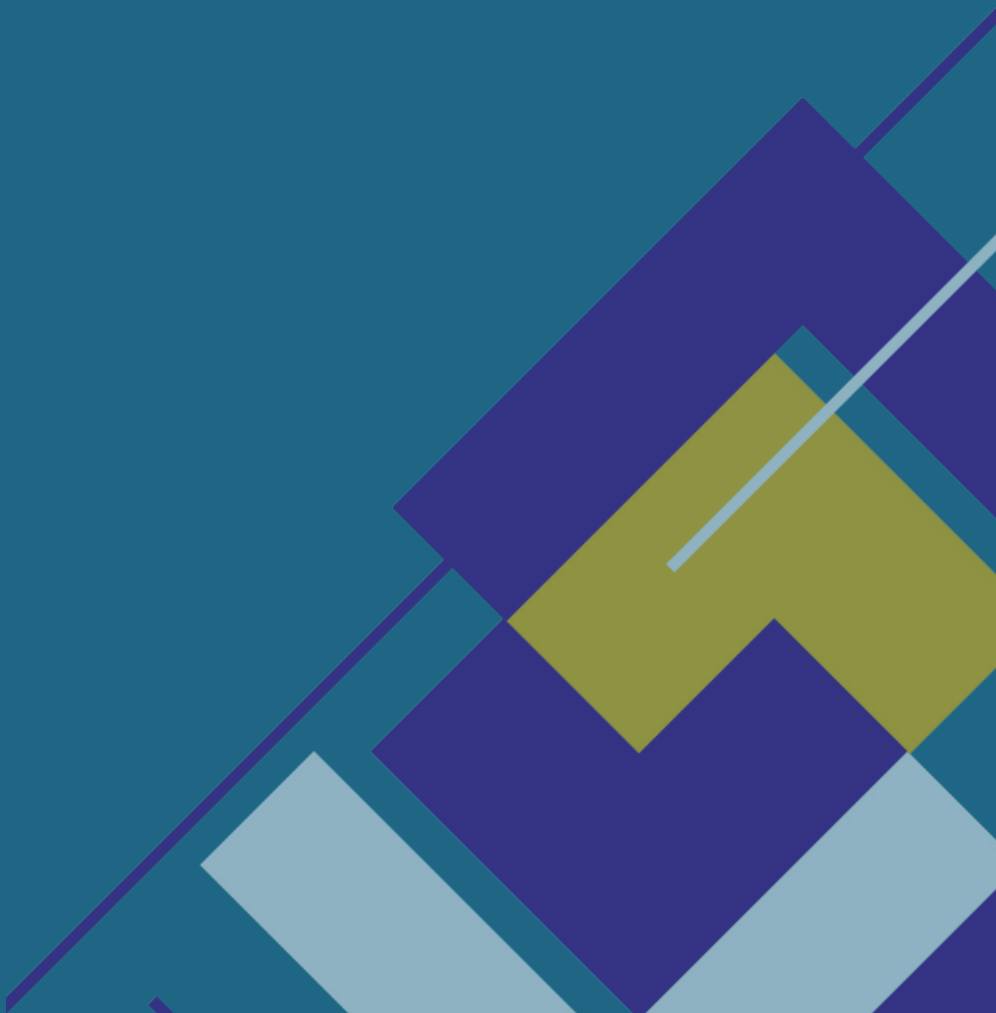
EuropaBio®
The European Association for Bioindustries

SME BioForum 2022

Advanced Therapy Medicinal Products



CONTENTS

Introduction

Advanced therapy medicinal products (ATMPs) are medicines for human use that are based on genes, tissues or cells. ATMPs can be used to cure, diagnose or prevent diseases. ATMPs are revolutionary therapies with unprecedented potential to address high unmet medical needs in rare (adult and paediatric) diseases, including genetic disorders, cancers or long-term illnesses. Increasingly in a single treatment, they can eliminate the need for unpleasant and long-term interventions that reduce the quality of life and the patient's active economic and societal role. ATMPs offer unique long-term benefits for patients and society. One of the main drivers for their discovery and manufacturing are small and medium-sized enterprises (SMEs).

Such therapies are opening a new frontier in medicine development, which translates into higher costs and risks than conventional and already established technologies. Among the most common challenges for SMEs working in the ATMP field is the lack of investment and how competitiveness can be unlocked. When we analyse the issue in further detail, we can easily conclude that it is not merely about financing but the investment environment as a whole. Public and private resources can be much more efficiently managed if Europe addresses entrepreneurship's main challenges to growth. SMEs face giant regulatory hurdles, a fragmented market and countless other challenges, including access to skills for each scientific and business stage.

