TRANSFORM MEP Interest Group Event

Launch of Charter for EU Cooperation to Enable Safe and Timely Patient Access to Advanced Therapies in Europe

Hosted by the MEP Interest Group on Transformative Therapies
13 October 2022

#MEPsforATMPs

European Alliance for Transformative Therapies

European Parliament

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Event held under the auspices of the Czech EU Presidency

EVENT REPORT

Executive Summary

On 13 October 2022, the TRANSFORM MEP Interest Group launched its TRANSFORM MEP Charter for EU Cooperation to Enable Safe and Timely Patient Access to Advanced Therapies in Europe. The Recommendations contained in the Charter are the culmination of TRANSFORM's multi-stakeholder collaboration over the past year, building on the Policy Asks for ATMPs developed around Regulatory and Access issues.

During discussion at the launch event, key points raised across the speakers and panel exchanges included:

- **The patient voice needs to be reflected** throughout the legislative and non-legislative initiatives. The potential of ATMPs for people living with a rare disease and (increasingly) for patients with more prevalent conditions is significant.

- **Europe should remain attractive for companies to invest and undertake clinical trials**, to ensure European patients receive transformative therapies quickly. The GMO rules relating to clinical trials for ATMPs are a major barrier, but the Commission is looking at suitable changes. **The regulatory system also needs to be streamlined and made flexible for ATMPs**, whilst maintaining safety standards.

- **Academics and hospitals play an important role in the cell and gene therapy ecosystem**, with many ATMPs originating in basic research. The challenge is translating this research into therapies for patients. Appropriate support and guidance from regulators and (public and private) investors – including industry partners – can support these institutions.

- The current review of the EU pharmaceutical legislation (including the proposed SoHO Regulation, and the revision of the General Pharmaceutical Legislation and Orphan Medicinal Products & Paediatric Regulations) is **an opportunity to update the regulatory framework and access environment to better suit ATMPs**. At the same time, there are also several non-legislative actions that can be taken to address current challenges.

- Cross-border access to care and **new access pathways premised on cross-border Member State cooperation should be supported by the European institutions,** playing a coordination role and enabling sharing of best practices.

Opening words

Ondřej Knotek MEP (Renew Europe, Czechia), Chair of the TRANSFORM MEP Interest Group opened the event.

> ***"The MEP Interest Group for Transformative Therapies is a group of members of the European Parliament from various political groups and nationalities, but with one common goal: to use the full potential of advanced therapeutic medicinal products … that are so innovative, high tech and life-transforming … [and] to enhance the access of patients to those therapies."***

- MEP Knotek noted that cell and gene therapies are often developed to address conditions where there are no other care options, so their potential for patients must not be underestimated. However, he noted that whilst "*the patients are ready, but we are still not able to deliver and meet their needs*" relating to access.
- There is a body of health-related legislation being analysed and this means there is "*an ideal opportunity to address the concrete [TRANSFORM] Recommendations in concrete legislation.*"
- He called for a dynamic, patient-centred, innovation ecosystem to address areas of medical need and ensure that regulatory requirements remain appropriate for the development of ATMPs.

The potential of innovative treatment options for the patient community

Luke Pembroke, Haemophilia & rare disease patient advocate, shared his personal experience as a patient.

- Luke was born with haemophilia and received an experimental gene therapy as part of a clinical trial in the UK. He stated that following the trial, "*gene therapy has truly changed my life*."
- He noted that the UK is "*a country that plays host to these pioneering trials, centres of excellence and top experts. Where you are born should not restrict your ability to access ATMPs, whether through a clinical trial or an approved setting. These innovative treatments should be made available for everyone, not the fortunate few*."
- Luke said that he was particularly pleased to see patient centricity at the core of the TRANSFORM Charter's Recommendations. For him, it is important that the current limitations of the regulatory framework are recognised, and the potential to create more equitable access to innovative therapies is explored through partnerships and sharing of expertise.

View from the Czech EU Presidency: The role of ATMPs in a strong EU health union

Tomáš Boráň, Director of the Marketing Authorisation Section, State Institute for Drug Control (SÚKL) gave his perspective, noting he was also previously a member of the EMA's Committee on Advanced Therapies.

> ***"Unfortunately, we have only 16 ATMPs authorised in the EU, compared to 25 in the United States. What is even less fortunate is that some marketing authorisations have been withdrawn or didn't come into real life [with the product not placed on the market]."***

- Mr Boráň noted that ATMPs are no longer exclusively being developed for rare diseases, but also more common conditions like diabetic peripheral neuropathy. He added, however, that "*from the 16 authorised ATMPs in the EU, only 6 of them are marketed in more than 10 Member States. There are*

still over half of Member States with 4 or less marketed ATMPs, and some Member States have no marketed ATMPs." Mr Boráň concluded that initiatives to improve access to ATMPs are therefore very important.

