Flash Report - Implementation of the Hospital Exemption in the EU and its Role in Boosting Innovation and Patient Access to Innovative Therapies – 21 November 2024

On 21 November, a full-day hybrid event, in Brussels and online, gathered officials from the National Competent Authorities (NCAs) and developers of Advanced Therapy Medicinal Products (ATMPs), both academic and private developers, which are actively involved in the implementation of Hospital Exemption (HE) in EU countries. Other stakeholders, including the EMA, the European Society of Blood and Marrow Transplantation (EBMT), pharmaceutical industry associations, scientific societies and academic biotech spin-offs, also delivered presentations and were engaged in useful conversations. This stakeholders' meeting was organised in the framework of the ongoing "Study on Hospital exemption in relation to the implementation of the Advanced Therapy Medicinal Products (ATMP) Regulation) EC) No. 1394.2007". An overview of stakeholders present during the meeting can be found in the Annex of this document.

Marina Rodés Sánchez from PredictBy Research and Consulting, representing the contractor opened the meeting and presented the agenda items.

Bruno Gautrais, Head of Unit at DG SANTE D2, welcomed the participants and pointed out that HE enables invaluable patient access to innovative treatments and facilitates the translation of research in European university hospitals and research centres into innovative medicines. **Agnes Mathieu-Mendes**, Head of Unit at HaDEA A2, provided an overview of the work and vision of the Agency, including the EU4Health Programme under which the HE is funded. **Paschalia Koufokotsiou**, Policy Officer at DG SANTE D2, provided some insights on the design of the HE study and presented the intended purpose of HE in EU Member States. Marina Rodés Sánchez then presented the study's methodology.

Evangelia Yannaki, Medical Director at the Hematology Department/Hematopoietic Cell Transplantation (HST) Unit and the Gene & Cell Therapy Center of G.Papanikolaou Hospital, in Thessaloniki, started the event with a keynote speech on "ATMPs development in hospitals". She offered insights into the critical role hospitals play in advancing ATMP development and presented two cases of investigational ATMPs developed in their hospital, specific T cells (CoV-2-STs) for the treatment of patients with severe COVID-19 and 3rd generation of T-cells for the treatment of blood malignancies. She also noted that the HE provision has not been transposed into the national legislation in Greece.

Next on the agenda were the presentations of national HE legislation provisions. **Raquel San José Rodríguez**, from the Advanced Therapies Unit (UTA) of the Healthcare office of the Region of Madrid, outlined the HE framework in Spain and the involvement of her unit in establishing a regional strategy for a comprehensive management of ATMPs, which led to the first advanced therapy of public ownership manufactured under HE in Spain. In total 5 ATMPs were authorised under the HE in Spain, and information on these products is publicly available. **Triin Suvi,** Head of the Biologicals Department of the State Agency of Medicines (SAM), presented an

overview of Estonia's HE system, which is regulated since 2022. In her presentation she noted an ongoing revision of the national HE rules due to the limited use of HE in Estonia. It was also highlighted that there are centrally authorised ATMPs in the EU, but they are not available to the Estonian patients. **Babs O. Fabriek,** Senior Clinical Assessor at the Medicines Evaluation Board in the Netherlands and alternate member of the EMA Committee of Advanced Therapies (CAT), shared the Dutch key rules of HE, including compliance with ATMP GMP requirements, small scale manufacturing and no alternative treatment options, such as registered products or clinical trials. It was emphasised, that a pre-application process allows for most of the HE requests to be awarded and no product related safety signals have been reported so far for HE products. **Manon Thamin**, a Regulatory Affairs Assessor in the Regulatory Affairs and Ethics Division at the French National Agency for the Safety of Medicines and Health Products (ANSM) and Member of the HMA Borderline Classification Group (BLCG), presented the national HE rules in France. In total 13 ATMPs were authorised for use under the HE and a new provision on peri-operative autologous HE-ATMPs has been established for the preparation, distribution and administration of HE-ATMPs within a hospital, as part of the same medical intervention as the tissue or autologous cell collection involved.

