The potential of advanced therapy medicinal products in Europe

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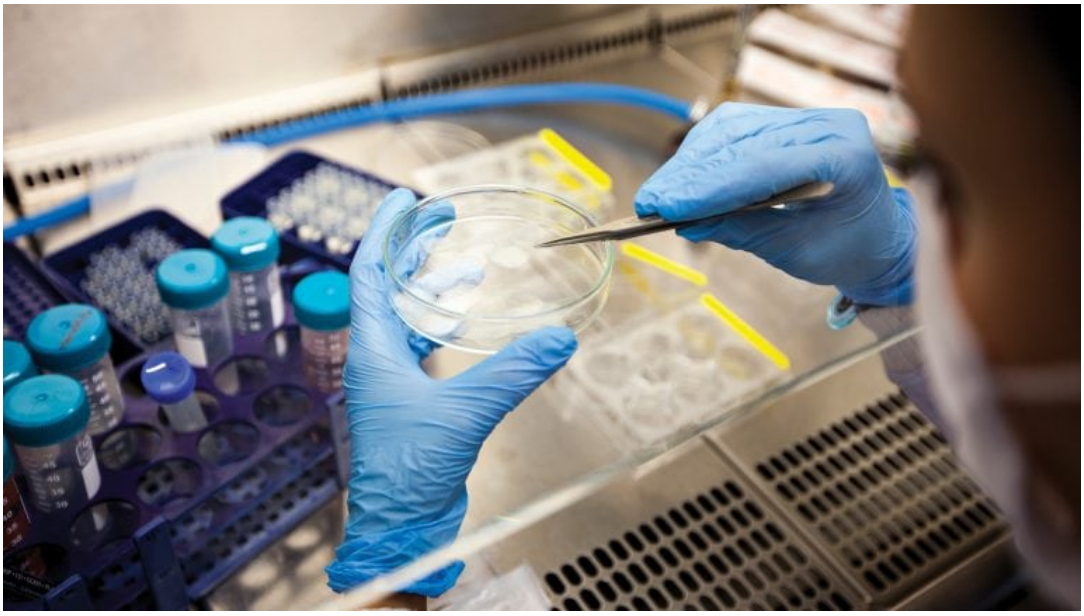

Together, the European Commission and the European Medicines Agency are working to bring game-changing advanced therapy medicinal products to the patients who need them.

So-called advanced therapy medicinal products (ATMPs) – the collective name given to gene therapies, somatic cell therapies and tissue-engineered products – are poised to transform the way we treat injuries and diseases today; in particular, they offer potential cures for severe, chronic diseases that currently don't have them or are too difficult or expensive to treat long-term.

Which ATMPs are approved in Europe?

Despite this promise, reimbursement challenges, stringent regulatory requirements and other obstacles are preventing ATMPs from reaching the patients who need them. So far, only ten advanced therapy medicinal products have received marketing authorisation in Europe since the entry into force of the EU's ATMP regulation. Of those, just six remain on the market:

- Alofisel is a somatic cell therapy product and was approved by the European Commission in 2018 to treat complex perianal fistulas in adults with Crohn's disease, when a conventional or biological medicine has not worked sufficiently;
- The tissue-engineered product Spherox was approved in 2017 for the treatment of cartilage defects in the knee of adults who are experiencing symptoms such as pain or movement problems;
- Zalmoxis is a somatic cell therapy product and was approved in 2016 as an adjunctive therapy in adults who have received a haematopoietic stem cell transplant from a partially matched donor due to a serious blood cancer such as leukaemia;
- A gene therapy product, Strimvelis was approved in 2016 for the treatment of severe combined immunodeficiency due to the rare inherited condition adenosine deaminase deficiency (ADA-SCID);
- Imlygic, also a gene therapy product, was approved in 2015 as a cancer medicine for adults with melanoma that cannot be surgically removed and that has spread to other parts of the body; and
- Holoclar is a tissue-engineered product that was approved in 2015 and is used in the eyes of adult patients to replace cells damaged on the surface of the cornea due to burns.

What role does the EU play in ATMP development?

