Gene Therapies

Navigating the Access Landscape with ATMPs

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Agenda

What are ATMPs and why are they important?

What are the challenges with valuing one-time ATMPs, such as gene therapies?

What should be priorities and next steps for patient access to ATMPs?

ATMP = advanced therapy medicinal product

Are payers, HTA bodies and healthcare systems ready for Advanced Therapy Medical Products?

And in particular for one-time therapies?

The healthcare industry is at an inflection point with the market now preparing for many cell and gene therapies to be approved over the coming years (hundreds in development)

Regulators have adapted to support timely access to ATMPs

Payers have a long way to go…

- To support timely patient access to these therapies, EMA regulators have established **specific approval pathways** and expert committees to ensure **appropriate assessment and expedited approval** of ATMPs
- The European Parliament formally introduced ATMPs as a class in 2007; the **European Medicines Agency's Committee for Advanced Therapies (CAT)** was subsequently established to accommodate the specific demands of this class of medicines
- However, most national payers and health technology assessment (HTA) bodies have not established specific mechanisms to adequately capture the full benefits of ATMPs.
- There are many systematic barriers that hinder ATMPs from reaching patients in need in a timely manner. In some cases, patients/families may resort to emotional crowdfunding campaigns rather than waiting for access to innovative ATMPs

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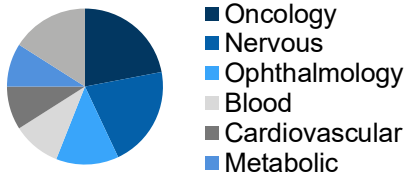
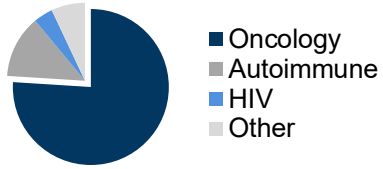
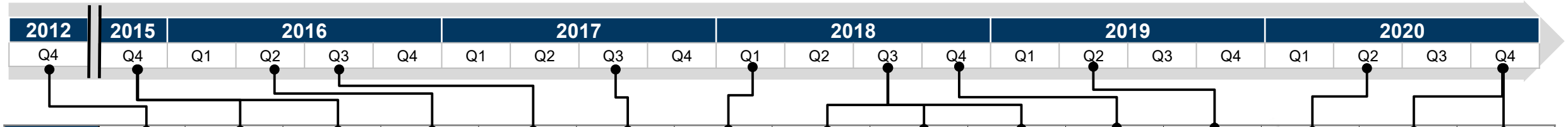
EMA is at the forefront of ATMP evaluation processes with well-defined regulations and classifications

EMA ATMP categories	Examples	EMA guidance classifications*	Therapeutic areas of pipeline products	Definitions
Gene therapies	Glybera, IMLYGIC, LUXTURNA, Strimvelis, zynteglo, onpattro	**64**	**To date, highly fragmented across multiple therapeutic areas** 	*Annex I to Directive 2001/83/EC* • Recombinant nucleic acid administered with a view to regulating, repairing, replacing, adding or deleting genetic sequence
Somatic cell therapies that contain cells or tissues	ZALMOXIS, ALOFISEL, KYMRIAH, YESCARTA	**70**	**To date, most experience in oncology** 	*Annex I to Directive 2001/83/EC* • Cells or tissues that have been subject to substantial manipulation with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action
Tissue-engineered medicines	HOLOCLAR, CHONDROCELECT™	**124**	*N/A*	*Article 2(1)(b) of Regulation (EC) 1394/2007* • Engineered cells or tissues administered to human beings with a view to regenerating, repairing or replacing a human tissue
Combined ATMPs	maci	**27**	*N/A*	*Article 2(1)(d) of Regulation (EC) 1394/2007* • One or more devices integrated with the medicine [cell/tissue with matric/scaffold]

While regulators are increasingly familiar with ATMP products, national payers have been slow to evolve

ATMP = advanced therapy medicinal product; *Number of EMA applications for guidance on classification of ATMPs. Representative of the number of products in development within each classification; Sources: EMA, FDA, IMS report

EMA-approved cell and gene therapies



ATMP	Glybera	HOLOCLAR	IMLYGIC	Strimvelis	ZALMOXIS	Spherox	ALOFISEL	KYMRIAH	YESCARTA	onpattro	LUXTURNA	zynteglo	zolgensma	TECARTUS	Libmeldy
MAA Holder	uniQure	Chiesi	AMGEN	Orchard therapeutics	MOLMED	CODON	Takeda	NOVARTIS	Kite	Alnylam	Spark	bluebirdbio	NOVARTIS	Kite	Orchard therapeutics
Therapy type	Gene therapy	Engineered tissue/stem cell	Gene therapy	Gene therapy	Stem cell therapy	Engineered Tissue	Stem cell therapy	CAR-T	CAR-T	Gene therapy	Gene therapy	Gene therapy	Gene therapy	CAR T	Gene therapy
Indication	Lipoprotein lipase deficiency	Limbal stem cell deficiency	Melanoma	ADA-SCID	HSC transplantation	Articular cartilage defect	Perianal fistulas in Crohn's disease	pALL DLBCL	DLBCL PMBCL	Transthyretin-mediated amyloidosis	Mutation-associated retinal dystrophy	Transfusion-dependent beta-thalassemia	Spinal Muscular Atrophy	Mantle cell lymphoma	Meta-chromatic leuko-dystrophy
Disease type	Genetic	Ophthalmology	Oncology	Immune/ Genetic	Oncology	Rheumatic/ Injury	Immune	Oncology	Oncology	Genetic	Genetic/ Ophthalmology	Blood/ Genetic	Genetic	Oncology	Genetic
EMA orphan designation	✓ (!)	✓	X	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	✓

