EMA
EUROPEAN MEDICINES AGENCY

The landscape for ATMPs in Europe 15 years after the initial introduction of the Regulation

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Vice-Chair - Committee for Advanced Therapies

The conception & birth: 2007 - 2009

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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

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the Opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the procedure laid down in Article 251 of the Treaty (2),

Whereas:

(1) New scientific progress in cellular and molecular biotechnology has led to the development of advanced therapies, such as gene therapy, somatic cell therapy, and tissue engineering. This nascent field of biomedicine offers new opportunities for the treatment of diseases and dysfunctions of the human body.

(2) Insofar as advanced therapy products are presented as having properties for treating or preventing diseases in human beings, or that they may be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting principally a pharmacological, immunological or metabolic action, they been defined in Annex I to Directive 2001/83/EC, but a legal definition of tissue engineered products remains to be laid down. When products are based on viable cells or tissues, the pharmacological, immunological or metabolic action should be considered as the principal mode of action. It should also be clarified that products which do not meet the definition of a medicinal product, such as products made exclusively of non-viable materials which act primarily by physical means, cannot by definition be advanced therapy medicinal products.

(4) According to Directive 2001/83/EC and the Medical Device Directives the basis for deciding which regulatory regime is applicable to combinations of medicinal products and medical devices is the principal mode of action of the combination product. However, the complexity of combined advanced therapy medicinal products containing viable cells or tissues requires a specific approach. For these products, whatever the role of the medical device, the pharmacological, immunological or metabolic action of these cells or tissues should be considered to be the principal mode of action of the combination product. Such combination products should always be regulated under this Regulation.

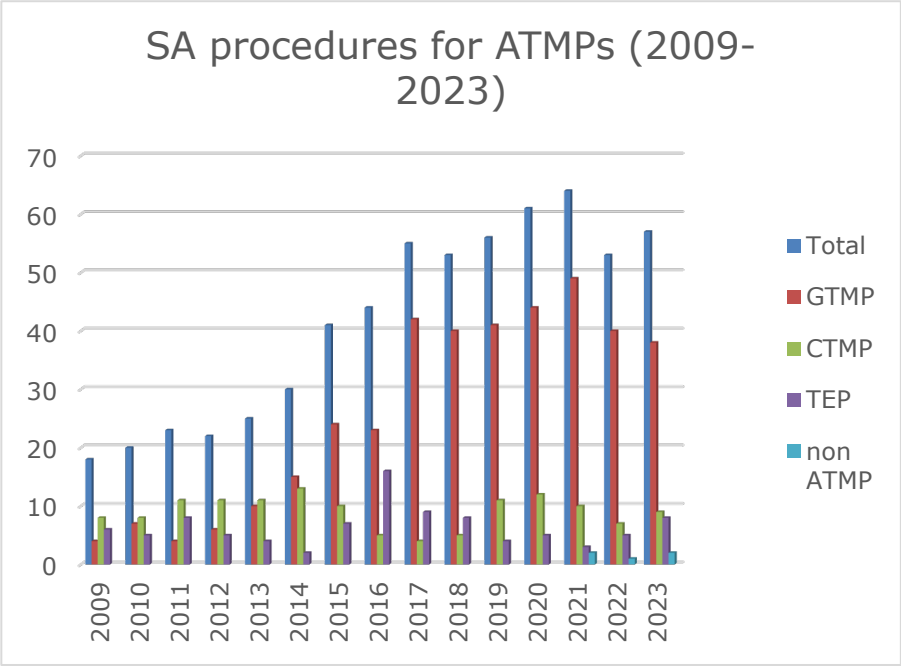
(5) Because of the novelty, complexity and technical specificity of advanced therapy medicinal products, specially tailored and harmonised rules are needed to ensure the free movement of those products within the Community, and the effective operation of the internal market in the biotechnology sector.