To boost this number, in October, the European Commission and European Medicines Agency (EMA) launched a joint action plan designed to foster the development and authorisation of high-quality, safe and effective ATMPs – for the benefit of not only patients but also EU innovation and competitiveness. The plan sets out 19 key actions aimed at improving the regulatory environment and arrived at through consultation with stakeholders at all stages of development.

As part of these actions, in November the European Commission published a series of new guidelines on Good Manufacturing Practices specific to ATMPs. The document sets out the obligations of the manufacturer and marketing authorisation holder or sponsor, and promotes a risk-based approach to development and testing. Its purpose is to ensure that ATMPs are consistently produced and controlled in compliance with high-quality standards.

Meanwhile, in line with action four of the plan, in February the EMA updated its procedural advice on the evaluation of ATMPs, which is intended to support medicines developers by

clarifying the regulatory process. According to the EMA, the revised guidance aims to reduce administrative burden and 'address specific needs of ATMP developers in the evaluation procedure for initial marketing authorisations'. It has also been designed to enhance collaboration between the three EMA bodies involved in assessing ATMPs, namely:

1. The Committee for Advanced Therapies, which is responsible for evaluating ATMPs on the basis of safety, quality and efficacy;
2. The Committee for Medicinal Products for Human Use (CHMP), which is responsible for human medicines; and
3. The Pharmacovigilance Risk Assessment Committee, which is responsible for assessing and monitoring the safety of human medicines.

Other measures laid out in the action plan include the revision of the EMA's guidelines on the safety and efficacy follow-up and risk management of ATMPs, which were recently released for public consultation, increased stakeholder assistance for SMEs and academia, and enhanced scientific support in the form of greater opportunities for early dialogue with expert teams.

Are there any new ATMPs on the horizon?

Elsewhere, the EMA is also encouraging the development of advanced therapy medicinal products through its dedicated Priority Medicines scheme (aka PRIME). The voluntary programme is aimed at medicines that target an unmet medical need and is intended to improve clinical trial design and accelerate the evaluation of medicines applications. This should have the overall effect of getting much-needed treatments to patients sooner.

In June, the EMA recommended marketing authorisation for two blood cancer ATMPs, Kymriah and Yescarta. They are the first two CAR T-cell therapies to have been given such a recommendation in the EU and are also the first medicines supported by PRIME to have received positive opinions from the CHMP. Both will need to be granted marketing authorisation from the European Commission before they can be made available to patients in the EU.

Nonetheless, their intermediate success is testament to both the benefits of PRIME and the wider work of the EMA in supporting ATMP development, while the launch of the joint action plan in October signals the European Commission's own firm commitment to the cell and gene therapy space. Combined, these efforts will hopefully result in more advanced therapy medicinal products reaching the market – and the patients who need them – in the not-too-distant future.

Phacilitate Leaders Europe

In September, stakeholders will gather in London, UK, for Phacilitate Leaders Europe, a two-day event dedicated to the development and commercialisation of advanced therapy medicinal products.

This year's event will focus in particular on three critical challenges:

1) Cost per patient: How can the cost of ATMPs be reduced from $500,000 (~€427,872) per patient to $30,000?

2) Payer acceptance: How will payers evaluate my product against the current standard of care? and

3) Lack of knowledge: How is the improved cost of goods, pricing models and open collaboration expected to impact the evolution of ATMPs' commercial success?

Addressing these questions will be speakers from the likes of the International Society for Cellular Therapy, EATRIS, and the UK's Cell and Gene Therapy Catapult. They will join representatives from AstraZeneca, Merck Ventures, MolMed and more in considering what's next for the evolution of ATMPs.

Phacilitate Leaders Europe is expected to feature dedicated sessions on the commercial success of advanced therapies, the key challenges in next-generation stem cells, and funding, patient access, and pricing and reimbursement issues.

Other sessions will reflect on the viability of ATMPs from an EU payer perspective, the best ways for the ATMP biotech industry to attract European, Asian and US investment, and how cell and gene therapies can achieve

> *commercial scale.*
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> *Taken as a whole, Phacilitate Leaders Europe is set to play a key role in ensuring that advanced therapy medicinal products and the industry continue to adapt, evolve and thrive long into the future.*
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> *To find out more about the conference, visit www.phacilitate-leaders-europe.com*

This article will appear in issue 6 of *Health Europa Quarterly*, which will be published in August.