities to introduce ATMPs in national healthcare delivery, delays in patient access, and strong health inequity across the EU. This absence of credible prospects of returns on investment disincentivises in turn reinvestment in the EU, as developers may shift R&D activities to regions with more supportive regulatory environment, delivery infrastructure and predictable reimbursement frameworks.

1 Advancing Early Discovery, Translation and Preclinical Research

Way forward

In the early stages of ATMP R&D, most of the basic research is conducted by the public sector. In contrast, the private sector tends to be more active in the later stages of the lifecycle.[x] Advancing early discovery and overcoming translational gaps requires EU strategies that fully leverage existing public funding resources and potential synergies between private and public developers. In addition, improving predictability through regulatory support and better access to infrastructure can enhance the attractiveness of the sector.[xi]

TRANSFORM Recommendations

1. Embed ring-fenced resources for ATMP early discovery and preclinical research into the next EU Multiannual Financial Framework

TRANSFORM calls on the European Commission to include in its forthcoming proposal on the Multiannual Financial Framework (MFF) a new, standalone and appropriately financed Framework Programme for Research and Innovation (the FP10), focusing on supporting excellence in early scientific discovery and basic research.

2. Support multistakeholder alignment on research priorities for patient-centric innovation

TRANSFORM recommends that the Life Science Strategy creates an EU-level multistakeholder innovation platform to help identify and connect key research areas.

This platform should be modelled upon existing concepts (e.g. 'Enhanced Dialogues'). The dialogues should aim towards the identification of scientific gaps, translational challenges and enabling technologies to overcome research silos and duplication, as well as clinical and commercial barriers.

3. Future-proof R&D through enhanced regulatory support

TRANSFORM reiterates the importance of expanding current frameworks for regulatory support and scientific advice, such as EMA protocol assistance, PRIME,[xii] and the EU biotech and biomanufacturing hub, making them available to medical biotech developers *by default*. Such frameworks will help de-risk the development of innovation and ensure EU funding translates into therapeutic solutions.[xiii]

4. Meet developers and patients' needs in R&D infrastructural capabilities

TRANSFORM calls on the European Commission to leverage the Life Science Strategy to boost EU research infrastructures and scale up current R&D capabilities, while expanding commercial and non-commercial developers' access to complex infrastructure across the EU.

High-quality facilities for ATMP production in the EU are scarce. The European Commission must complement national efforts in enhancing R&D capacity through EU co-funded ATMP innovation hubs. The European Commission must also develop fit-for-purpose access rules and roadmaps to facilitate their use.

5. Nurture EU talent to support the ATMP sector

TRANSFORM calls on the European Commission to secure the expertise necessary to support ATMP R&D. The EU is facing a healthcare workforce crisis. This is also impacting the ATMP sector across these medicines' lifecycle. The European Commission must facilitate the cross-border flow of scientific knowledge and expertise, especially in multidisciplinary contexts. This action should be complemented by increased investment in talent development to ensure the EU trains, attracts and retains skilled life science professionals from different domains.

2 Accelerating Development and Boosting EU Clinical Trial Activity

Way forward

Developers often face significant challenges in clinical research, from securing the necessary funding to run clinical trials (CTs) to navigating complex regulatory requirements. This period is critical for ensuring ATMPs' success and demonstrating their safety and efficacy. Streamlined, adaptive regulatory frameworks, coupled with better access to risk capital, can reduce delays, improve business predictability for developers, and create an environment favourable to the development of ATMPs.

TRANSFORM Recommendations

1. Simplify regulatory requirements for investigational ATMPs

TRANSFORM reiterates the need for a risk-based approach to CT applications for investigational cell and gene therapies under the GMO legislation.

Genetic material used in ATMPs is typically *non*-replicant, specific to human cells, and unable to survive in open environments. Furthermore, ATMPs are manufactured and handled in controlled clinical settings and administered directly to patients under strict biosafety protocols. The genetic material used in ATMPs has been validated through repeated testing, use and post-market surveillance over several years. Considering the Commission's proposal under the Pharmaceutical Package regulation to exempt ATMPs for compassionate use from the Environmental Risk Assessments, TRANSFORM encourages the European Commission to consider other cases where patient benefits outweigh environmental risks, and whereby a complete derogation from these requirements could be applied to all ATMPs *by default*.