- Regulation 1394/2007 of 13.11.2007
- In operation since 30.12.2008:
  - Establishment of the Committee for Advanced Therapies (CAT)
  - Provides definitions & procedures for ATMPs
  - Incentives for developers
- First CAT meeting: January 2009

Challenges with ATMPs

- Complex products to develop, manufacture, characterise, test
- Evolving technological and scientific breakthroughs
- Tailored non-clinical development programmes developed prior to FIH studies
- Concomitant therapies, e.g. conditioning therapy, immune suppression
- Novel toxicities with potential unknown risk e.g. insertional mutagenesis events
- Specific post-authorization obligations to address remaining uncertainties and to build regulatory knowledge base
- Lack of precedent cases for regulatory decision making

ATMP pipeline



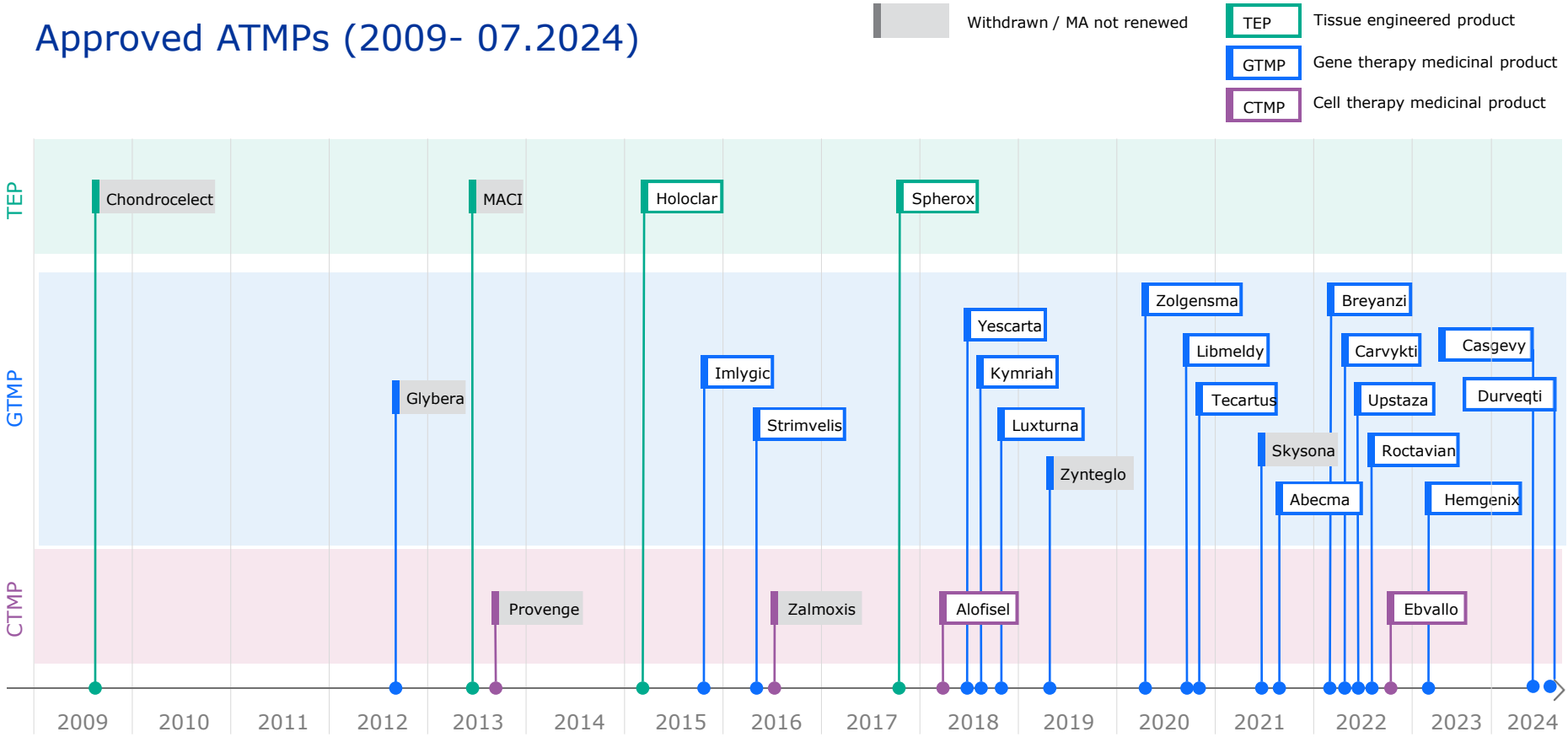
Predicted submission rate 10/year.