- He highlighted that most ATMPs are initially developed in an academic setting, and then need to be transferred into Phase III trials. Academics therefore need investor support to achieve marketing authorisation. Mr Boráň also referenced the EMA's new pilot to support academic developers of ATMPs through regulatory processes, praising this step because "*[if] even at the stage of clinical trials academia can avoid mistakes, this can support the availability of ATMPs*."
- Early communication with HTA bodies is vital for Mr Boráň. He flagged this Recommendation in the Charter as particularly important to avoid delays in products coming to the market. He added that "*compared to the US, the marketing authorisation process in the EU is longer and less predictable, and we need to build better capacity at EMA level*".
- He finally noted linkage between the decline in the number of clinical trials for ATMPs in Europe with the non-harmonised approach to approval for clinical trials and genetically modified organisms (GMO).

Solutions across the R&D lifecycle to build a European system fit for transformative therapies

Victor Maertens, Government Affairs Manager, EUCOPE reflected on the TRANSFORM Charter and the opportunities there are to take its Recommendations forward.

> ***"By bringing together these different perspectives [in TRANSFORM], hopefully we can look for some solutions to shared challenges and chart a path forward."***

- He opened by saying that ATMPs signify an important shift in how to approach treatment, particularly in the case of potentially 'one-off' applications. This means we must balance system sustainability with the drive for long-term, disruptive innovation.
- Mr Maertens said that "*it is important to reflect on some of the opportunities we see ahead of us. We have the General Pharmaceutical Legislation, the Orphan legislation, the Pediatrics legislation and the proposed SoHo Regulation all coming, and there will be important elements where we can look at some of the challenges [for ATMPs] and drive innovation and, more importantly, access.*"
- He noted the importance of initiatives such as early dialogue between various stakeholders involved in the development of ATMPs and underlined the need for new thinking on clinical trials.
- At the same time, he flagged things that can be done outside of legislation to support innovation and access for ATMPs, such as sharing best practices and the improvement of the care infrastructure, to name a few.
- He concluded that a holistic perspective is vital for ATMPs when reviewing the development ecosystem, and highlighted that this is what TRANSFORM has done, by considering the full lifecycle of cell and gene therapies in its Charter.

Panel 1: Future-proofing the EU's regulatory framework to accommodate innovative therapies: opportunities within the current review of the legislative acquis

- **Billy Kelleher (Renew Europe, Ireland)**, TRANSFORM MEP Interest Group member
- **Stefaan Van der Spiegel**, Team leader – substances of human origin, Unit D2: Medical products: quality, safety, innovation, DG SANTE, European Commission
- **Eleni Antoniou, Senior Policy Officer**, Thalassaemia International Federation
- **Gilles Vassal**, Pediatric Oncologist Gustave Roussy, SIOP Europe board member
- **Laila Syed**, Vice President Global Regulatory Affairs, Rare Disease & Serious Chronic Disease, Novo Nordisk

- **MEP Kelleher** "*We can have a lot of research and innovation but until we have a system in place that can assess the efficacy of a medicine through the health assessment technology and then make it available to patients with timely reimbursement, we are always going to have difficulty in incentivizing and rewarding innovation and creativity in medicines, particularly in [ATMPs].*"
  Despite health being mainly a national competence, MEP Kelleher called for more centralised, cross-country coordination on information sharing, HTA, clinical trials and newborn screening rules. Patients must be able to access the best standard of care regardless of their Member States' financial status. At the same time, the system needs to stay nimble to allow that assessment to evolve with the science. MEP Kelleher stated that a clear development and reimbursement pathway, such as by establishing dedicated funds, needs to be put in place for innovative therapies, to move away from a system where therapies are available only where there is budget surplus.

- **Stefaan Van der Spiegel** *"There is a need for legal clarity in the distinction between ATMPs and SoHO. The proposed SoHO Regulation does not alter the borderline which is set by the scope of the pharma legislation. However, in order to achieve more legal clarity, the SoHO Regulation proposes much more cross-sector coordination between authorities, at national level, as well as at EU level. The proposed SoHO Coordination Board can consult equivalent bodies in other legal sectors, like CAT to provide coordinated advises on borderline cases."*
  Mr Van der Spiegel reflected on the importance of the proposed SoHO Regulation for ATMPs, as most ATMPs originate in these substances. He noted that the proposal will provide for more harmonized EU-wide requirements for ATMP starting materials and will address concerns raised to make sure there is transparency and common approaches to SoHO and ATMPs across Member States, and learnings are captured. He confirmed that the challenges around GMO rules and clinical trials in ATMPs are on the radar of the European Commission.

