Scientific Symposium on Advanced Therapy Medicinal Products - ‘Contribution, evolution, revolution’

Interventions on behalf of ARM / EFPIA / EUCOPE / EuropaBio

10th October 2024

efpia
European Federation of Pharmaceutical Industries and Associations

EuropaBio®
The European Association for Bioindustries

EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

Alliance for Regenerative Medicine

What challenges will arise from ATMPs under development?

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Outline

- The CAT's important contributions to the ATMP sector in the EU and globally
- EU ATMP landscape today
- Current and future opportunities for ATMPs
- Importance of the new structure for ATMPs & SA
- GPL revision and HTA Regulation: possible implications
- Global harmonization and convergence for ATMPs

The Committee for Advanced Therapies

Acknowledgment

- Tremendous progress in creating clear delineation of ATMP classifications
- Critical role in providing scientific advice on behalf of the EMA to developers
- Pivotal role in approving, often first in the world, groundbreaking therapies addressing unmet medical needs
- Representation of all member states
- 15 years of expertise and experience in assessing pre- and post approval ATMPs in the EU

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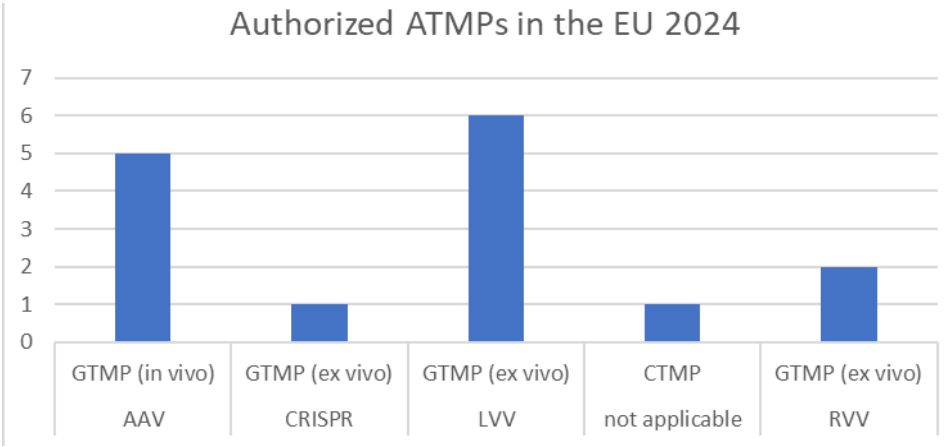
EU ATMP product landscape today

Initial Evaluation of Marketing Authorisation Applications (MAA) for ATMP						
	2009-2020	**2021**	**2022**	**2023**	**2024***	**Total**
Submitted MAAs	32	3	1	3	5	44
Positive draft Opinion	18 i	2	6	1	1	28#
Negative draft opinions	4 i,ii,iii	0	0	0	0	4
Withdrawals	8 ii, iv	0	1v	1vi	0	10
Ongoing MAAs						7



Corresponding to 27 ATMPs (see List of authorised ATMPs)
i One negative draft opinion and two positive draft opinions for the Glybera
ii Negative draft opinion and withdrawal for the Cerepro
iii Two negative draft opinions for Heparesc
iv Luxceptar, Roctavian, Artobend
v Sitoiganap
vi Lumevoq

Adapted from : EMA/CAT/177024/2024

ATMP product landscape today continued

Q2 2024 Sector Data

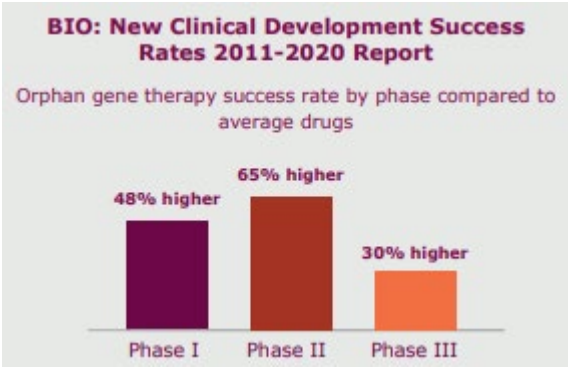
GlobalData.