- Lots of activity (SA, PRIME, classifications)
- Most gene therapies
- Great mix (academic, SMEs, large pharma…)
- Similar forecast to FDA

but:

- COVID-19 impact on clinical trials
- Attrition rate high
- Development delays very frequent

Approved ATMPs (2009- 07.2024)



EMA initiatives to facilitate ATMP development

- Innovation Task Force (ITF)
- Scientific advice (SAWP)
- Guideline publication
- PRIME scheme
- Accelerated assessment
- ATMP pilot for academia and non-profit organisations
  - Up to five ATMPs addressing unmet medical needs

The **PRI**ority MEdicines (PRIME) programme

Medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation.

- Potential to address to a significant extent an unmet medical need

Reinforce scientific and regulatory advice

- Foster and facilitate early interaction
- Raise awareness of requirements earlier in development

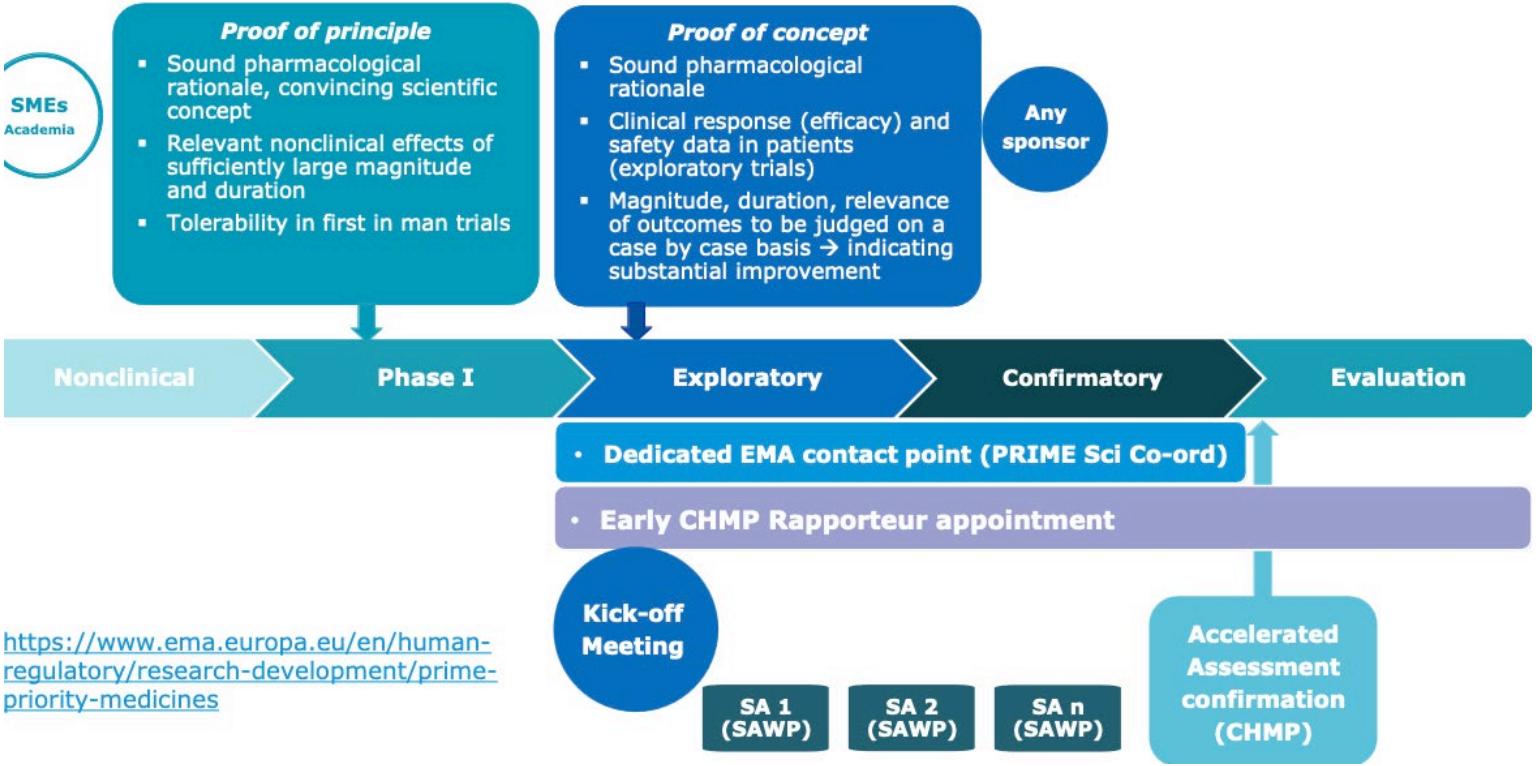
Optimise development for robust data generation