2. Ensure a regulatory system fit for ATMPs

TRANSFORM supports a regulatory sandbox approach to requirements impacting CT starts and marketing authorisations in the EU.[xiv]

The **Clinical Trials Regulation** has failed to address the EU 's fragmentation: differences in information requirements and the absence of bespoke frameworks for the transferability of CT applications across jurisdictions continue to hinder the implementation of (multi-country) CTs in the EU. **TRANSFORM urgently calls to address these and other duplications of effort and inefficiencies by streamlining the Clinical Trials Regulation.**

TRANSFORM notes that the **In-Vitro Diagnostics Regulation** negatively impacts clinical trial starts in the EU. Furthermore, additional costs (such as CE marking) limit the scale up of IVDs in the EU[xv] and pose operational challenges for combined CTs requiring in-vitro testing. [xvi] **TRANSFORM urges the European Commission to streamline the current framework for in-vitro diagnostics and minimise duplication with overlapping pieces of legislation, including the Clinical Trials Regulation.** Additional streamlining in other legislation impacting ATMP R&D, such as the Regulation on Substances of Human Origin (SoHO), could further support developers. **The European Commission should open an impact assessment and public consultation with all stakeholders on the SoHO Regulation, with a view to revise the provisions applicable to ATMPs.**

Finally, **the European Commission and affiliated expert bodies should issue harmonised guidelines and recommendations on process frameworks for CT designs, data package reviews, alternative evidence sources (e.g., real-world data, surrogate endpoints) and other considerations, to help regulators at all levels systematically recognise and take into account ATMP specificities in their decisions.**

3. Facilitate access to EU capital markets

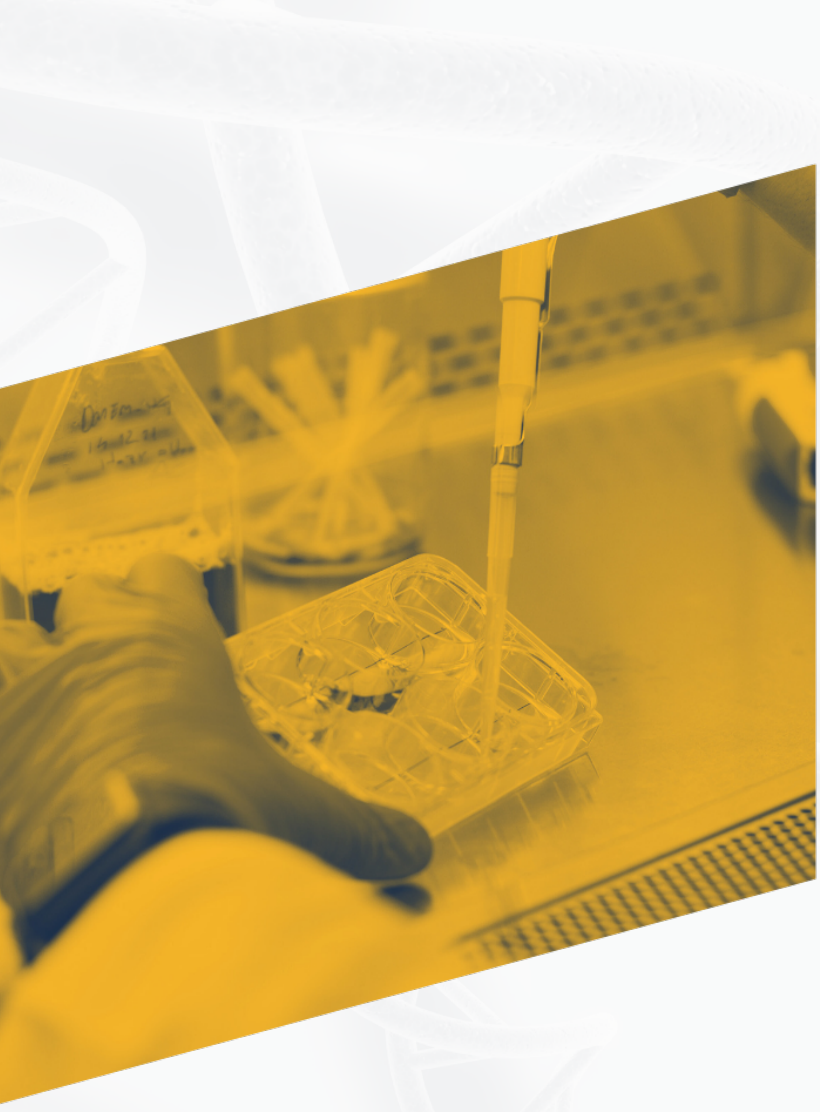
TRANSFORM recommends leveraging the upcoming Savings and Investment Union to facilitate access to capital for ATMP developers.