Withdrawn

Key takeaways

- ATMPs experience **unique and unprecedented challenges** around manufacturing, payment models, real-world evidence generation, and value vs. economic impact assessments leading to **complex product launches** and **unpredictable market uptake**
- **Key learnings** can be extracted from both **successful** and **less successful** ATMP launches to better prepare the market for new products in the future

ATMP = advanced therapy medicinal product

Valuing and paying for one-time treatments with conventional assessment and financial frameworks poses significant challenges due to inherent differences between treatment types

	Conventional Therapies	One-time Therapies
Admin	Repeated, often **chronic administration** for months or years	One-time administration designed to **address the underlying root cause of disease**
MOA	Treatment focused on **improving symptoms** of a disease	Potential to **halt disease progression** for the underlying condition
Duration	**Treatment must be continued** for sustained effect	**Sustained effect** with major health gains long after administration; **potential for lifelong benefit**
Access	**Well-established path** to access & reimbursement	**Customized path** to access & reimbursement required that **addresses budget impact of high upfront cost** and potential **long-term outcome uncertainties**

Both conventional and one-time **therapies should be assessed with a consistent and holistic definition of value** encompassing **inherent treatment value, value to patients, the healthcare system, and society**

Payers have a short-term focus and lack the necessary tools to properly evaluate one-time therapies with life-long impact

One-time treatment

Upfront cost

Long-term benefit

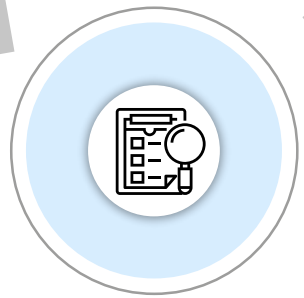
- National payers **struggle to assess** the total value given the long time horizons
  - Key payer concerns include assessing impacts on **mortality and morbidity**, **durability of treatment effect**, **inability to stop treatment**, and **appropriate cost offset frameworks**
- In cost-effectiveness markets (e.g., England) **payers question the QALYs produced by models**
- Upfront costs > $1M/patient can pose **significant budget impact problems**
  - Annuity-based models address this issue, but often payers cannot manage the administration or are limited by legal/cash flow constraints
- HTA bodies often demand **comparative evidence versus standard of care**
  - Many ATMPs **will not have developed the evidence traditionally required** by payers due to the nature of these technologies addressing orphan diseases
  - **Innovative HTA modelling using small data-sets** is unfamiliar to some payers

There are several key steps to the Market Access process before a therapy is reimbursed and accessible to patients

Pre-launch | Post-CHMP/MA | 4 – 6 Months | 6 – 9 Months | 12 – 24 Months

HTA dossier prepared by the Marketing Authorisation Holder

HTA dossier submission; Payer completes clinical/benefit assessment



Coverage decision based on clinical benefit

Price negotiations between payer and Marketing Authorisation Holder

Reimbursement achieved

During these stages, the Marketing Authorisation Holder leverages important EMA documents including EPAR and SmPC

Alliance for Regenerative Medicine's ideas and recommendations to improve future access to ATMPs across Europe

ARM's recommendations can enable broader access to patients and rapid uptake of ATMPs in the future

A quick adoption of new payment models such as conditional reimbursement, pay-for-performance, and annuity-based payments

ATMP-dedicated funds allowing health systems to invest in ATMPs that offer the potential for long-term benefits

Improved health technology assessment (HTA) methods, using real-world evidence (RWE). Develop the **infrastructure required to collect and use high-quality RWE**

Create more opportunities for early dialogue between ATMP developers and payers, supported by increased EU funding

Development of pan-European initiatives to ensure timely and effective access to **cross-border healthcare** for patients

We are seeking pathways to develop an actionable plan to collaborate with EMA and national payers. Working together, we can transform the ATMP landscape

Source: 2019 - Alliance for Regenerative Medicine (ARM):- Getting Ready: Recommendations for Timely Access to ATMP's in Europe (www.alliancerm.org)

In conclusion

Collaborate with EMA and national payers wherever possible to improve access to ATMPs moving forward

Facilitate dialogue between the stakeholders: pharmaceutical companies, national payers and regulators

A simultaneous **Clinical and Economic Assessment** process may be helpful to expedite access