- **Eleni Antoniou** "*Patients must be at the centre…Patients call for collaboration, harmonization of processes, [and] interoperability of the different mechanisms that exist in Europe."*
  Ms Antoniou said that safeguarding patients' right to health implies finding effective routes to patient access. She stressed the importance of infrastructure – namely registries – for the collection of real-world evidence to support cell and gene therapies' development and monitoring. During the upcoming legislative revisions, patients' views must be effectively taken into consideration. She agreed with other panelists that safety standards are crucial for patients, regardless of the access pathway.

- **Gilles Vassal** "*In light of recent market failures, having academic teams fully qualified to develop and provide access to these therapies for patients, including under GMP standards, is very important."*
  Prof Vassal underlined the importance of early, multi-stakeholder dialogues, starting from the definition of R&D priorities. He also argued that data collection is crucial, both inside and outside clinical trials, to improve access timelines and increase patient safety post marketing authorization, whilst reducing uncertainties for HTA Agencies and regulators.

- **Laila Syed** "*We must modernise the EU, but not just its regulatory framework; also how it attracts investment. An important factor for a developer when embarking in an investment is whether there is a robust regulatory framework: predictable, strong, and agile regulatory bodies*."
  Ms Syed said that the regulatory framework is currently not fit for purpose for innovative treatments such as ATMPs. She called for a reassessment of the GMO requirements for ATMPs, as these rules add up to 6 months of time when doing first human dose trials. Moreover, she endorsed minimum, standardised safety requirements for the use of Hospital Exemption across Member States, to ensure these products are held to the same safety standards as "conventional" ATMPs. Moreover, she highlighted that the concept of RWE is not new, indeed what is more important in the context of ATMP development is the net value and grade of this generated evidence, both for the regulators as well as HTA Agencies and Payers.

- From the audience, **Dr Esteve Trias-Adroher** spoke about his experience participating in the EMA pilot to support academic organisations develop ATMPs. He highlighted that safety and quality requirements for treatments under Hospital Exemption in Spain are very high, and that this is key to ensure patients receive the best standard of care.

Panel 2: New approaches to foster safe and timely patient access to ATMPs in Europe: realising agreed EU-level actions and building on national learnings

- **Ondřej Knotek (Renew Europe, Czechia)**, TRANSFORM MEP Interest Group Chair
- **Simone Boselli**, Public Affairs Director, EURORDIS-Rare Disease Europe
- **Dr Donato Bonifazi**, Coordinator, European Paediatric Translational Research Infrastructure (EPTRI)
- **Prof Mor Dickman**, ATMP expert and custodian of European Cornea and Cell Transplantation Network (ECCTR), EU-EYE representative
- **Tay Salimullah**, Vice President, Global Head Value & Access, Novartis Gene Therapies

- **MEP Knotek** "*We cannot reach our goals on the individual Member State level: there will never be enough capacity, never enough resources, never enough knowledge. So, this is an agenda that needs an EU answer*."
  Mr Knotek called for Member States to work towards reducing fragmentation and health inequalities. More resources are needed to upgrade HTA and regulatory capacities across the bloc. The MEP said that the EU must do more to ensure effective access to cross-border healthcare, as this is crucial for access to ATMPs. MEP Knotek agreed to investigate the possibility of an own-initiative report from the Parliament to bring the TRANSFORM Charter recommendations forward.

- **Simone Boselli** "*Regional collaborations to support HTA and pricing and reimbursement negotiations, such in BeNeLuxA, are a cornerstone for success in improved patient access to innovative therapies*."
  EURORDIS is a strong advocate for the harmonization of Newborn Screening practices in Europe, despite the Member States' reluctance. Mr Boselli agreed that a lifecycle perspective is critical to improve access and put Europe on the forefront of medical innovation in rare diseases.

- **Donato Bonifazi** "*There is no body with leadership in boosting innovative research in the EU. To increase research, we need to change the paradigm...to increase basic research in the academic environment and then make it accessible to patients*."
  Mr Bonifazi said that academic research and innovation must be better funded and supported. Neighbouring regions must cooperate to ensure better access to cross-border care as references

centers do not exist in all Member States. He advocated for focusing on unmet needs, particularly for pediatric patients.

- **Mor Dickman** "*We have seen how regulatory authorities throughout the world can come together [during the COVID pandemic]…the FDA is…a partner for Europe. We need to work together and harmonise our processes with the US to ensure there is one way to the patient*."
  Prof Dickman said that the Hospital Exemption can be a way to ensure access if there is a case where a company with an authorized treatment withdraws from the market. He noted that there is a need for funding for registries to ensure their sustainability, as cornerstones of medical research, especially in rare diseases: they allow for the collection of long-term data, including patient-reported outcomes, which contributes to evidence gathering in HTA processes.