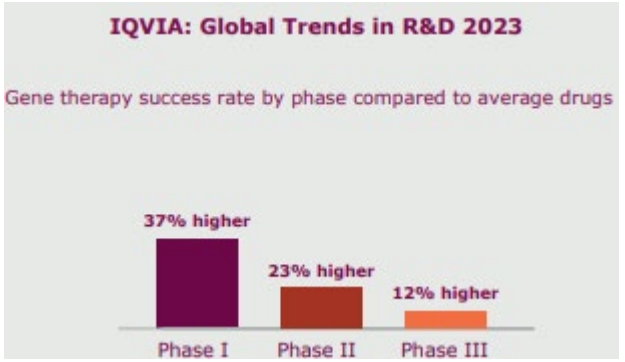
GlobalData is ARM's data partner.

2024	Developers (Snapshot Value)	Clinical Trials (Snapshot Value)	Investment (Q2 2024 Total)
North America	1,243	974	$3.8B
Asia Pacific	1,000	784	$0.1B
Europe	579	341	$0.3B
Total	2,919*	1,851*	$4.2B*

*Totals refer to unique quantities and includes data from other regions not shown

More data breakdowns available at www.alliancerm.org/data



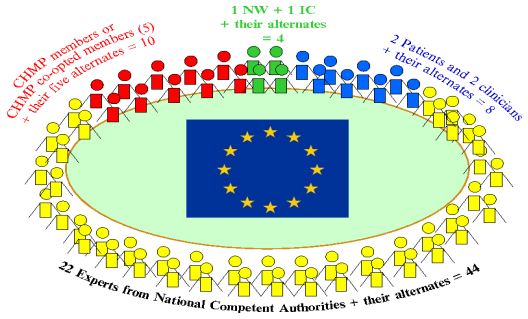


Source: [ARM August-2024-Sector-Snapshot]

Overcoming challenges for ATMPs in the EU

- Streamline EMA structure while maintaining strong expertise in ATMPs
- CT design and evidence generation including LTFU
  - Scientific advice (SA) through development phases to ensure harmonized, aligned feedback
  - ATMPs-appropriate methodologies for new EU Joint Clinical Assessment (HTA Regulation) with recognition of evidence from single arm trials and RWE
- Fragmented regulatory framework (ATMP, SoHO, GPL)
  - Improve interface/convergence between different frameworks, in particular with IVD and MD, SoHOs
- Future proofing and flexibility to reflect fast scientific progress

Maintain strong expertise in ATMPs



Reference: Bettina Klug, Patrick Celis, Melanie Carr, Jens Reinhardt, Chapter Seventeen - Regulatory Structures for Gene Therapy Medicinal Products in the European Union, Editor(s): Theodore Friedmann, Methods in Enzymology, Academic Press, Volume 507, 2012, Pages 337-354,

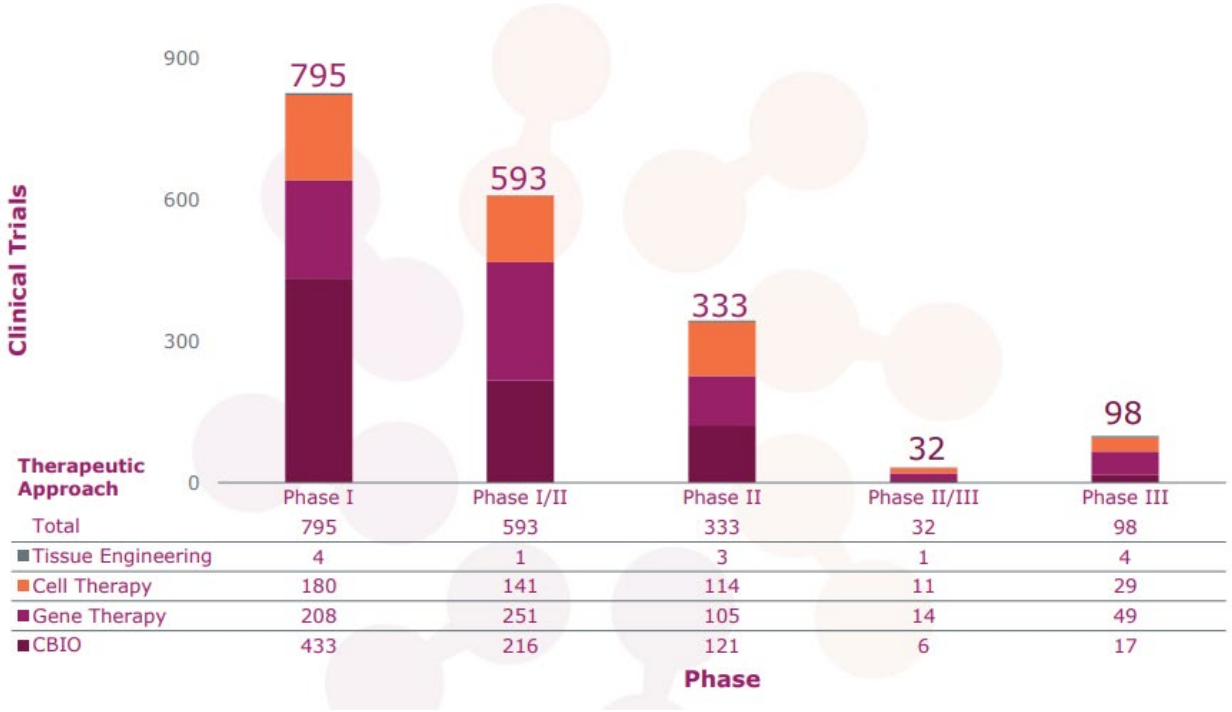
- Ensure the expertise of CAT is not lost and integrated into the WP approach
- Ensure patient input is maintained & strengthened
- Experts are engaged in horizon scanning, training and education
- Dissemination of learnings and knowledge across the network
- Equal access to knowledge, expertise, horizon scanning, training and education across all EU member states