The European Commission must develop bespoke investment tools and complementary blended finance instruments to increase the critical mass of risk capital available in the EU. National boundaries in access to funding should be removed in order to support the growth of EU small- and medium-sized developers and limit the risk of offshoring.

4. Enhance patients' role throughout ATMP research and development

TRANSFORM calls for measures aiming to ensure that patient voices are meaningfully involved in the development of ATMPs, and especially in clinical trials.

Patient involvement across the lifecycle of ATMPs is critical to ensure that these medicines meet patients' needs and fit within the existing clinical practice. Patient organisations often rely on volunteers and have limited resources to take part in this critical work. It is therefore crucial to invest in patient education, involvement in CT design, and identification of research priorities. TRANSFORM also urges the European Commission to revisit funding criteria for patient organisations' involvement in CTs, as under current frameworks, patient organisations have limited access to funding and are unable to facilitate effective patient involvement in CTs.



3 Fast-tracking innovation uptake for a flourishing EU biotechnology ecosystem

Way forward

A key focus of the Life Sciences Strategy must be effective innovation uptake to ensure this sector's sustainability. As such, the Strategy must address bottlenecks at the market entry stage since only consistent and predictable healthcare system uptake can spur a sustainable research, development and reinvestment cycle that will fuel the EU's life sciences ecosystem. Enhanced real-world data collection and use, infrastructural upscaling in healthcare delivery, and cross-border flows of expertise and patients are key measures to include in the future life sciences toolkit.

TRANSFORM Recommendations

1. Connect healthcare capabilities through cross-border access to healthcare and European Reference Networks

TRANSFORM recommends fully leveraging European Reference Networks (ERNs) in developing innovative, streamlined, standardised national and cross-border care pathways.

TRANSFORM supports the European Commission's Joint Action on integrating ERNs into National Healthcare Systems (JARDIN) and calls for additional EU-level projects and pilots expanding the *cross-border*, interconnecting role of ERNs, empowering them to operate as effective catapults for innovative technologies.

TRANSFORM also calls on the European Commission to revisit the cross-border healthcare (CBHC) framework and harness its potential in improving patient access across the EU. To this end, TRANSFORM asks the European Commission to examine the implementation of existing financial compensation mechanisms between Member States as outlined in the CBHC Directive. The European Commission should also look into the interplay between the CBHC Directive and Social Security Regulation in order to clarify the provisions and address the practical barriers that exist, such as the need for upfront payment by patients. Finally, National Contact Points should legally assume a more prominent role in patient and clinician education around CBHC pathways and the available infrastructures in EU centres of excellence.

2. Expand genomic screening programmes in the EU

TRANSFORM calls on the European Commission to support Member States in expanding newborn screening (NBS) and other early diagnosis programmes.

Early and correct diagnosis is critical to ensure ATMPs can be administered within the short time frame in which these therapies can bring the greatest clinical benefit. Existing frameworks, such as the ERN Expert Platform for Newborn Screening, should be formally engaged in developing EU guidelines for NBS, diagnosis and genetic testing from best practices in national programmes The European Commission should therefore support the work of the ERN Expert Platform in developing unbiased scientific information, evidence, and comparative data to assist Member States in making informed decisions about their NBS policies.