- Focus efficient development
- Promote generation of robust and high-quality data

Enable accelerated assessment

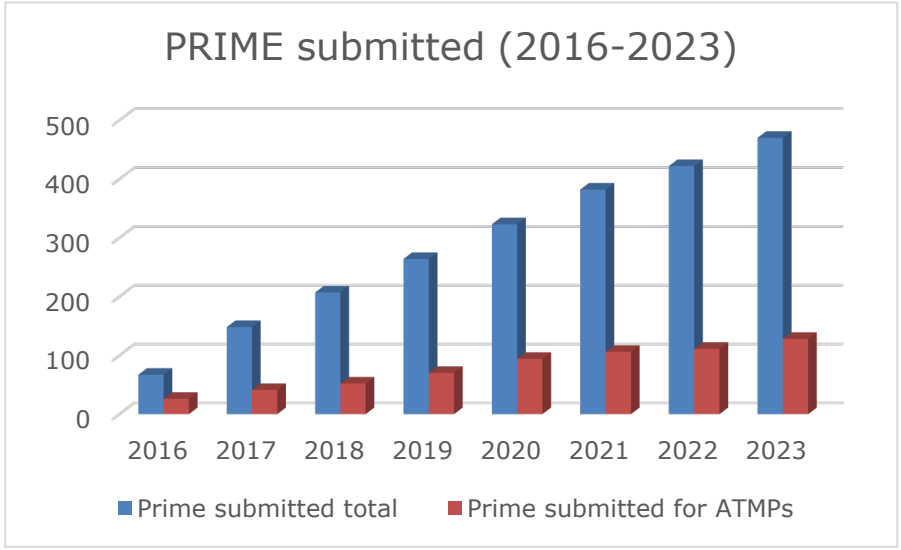
- Promote generation of high-quality data
- Facilitated by knowledge gained throughout development

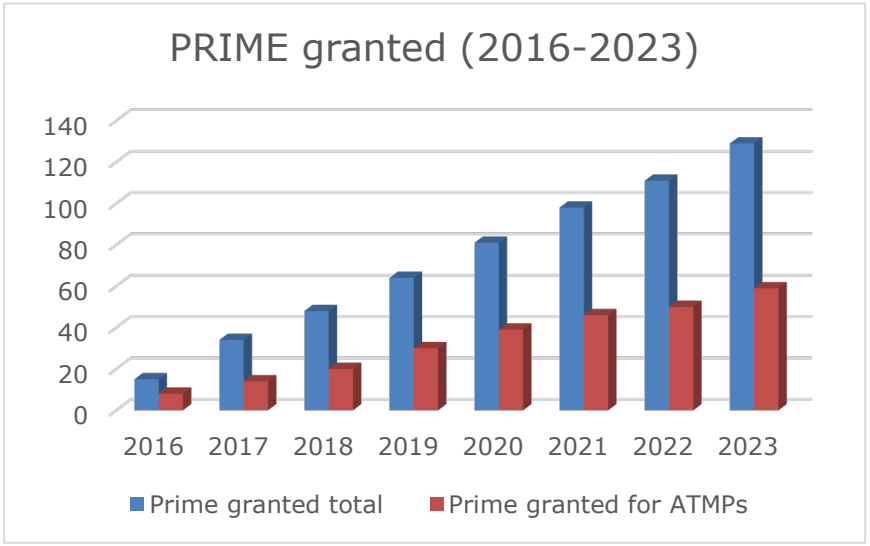
The **PRI**ority **ME**dicines (**PRIME**) programme



https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

ATMP PRIME: submissions and successes (2016-2023)