Participants then engaged in three breakout sessions to delve into key aspects of Hospital Exemption (HE).

- **What are good examples of national practices on HE, and what are their effects on patient access to ATMPs?**
- **For which therapeutic indications have HE-ATMPs been used in your country? To what extent have HE-ATMPs served patient's needs?**
- **Has HE enabled the translation of deep science into innovative products in your country? Can you provide some examples?**

The afternoon sessions started with the presentations of product journeys. **Maria Pia Cicalese**, Physician and Scientist at the Paediatric Immunohematology Unit at the San Raffaele Hospital and Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy, highlighted in her presentation three case studies in which the HE scheme was used to enable patient access to innovative therapies as an alternative to already approved ATMPs. Telethon Institute for Gene Therapy (SR-Tiget) is the first non-for-profit organisation that holds manufacturing and distribution rights for an approved ATMP. **Alexandra Karström,** Assistant Head of the Department of Plastic and Maxillofacial Surgery and Head of the Tissue Establishment at Uppsala University Hospital in Sweden and Qualified Person under the HE framework, presented a HE case on burn care. It involves the treatment of severe burns with use of autologous cultured keratinocytes manufactured under the HE as life-saving and last resort treatment for burns. **Julio Delgado,** Associate Professor and Head of the Onco-immunotherapy Unit and Department of Haematology at the Hospital Clinic de Barcelona presented the product journey of two CAR-T cell therapy products developed under the HE in Spain. The first is the ARI-001, which was made available under the HE in 2020 and received PRIME designation and was included in the EMA's pilot programme of enhanced support for academic ATMP developers. The second is the ARI0002h for multiple myeloma.

The following item in the agenda was a presentation on the **EBMT registry by Ana Alarcón Tomás,** Hematologist at the Hospital Universitario Puerta de Hierro Madrid and Co-Chair of the CAR-T Subcommittee withing the Cellular Therapy and Immunobiology Working Party at EBMT. She shared the experience of the last 50 years of the EBMT registry, with over 500 centres in 70 countries worldwide and over 10,000 patients treated with CAR-T cell therapies. The EBMT also collects data related to HE, for example in a survey on the use of mesenchymal stromal cells (MSC) produced in academia (HE) which proved to be a viable treatment option for steroid-refractory acute graft versus host disease (GVHD).

The final session focused on **"Supporting academic ATMP developers and competitiveness of the EU biotech secto**r." **Caroline Pothet**, who manages the Office of Advanced Therapies and Haemato-oncology at the EMA, presented EU regulatory tools supporting academic developers of ATMPs. EMA key support tools for academia include the Innovation Task Force for early academic briefing, scientific advice and protocol assistance and PRIME scheme to support development of medicines that target an unmet medical need. Additionally, she highlighted the academic support pilot for academic developers that has been launched in 2022, with currently selected three products for regulatory support and fee incentives. **Hans-Dieter Volk,** founding Director of the Center for Regenerative Medicine in Berlin and CEO of a spin-off company of the Hospital Charité in Berlin, spoke about the need for specialised laboratories that combine innovation, flexibility and quality assurance in order to support academic developers of ATMPs. He also presented new laboratory methods for the analysis of identity, phenotype and functionality of CGT products and for the monitoring of the therapy response of patients. **Denis Dufrane**, Co-founder and CEO of Novadip, presented a case study that HE can serve for a biotech start up. The company Novadip was created because of the development of a successful product NVD0003, a single treatment to cure large bone defects and disease without amputation, which was made available under the HE in Belgium for rare paediatric indications.

The event concluded with a recap by the contractor and DG SANTE. Participants were informed about upcoming follow-up activities and encouraged to contribute to the forthcoming public survey related to the outcomes and findings of the study and the HE stakeholder event. The findings and takeaways collected during the event will be included in the study results and the final analysis report.