Current and future opportunities for ATMPs

Table 2: The Top Emerging Technologies in C&GT identified by the described methodology

Rank	Technology
1	Engineered T cells for Autoimmunity
2 (tie)	*in vivo* CAR-T cell Engineering
3 (tie)	Synthetic Biology
4	Non-double-stranded break-inducing Gene Therapies
5	iPSC-derived Therapies
6	Engineered Immune Cells
7	Nonviral Gene Therapy Delivery
8	Capsid Engineering
9 (tie)	Bioengineered and Xenotransplanted Organs
10 (tie)	Secretome and Exosome-based Therapeutics
11 (tie)	Alternative RNA Therapeutics

Source: ARM- 2024 Emerging technologies shaping cell and gene therapy

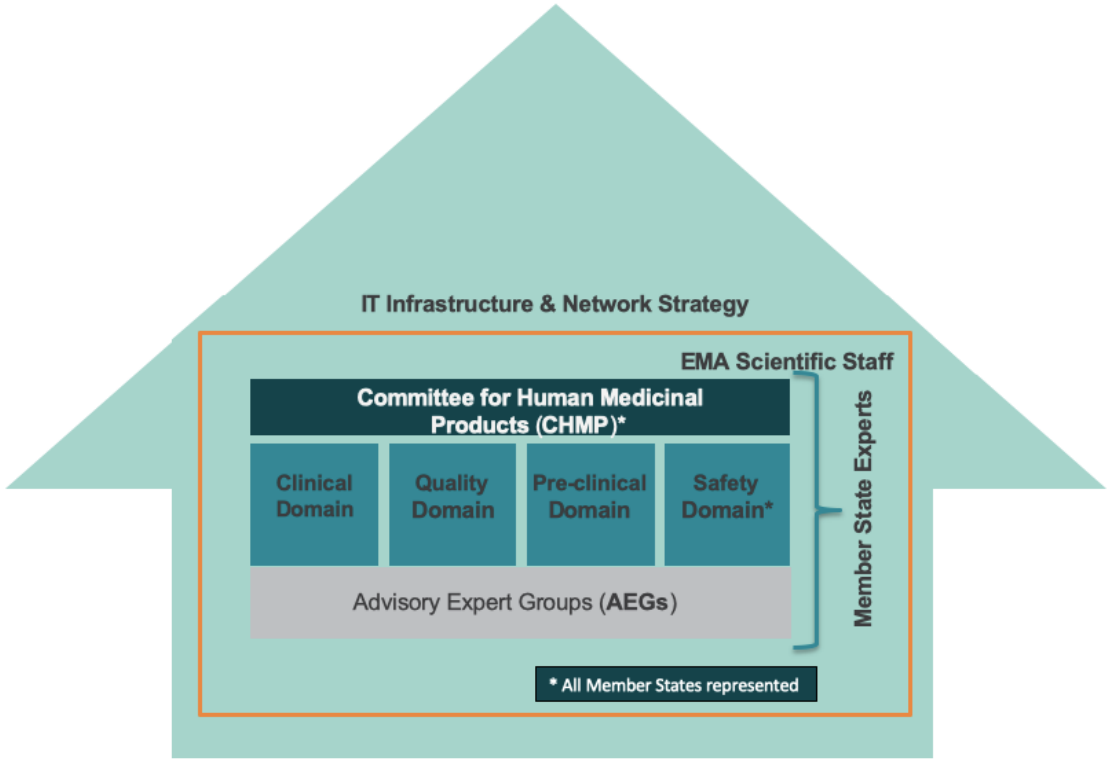


Source: ARM- Clinical Trials as of July 2024

Current and future opportunities for ATMPs in the EU – additional areas of interest