3. Help developers, HTA/Payers and governments overcome access issues

TRANSFORM is committed to exploring access issues in dialogue with institutional partners. Recognising Member States' primary competence in this area, we urge the European Commission and national governments to act on identified best practices in consultation with developers, healthcare professionals and patient representatives. The EU should prioritise:

1) **Sharing best practices and key learnings from national implementation of novel payment models for innovative therapies.** TRANSFORM calls for these new reimbursement models to be integrated into national P&R decision-making processes. Furthermore, there needs to be enhanced clarity on core parameters for outcome-based models and indicators tracking

ATMPs' clinical and socio-economic value (including enhanced patient productivity and health system performance). TRANSFORM calls on the European Commission to support Member States through consolidated guidelines. Early access programmes should be co-developed and expanded to unblock systemic barriers and support evidence generation for P&R.

2) **Review EU legislation that may obstruct access to ATMPs in Member States, including current EU Accounting Rules.** Under the current accounting frameworks, Member States must account for the full cost of ATMPs in the year of purchase, effectively preventing the implementation of payment models that spread costs over several years or contingent on long-term outcomes. TRANSFORM calls for a harmonised and clarified EU accounting framework for annuity and performance-based payments, allowing payers to record expenditures in alignment with payment schedules or outcome delivery.

3) **Ensuring that other harmonising/centralising legislation, such as the EU HTA Regulation applying to ATMPs as of January 2025, does not lead to duplication or delays and remains fit-for-purpose.** The Joint Clinical Assessments (JCAs) must reflect the unique characteristics of ATMPs. Due to the rarity of the targeted diseases, the novel mechanisms of action of these therapies, and ethical considerations, ATMP developers cannot develop data dossiers fitted to the 'gold standard' in evidence generation, particularly in running randomised clinical trials (RCTs). As such, we ask that alternative evidence resources for comparative effectiveness, such as RWE and data from single-arm trials, be adequately valued in light of the difficulties in developing RCTs for investigational ATMPs.

4) **Adhere to established ATMP production and distribution mechanisms for continued patient access, without prejudice to quality, efficacy and patient safety standards.** The centralised marketing authorisation procedure should remain the 'gold standard' of ATMP regulatory approval. TRANSFORM recognises the value of hospital exemption (HE) in situations where treatment may be lifesaving, but no commercial or investigational interventions are available.[xvii] TRANSFORM calls on the European Commission to develop guidelines and legislative tools that can:
   - ensure quality and safety in the application of HE while maintaining a streamlined and affordable authorisation procedure,
   - enhance data collection capacity, including real-world data, to monitor the long-term safety and efficacy of ATMPs administered under HE and to generate greater visibility on its use, and
   - harmonise the implementation of HE rules across Member States.

[i] Gene therapies use genetic material to treat or prevent diseases by modifying, replacing or inactivating specific genetic material, while cell therapy centres around replacing or regenerating human cells, tissues or organs using the patient's own cells (autologous) or a donor's (allogeneic). Tissue engineering combines a scaffold, i.e., a structure on which tissue, cells and other active molecules are grown and then placed onto a person's functional body tissue.

[ii] Horgan D, Metspalu A, Ouillade MC, Athanasiou D, Pasi J, Adjali O, Harrison P, Hermans C, Codacci-Pisanelli G, Koeva J, Szucs T, Cursaru V, Belina I, Bernini C, Zhuang S, McMahon S, Toncheva D, Thum T. 2020. Propelling Healthcare with Advanced Therapy Medicinal Products: A Policy Discussion. *Biomed Hub*. 3;5(3):130-152. doi: 10.1159/000511678. PMID: 33987187; PMCID: PMC8101061.

[iii] Alliance for Regenerative Medicines. 2024. Cell and Gene Therapy Sector Data: Q2 2024: Therapeutic Developers. https://alliancerm.org/data/

[iv] Ten Ham RMT, Hoekamn J, Hovels AM, et al. 2018. Challenges in advanced therapy medicinal product development: a survey among companies in Europe. *Mol Ther Methods Clin Dev*, 11:121–130.

[v] These legislation include, but are not limited to ATMP Regulation, the In-Vitro Diagnostics Regulations (IVDR), two Directives on Genetically Modified Organisms (GMOs), and the Regulation on Substances of Human Origin (SoHO).