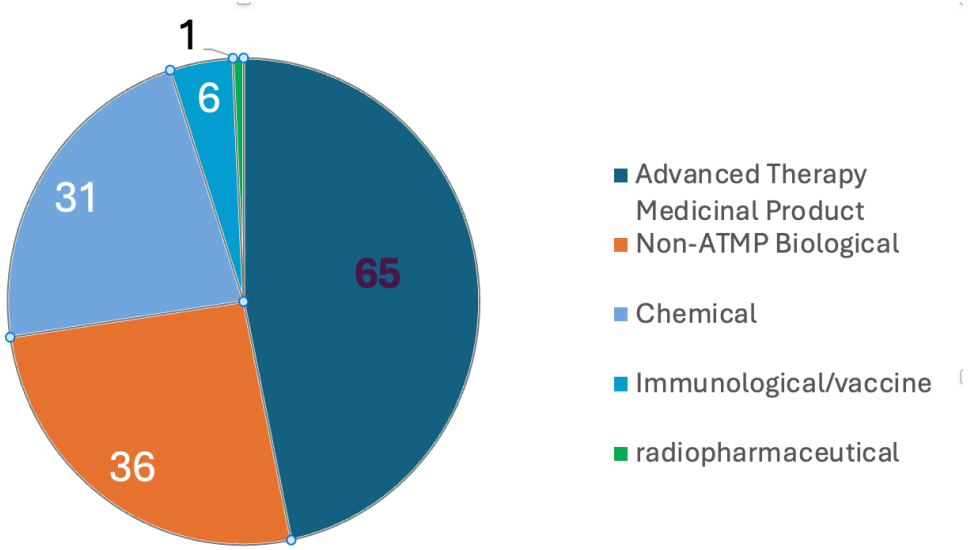




https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines

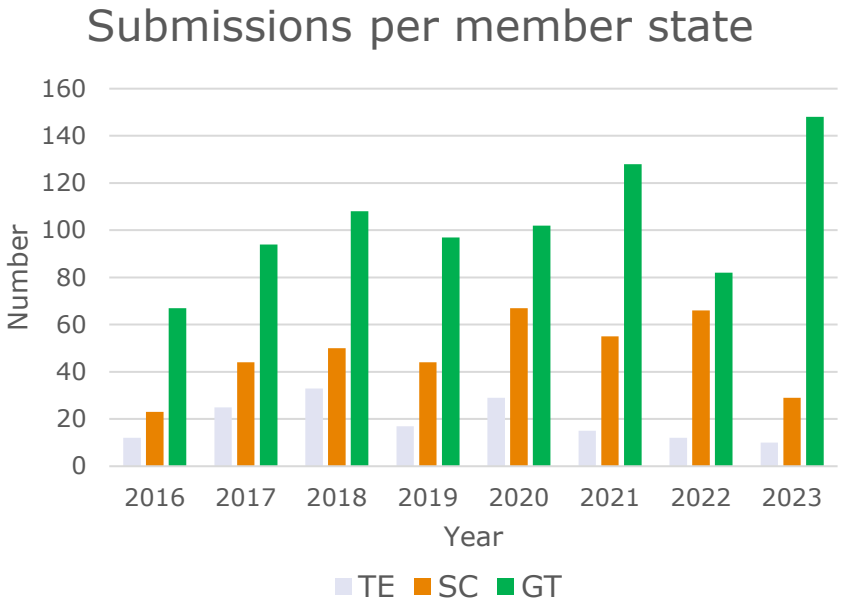
PRIME - ATMPs 27% of applications, 47% of products granted