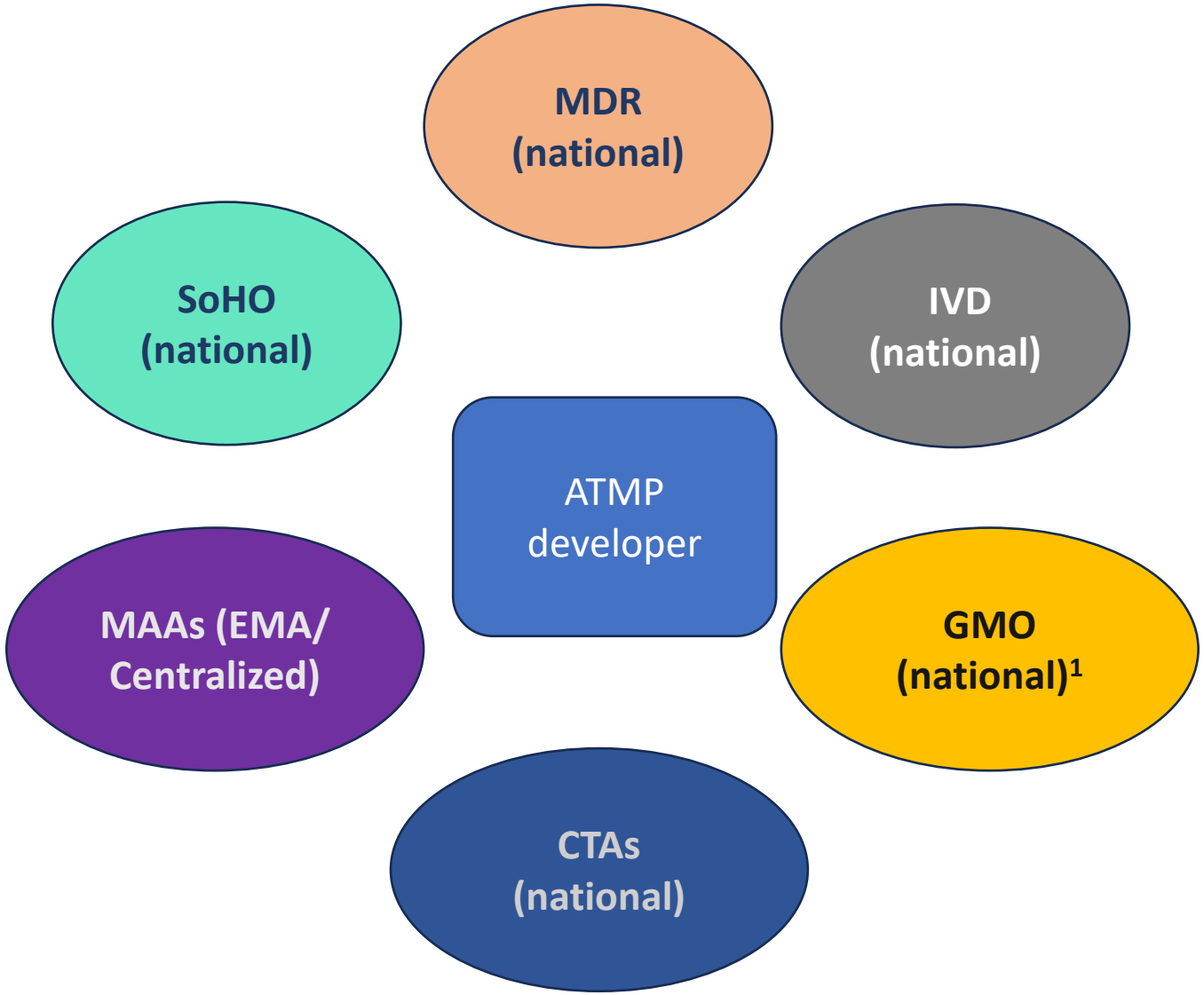
- **Clinical**
  - Pediatric development
  - Validated endpoints/biomarkers
  - Immunogenicity control
- **Non-clinical**
  - Animal species selection
  - Pharmacodynamic biomarkers
  - Dose translation animal to human
- **CMC**
  - **Analytical procedures:**
    - Complex testing requirements for drug products
    - Limitations to real time release and/or parametric release
    - Mostly non-compendial assays
    - Statistically complex and lacking EMA guidances on (statistical) expectations
  - **Raw materials:**
    - Consistent, harmonized classification of raw materials and standard/regulatory qualifications and/or use of master file mechanisms as applicable
    - Guidelines for establishing comparability between different raw material inputs
  - **Point of Care**
    - Clear definitions & more inclusion in updates to EU & EMA regulations & guidance(s)
  - **Manufacturing process**
    - Speed of development
  - **Platform Technologies**