[vi] Research, C. F. D. E. A. (2024, May 29). *Platform Technology Designation Program for drug development*. U.S. Food And Drug Administration. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/platform-technology-designation-program-drug-development

[vii] European Commission. 2024. The future of European Competitiveness. Part B | In-depth analysis and recommendations. https://European Commission.europa.eu/document/download/ec1409c1-d4b4-4882-8bdd-3519f86bbb92_en?filename=The%20future%20of%20European%20competitiveness_%20In-depth%20analysis%20and%20recommendations_0.pdf

[viii] European Committee of the Regions. 2025. Shortage of healthcare workers and agri-food supply chain on the agenda of the first NAT meeting of the new mandate. https://cor.europa.eu/en/news/shortage-healthcare-workers-and-agri-food-supply-chain-agenda-first-nat-meeting-new-mandate#:~:text=chair%20of%20NAT.-,Healthcare%20workforce,areas%20%E2%80%94%20face%20significant%20staffing%20issues.

[ix] Charles Rivers Associates. 2022. Factors affecting the location of biopharmaceutical investments and implications for European policy priorities. Final Report. Prepared for European Federation of Pharmaceutical Industries and Associations (EFPIA). https://www.efpia.eu/media/676753/cra-efpia-investment-location-final-report.pdf

[x] Chakravarthy, R., Cotter, K., DiMasi, J., Milne, C., & Wendel, N. (2016). Public- and Private-Sector contributions to the research and development of the most transformational drugs in the past 25 years: from theory to therapy. Therapeutic Innovation & Regulatory Science, 50(6), 759–768. https://doi.org/10.1177/2168479016648730

[xi] Murray, A. J., Cox, L. R., Adcock, H. V., & Roberts, R. A. (2024). Academic drug discovery: Challenges and opportunities. Drug Discovery Today, 29(4), 103918. https://doi.org/10.1016/j.drudis.2024.103918

[xii] While the PRIME scheme offers significant regulatory support to developers through early dialogue on data-generation plans and accelerated assessment, the scope of the scheme remains to be determined by the Pharmaceutical Package, potentially leaving out a significant number of ATMPs.

[xiii] Committee for Orphan Medicinal Products and the European Medicines Agency Scientific Secretariat. (2011). European regulation on orphan medicinal products: 10 years of experience and future perspectives. *Nat Rev Drug Discov*. 10(5):341-9. doi: 10.1038/nrd3445. PMID: 21532564.

[xiv] *Advanced therapy medicinal products: Overview*. European Medicines Agency (EMA). https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview

[xv] Rare diseases diagnostics should be exempt from the Vitro Diagnostic Medical Devices Regulation. (2024, February 8). https://www.eshg.org/news/newsdetails?tx_news_pi1%5Baction%5D=detail&tx_news_pi1%5Bcontroller%5D=News&tx_news_pi1%5Bnews%5D=65&cHash=0fee970cabb98a6e12d6882371fe4ad5

[xvi] IQVIA. 2024. Assessing the clinical trial ecosystem in Europe. Final Report. Prepared for European Federation of Pharmaceutical Industries and Associations (EFPIA) and Vaccines Europe. https://www.efpia.eu/media/o2gjnmfu/efpia_ve_iqvia_assessing-the-clinical-trial-ct-ecosystem.pdf

[xvii] Hospital exemption should be used in areas of unmet medical need where there is a lack of availability of/ access to other treatment options, such as an authorised therapy, an investigational product in the context of a clinical trial, or a compassionate use programme for which a patient may be eligible. A clear distinction should also be made between ATMPs prepared under hospital exemption for individual patients and those developed by public bodies more broadly.

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.

The work of the TRANSFORM Secretariat, provided by FIPRA, is enabled by funding from 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.

The European Medicines Agency (EMA) is an Observer to the Alliance

- European Society of Gene and Cell Therapy (ESGCT)
- ReNEW Consortium - Stem Cell Medicine
- European Federation of Neurological Associations (EFNA)
- Retina International
- World Duchenne Organisation (WDO)
- International Patient Organisation for Primary Immunodeficiencies
- Thalassaemia International Federation (TIF)
- European Haemophilia Consortium (EHC)
- Rare Diseases Europe (EURORDIS)
- European Paediatric Translational Research Infrastructure (EPTRI)
- Childhood Cancer International (CCI EUROPE)
- European Society for Paediatric Oncology (SIOP Europe)
- European Association for Haemophilia and Allied Disorders (EAHAD)
- European Association of Hospital Pharmacists (EAHP)
- GBS | CIDP Foundation International
- European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)