On 31 May 2022, EuropaBio - the European Association for Bioindustries, held its SME BioForum, a new activity in 2022 within the framework of its SME Platform. This first session focused on ATMPs. The session connected SMEs from different European countries, market applications, technology platforms and stages of growth. The Forum addressed biotechnology commercial development challenges and how the European landscape impacts their ability to grow and deliver to market.

Foreword

Andrew Topen,
Novartis Chair of EuropaBio Board, 2020 - 2022

Welcome to EuropaBio's report from the first edition of the SME BioForum. This is a time of unprecedented change for Europe, and the significance of science in lives of citizens. The voices of SMEs, large companies, patients and national ecosystems must speak together and be heard for science for continue progress in addressing clinical needs and a healthy Europe.

The importance of the biotechnology industry has touched upon everybody's lives. Science can often be a difficult concept to communicate, however in the last two years, we have seen it on the front page of newspapers and at the top of the agenda for politicians and citizens.

The voice of SMEs is of particular significance. They represent the pipeline through which Europe's excellence in research is translated and matured, both for patient and economic benefit to Europe. It is critical that SMEs can mature innovations more quickly to patients and the market, so that Europe is globally competitive.

Europe, through the EU and Member States has the power to make this happen, through the regulatory and cross-border framework that brings speed, access and Europe's critical mass to new technologies. This unlocks investment at a scale that enables the competitiveness that SMEs need. The SME BioForum dedicated to ATMPs is an opportunity for EuropaBio to bring SME voices and recommendations to policy makers that will shape their environment for success. To the European Commission, to create strong frameworks for technology maturation, and to European governments to enable access and international alignment so that all patients can benefit from your innovation.

The SMEs represented through this report are a combination of direct EuropaBio Members and companies nominated through Member National Associations. We thank them for the insight into their pathway for medicines development and for the strong message that EuropaBio brings to the stakeholders who determine Europe's biotech landscape.

ATMPs are revolutionary, changing the paradigm of therapies and medical care, especially for rare and ultrarare diseases. From this revolution, we are witnessing ATMP evolution to address non-rare diseases and solid tumours.

SMEs are essential. They are the most stimulating environment for cell and gene therapy-based product creation, development, and transfer to large companies

This initiative, and future Forums currently being developed by the SME Platform, and taking advantage of the National Association involvement, will contribute to creating the much-needed network of professionals and experiences for the development of innovative life-changing therapies.

Maria Luisa Nolli
Chair of EuropaBio SME Platform, 2021 - 2023

Regulatory pathways

The ATMP development field is recent and fast-evolving. While technology progresses rapidly, national regulators must learn and adapt quickly to support the development and approval of new cell and gene therapies.

The European Medicines Agency (EMA) and the EU regulatory network have to deliver a streamlined, flexible and coherent regulatory system, with good coordination between the EMA and the Member States, optimising support for new advances in health innovation and accelerating patient access.

Challenges

One of the main challenges for SMEs in the ATMP field is their financial capacity. With significantly fewer resources when compared to larger companies, SMEs are particularly vulnerable to market access delays. For small companies, delayed decisions mean not being financially viable in the short term and, therefore, not able to reach the market and patients.

Member States have different interpretations of the Clinical Trials Authorization regulation, leading to diverse practices across Europe. As companies must provide unique data across multiple countries, the fragmentation of a single ecosystem for clinical trials creates delays, loss of competitiveness and hinder innovation.

ATMP clinical trial conditions differ significantly across Europe. Times for approval can range from a few months to over one year, depending on region and member state. SME success is heavily dependent on engaging with national regulatory authorities at an early stage, ideally before clinical trial application, to ensure faster approval.

Clinical trials for ATMPs, such as gene therapies, need to comply with EU GMO legislation, which was not designed for medicinal products. These therapies are required to undertake approval procedures by different GMO competent authorities in each Member State, leading to a fragmentation of regulatory practices and loss of competitiveness.

Recommendations

Reinforce EMA and national regulatory agency resources to allow for faster approval times

Considering the latest developments in the ATMP field and the European Medicines Agency mandate extension, the agency should be better equipped to integrate accelerated pathways for these therapies. Improved resources must be allocated at the national and European levels to support regulators and reduce approval times.

Promote EMA/Member States centres of excellence

EMA's contribution to the ATMP field has been significant - including establishing a Committee for Advanced Therapies (CAT), facilitating centralized procedures with a one-stop-shop for regulatory discussion with authorities, and through the PRIME scheme with fast-track procedures for ATMP development. To build on these efforts, EMA should take better advantage of national expert advice on topics where member state regulatory authorities are more experienced. SMEs recommend the creation of EMA/Member State "centres of excellence" for specific topics to ensure expert, accessible and consistent scientific advice.