Importance of the new structure for ATMPs & SA



- Given the complexity of ATMP development & the often shortened development timelines:
  - earlier meetings (pre-clinical and pre-CTA to pre-MAA) and continuity of contacts to ensure consistency and currency of SA
  - Ensure discussions/meetings available for complex development questions
  - within PRIME and also outside when justified
- Benefits:
  - creates clarity on drug development expectations in a dynamic environment
  - Regulatory processes and governance (and resources) of EMA and the Network need to support this, ultimately enabling an informed and streamlined assessment for ATMPs that progress to MAA

Complexity in the legislative framework of the EU



[1] Will transition to EMA/CHMP centralized

EU ATMP impact of changes to the legislative framework

Additional GPL proposals with important ATMP touch points

- Exclusivity changes: max. protection requires launch in all 27 MS within 2 years – practicalities for ATMPs
- Hospital Exemption: retain and clarify definition of “non-routine basis” to ensure harmonized interpretation across EU Member States
- Regulatory sandbox
- Use of a quality master file mechanisms in support of ATMPs (e.g. viral vectors, gene editing tools, cell culture media etc.), also allow for a platform master file
- GMO process simplification:
  - Explicitly confirm that no additional national requirements or submissions related to GMO will be required
  - As earlier requested (see also position paper) by ARM, EFPIA, EuropaBio, and Vaccines Europe, a science-based derogation of currently applicable GMO laws for a broad range of GMO investigational medicinal products (GMO-IMPs) that would be used in clinical trials.
- Adapted regulatory framework for “less complex ATMPs”
- Definitions for "complex" ATMPs?
- Growing availability and importance of RWD/RWE incl. registries and how use of alternative data sources

Recent industry association (EFPIA) publications and position papers :

- Clinical Trial Applications for Investigational Medicinal Products that Contain or Consist of Genetically Modified Organisms: Industry Experience under the European Union Clinical Trial Regulation (536/2014) EFPIA. *Cell & Gene Therapy Insights.* 30 April 2024; 10(6), 375–395.
- **Definition of a GTMP** position paper

HTA Regulation and EU Joint Clinical Assessment

- The EU Joint Clinical Assessment (JCA) has the potential to facilitate patient access to ATMPs but only if it takes into account their specificities
- The Methodological Guideline for Quantitative Evidence Synthesis: Direct and Indirect Comparisons puts huge emphasis on randomized clinical trials (RCTs) without considering that more than 50% of ongoing gene therapy pivotal clinical trials are single arm or non-randomised
- EU JCA reports that would deem non-RCT evidence not sufficient to prove added clinical benefit are likely to hamper access to ATMPs in the EU
- The EU HTA Coordination Group and JCA assessors must take a more flexible approach when RCTs are not feasible/ethical by accepting evidence from single arm trials and RWE to fill remaining uncertainty

Future proofing and additional flexibility

- ATMPs are still developing and evolving
- Fast scientific progress is leading to a rapidly evolving ATMP landscape with more diverse and complex technologies
- The GPL should be an adaptive framework that does facilitate access without reducing the appropriate regulatory EU level oversight and GxP guardrails

Global harmonization & convergence for ATMPs

- Harmonize testing requirements for starting materials
- Harmonize & recognize classification
- Facilitate reliance, recognition and collaboration across ATMP lifecycle
- Encourage harmonization of accreditation and standardization programs
- Waive in-country testing
- Use of “universal label” and electronic options
- Harmonize and streamline ATMP-GMO risk assessment
- Harmonize requirements for LTFU