- **Tay Salimullah** "*There must be a huge pivot in the [data] standards we are used to in, for example, cardiovascular trials with thousands of patients and Phase III data. The reality is that there will be data that matures over time [for ATMPs]. We must find a way to acknowledge elements of value [for ATMPs] beyond just the trial data, such as through real-world evidence*."
  Mr Salimullah believes joint clinical assessments could be a key to unlock timelier approval processes for ATMPs. He stated that bringing best practices to all Member States in Newborn Screening and Diagnostics actions is crucial to ensure the effectiveness of ATMPs. Finally, he recalled the pressing need to incorporate innovative access models, such as outcomes-based agreements, to address uncertainties for these therapies.

Conclusions and next steps – TRANSFORM's commitment to ensure safe and timely patient access to ATMPs in Europe

Tomislav Sokol (EPP, Croatia), TRANSFORM MEP Interest Group member closed the event.

"*The first priority is stimulating research innovation. This means engagement with industry…Incentives for research and innovation can take several forms, from market exclusivity to using more real-world evidence in assessments, to other financial incentives. The second priority is enabling access. Pricing and reimbursement decisions are made by Member States, but we can still do a lot [at EU level]*."

- MEP Sokol said that health inequalities must be addressed through harmonization, where it is possible. He stated that the EU HTA Regulation was a missed opportunity for streamlining, as now we have 28 HTA systems, rather than 27. Still, much can still be done to improve the in-market access pathway, including the promotion of new and innovative access pathways like pay for performance.
- As rapporteur of the European Health Data Space proposal, the MEP will ensure secondary data is usable for research and innovation. Data interoperability will also be a key priority for him.

About the European Alliance for Transformative Therapies (TRANSFORM)

We invite you to join the TRANSFORM Community on Twitter and LinkedIn and keep an eye on the website to continue this important discussion online and to stay updated about the TRANSFORM MEP Interest Group and Alliance of experts' 2022 plans.

If you did not attend the event or if you wish to re-watch the discussion, you can access the recording and the MEP Charter Launch video here:

https://transformalliance.eu/event/mep-interest-group-2022-conference/

You can read the TRANSFORM MEP Charter for EU Cooperation to Enable Safe and Timely Patient Access to Advanced Therapies in Europe here:

https://transformalliance.eu/charter/

You can read the TRANSFORM Policy Asks on the Regulatory Framework for ATMPs launched on 16 June 2022 here:

https://transformalliance.eu/wp-content/uploads/2022/06/TRANSFORM-Policy-Asks-on-Regulatory-Framework-for-ATMPs_FINAL_June2022.pdf

You can read the TRANSFORM Policy Asks on Access to Authorised ATMPs launched on 31 March 2022 here:

https://transformalliance.eu/wp-content/uploads/2022/03/TRANSFORM-Policy-Asks-for-Access-to-Authorised-ATMPs.pdf

You can read the TRANSFORM MEP Interest Group Policy Asks on Cross-Border Healthcare launched on 10 November 2021 here:

https://transformalliance.eu/wp-content/uploads/2021/11/TRANSFORM-MEP-Interest-Group-Five-Asks-on-Cross-border-Access-to-ATMPs-1.pdf

You can read the TRANSFORM Recommendations for Actions in the context of the Pharmaceutical Strategy for Europe launched in June 2021 here:

https://transformalliance.eu/wp-content/uploads/2021/06/TRANSFORM-Recommendations-Version1.0_June2021-1.pdf

The European Alliance for Transformative Therapies (TRANSFORM) is a multi-stakeholder Alliance that connects Members of the European Parliament (MEPs) and policy-makers 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 sustainability of healthcare systems.

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The European Medicines Agency is an Observer to the Alliance.

EFNA – European Federation of Neurological Associations

RI – Retina International

WDO – World Duchenne Organization

IPOPI – International Patient Organisation for Primary Immunodeficiencies

TIF – Thalassaemia International Federation

EHC – European Haemophilia Consortium

EURORDIS – Rare Diseases Europe

EPTRI – European Paediatric Translational Research Infrastructure

CCI Europe – Childhood Cancer International Europe

SIOP Europe – the European Society for Paediatric Oncology

EAHAD – European Association for Haemophilia and Allied Disorders

EU EYE – European Alliance for Vision Research and Ophthalmology

EUCOPE – European Confederation of Pharmaceutical Entrepreneurs