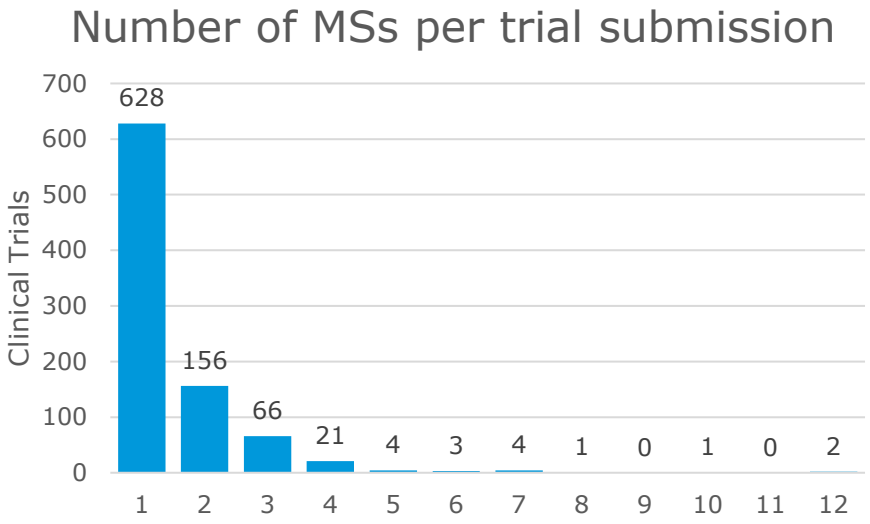
ATMP	65
Non-ATMP Biological	36
Chemical	31
Immunological/ vaccine	6
Radiopharmaceutical	1
Total	**139**



From Kevin Cunningham, EMA

ATMPs in development - Clinical trial submissions in the EU 2016-23





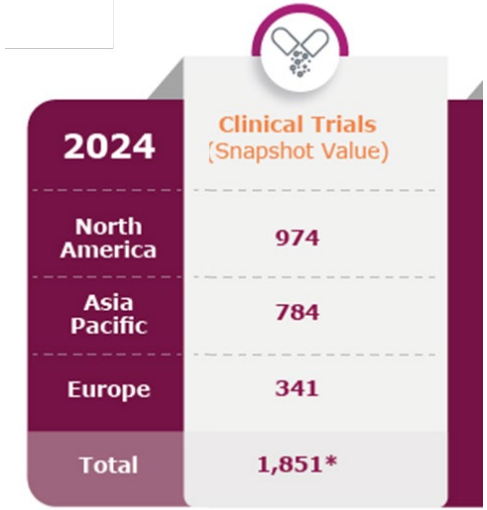
Preliminary curated analysis (EudraCT **and** CTIS) submissions and number of member states concerned

Follow-on from

CTs 2009-2016 - Boran et al. DOI: 10.1089/humc.2016.193 (from IG Reischl 2024)

Some future challenges for ATMPs in Europe

- **Rapid pace** of science (e.g. gene editing & platform technologies) will increase product complexity and challenge regulation
- Increase in global access to ATMPs will be facilitated by regulatory **convergence** (e.g. between EMA, FDA etc)
- Requirement for sustained **long-term follow-up** for more ATMPs
  - Potential use of combined **registries** for data collection and monitoring (e.g. World Federation of Haemophilia registry)
- Implementation of **EU Pharma Legislation**
- Opportunity to increase **innovation** and R&D **investment** in the EU



Source EFPIA Oct 2024

ATMP future development in Europe

- This is an ever-evolving **complex field**
- **ATMPs are medicinal products** and their quality, safety and efficacy needs to be demonstrated on a product-specific basis
- **Robust and reproducible data** are required
- Clinical trial procedures and interface aspects need to be **clear from the start**
- **Exemptions** for individual needs, when implemented, need to be clearly defined
- **Complexities** including combined products and companion diagnostics need to be considered
- Need for close interaction with **patients** – the CAT is unique with patient representatives
- **Patient access** needs to be facilitated with the implementation of the HTA regulations

Thank you!

Further information

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