Background slides

Proposed changes market exclusivity/data protection

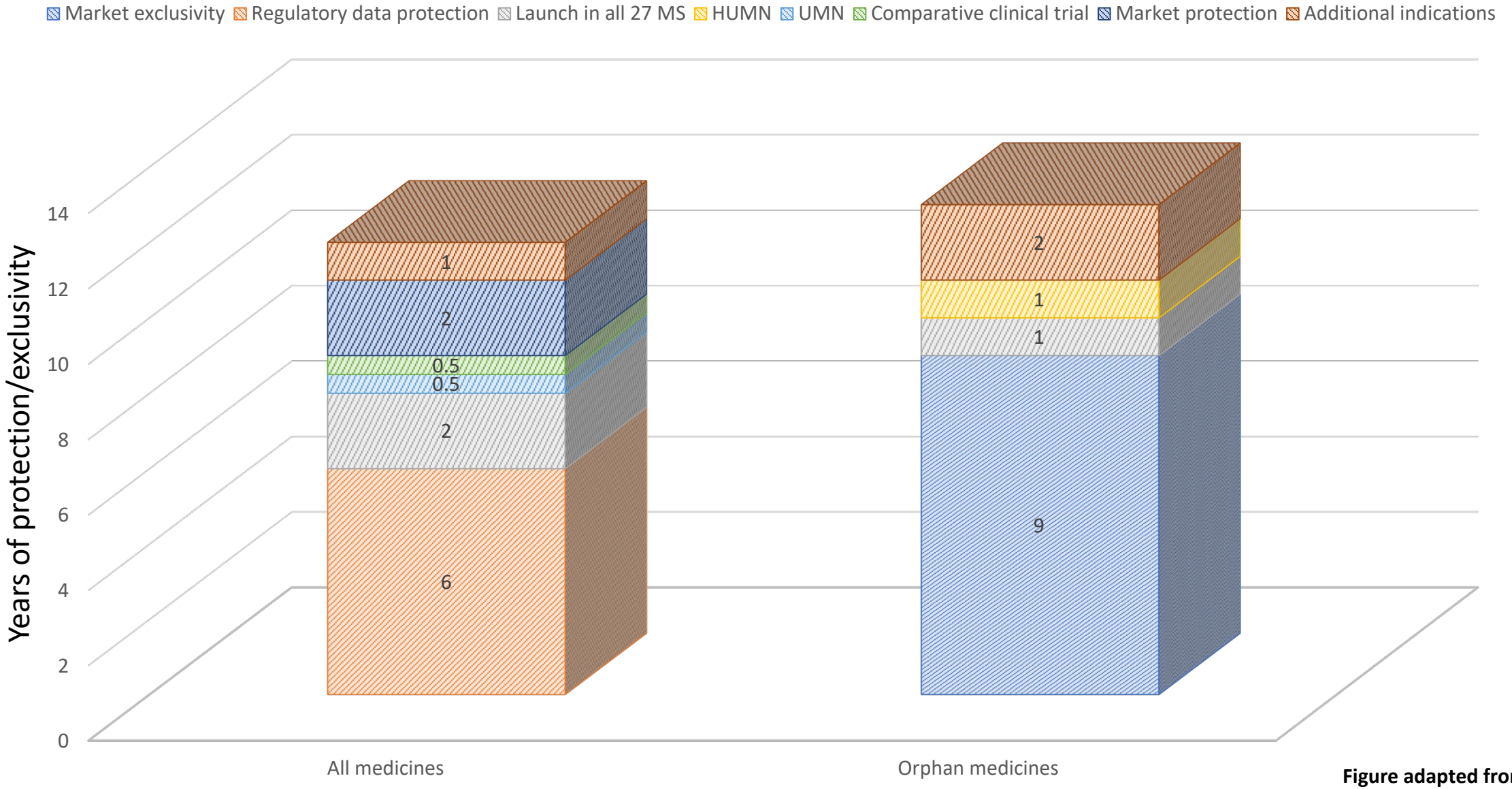


Figure adapted from: EMA webinar on revision of the pharmaceutical legislation

ATMPs for the next 15 years

Jacquelyn Awigena-Cook, BMS

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The Road Ahead for ATMPs in Europe

2024

Rapid pace of science and likely increase in product complexity in the future will require flexibility

- ATMPs targeting indications beyond haematology-oncology & rare diseases
- Increase in global access to ATMPs facilitated by regulatory convergence and harmonization efforts
- Sustainability of long-term follow-up where more ATMPs become available
- Timely implementation of improvements in EU General Pharma Legislation
  - ➢ Future proof definitions and regulatory mechanisms
  - ➢ Streamlining of structures and processes while retaining expertise
- Opportunity to increase innovation and R&D investment in EU

2024	Clinical Trials (Snapshot Value)
North America	974
Asia Pacific	784
Europe	341
Total	1,851*

Source: ARM August-2024-Sector-Snapshot

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