Foster early engagement with national regulatory authorities

National regulatory authorities should engage in early dialogue with SMEs to support the development of ATMP clinical trials and provide flexibility in changes in good manufacturing practices when scaling up. This process flexibility allows for a more cost-efficient and sustainable process earlier in development.

Simplify GMO requirements for ATMP clinical trials

The European Commission should consider re-evaluating GMO requirements for ATMP Clinical Trials. These requirements must be simpler and less cumbersome, allowing for faster clinical trial approval and making European SMEs more globally competitive.

> *"Throughout the pandemic, we have seen COVID review timelines dramatically different from the past. In the UK, we submitted a clinical trial application on Thursday evening, and it was approved by Monday morning. If we could continue to move at that speed, we could create wonders. The regulators, including EMA, have been excellent and have shown what they can do."*
>
> **Mads Jellingsø,**
> Chief Commercial Officer, UNION Therapeutics A/S

Market fragmentation

Healthcare systems are very different across Europe. Member States have distinct regulatory practices and experiences that condition how each country and region perceives and assesses value. It is essential to ensure that decision-makers regard ATMP costs as investments in patients, sustainable healthcare systems and society.

For European SMEs' growth and survival, it is fundamental to achieve more regulatory harmonization across Europe to ensure that therapies find their market with appropriate pricing and reimbursement decisions and that medicines are available to patients.

Challenges

The European market is fragmented, with complex and lengthy regulatory approvals for clinical trials and biomanufacturing processes. It has different regulatory authorities and ethical committees. This fragmentation is hindering innovation, competitiveness and access to life-changing therapies.

Alongside significant regulatory hurdles, ATMP SME developers face lengthy reimbursement decisions. Considering SMEs' limited financial resources, market access delays often force these companies to leave the market, leaving patient needs unmet for reasons beyond science. There needs to be greater awareness of ATMPs' pathway and potential, not only for regulators but also for policymakers and broader society.

Reimbursement decisions across Europe are slow, and the reimbursement methodology is outdated. While companies and public authorities strive for new early access pathways (e.g., through PRIME) reimbursement processes use long-standing methods fixed on long-term outcomes. It is inefficient and not beneficial to patients to have fast-track to market and registration procedures if reimbursement is linked with long-term observation.

Recommendations

Harmonise national requirements for the development of ATMPs

SMEs need streamlined, flexible, and coherent regulatory practices and requirements to address the European market fragmentation. National requirements for clinical trials and patient registries should be harmonised to reduce the gap between Member State approval times and enhance equity of access.

Greater dialogue on the value and importance of ATMPs

Engaging in comprehensive and inclusive dialogue with policymakers is essential to clarify the value of these therapeutics and raise awareness of their importance for patients, having faster reimbursement decisions.

Adapt Health Technology assessments and consider innovative payment models

Assessment methodologies must be adapted. Developing and encouraging faster regulatory pathways is inefficiency if we do not accelerate health technology assessments and reimbursement decisions. Other actions should also be further explored, including grace periods to allow for long outcome data collection and innovative payment models to address high up-front costs.

> *"ATMP development in Europe is very challenging, especially for SMEs. ATMP developers face strong pushback from regulators and payers to obtain marketing authorization and reimbursement. One of the main issues is the fragmentation of regulatory bodies, which is contributing to a less attractive environment for clinical trials in Europe."*
>
> **Ahmed Bouzidi, Ph.D.**
> Managing Director Europe & VP International BD, Trinomab Biotech

Other bottlenecks for growth

ATMP development advances alone do not deliver products to patients. The development pathway requires diverse skills to enable SMEs to succeed in delivering treatment solutions.

European SMEs face personnel shortages at almost every step of the ATMP development chain, with Europe struggling to meet the demand for advancing skill sets through current education and training programmes. Higher education authorities, SMEs, and other educational institutions must come together to prepare the next generation of ATMP professionals and fill the skill gap.

One of the most significant bottlenecks for SME growth and technology maturation is access to professional skills. This experience gap can only be addressed in the short term by greater public and private collaboration with practices and information sharing.

Challenges

ATMP SMEs lack experienced professionals in key areas, such as biomanufacturing and scale-up processes. Demand for such skills is cross-sectoral, and SMEs within biotechnology are unable to compete with established large sectors in Europe or with their peers in markets beyond Europe. There is an urgent need for support in skills development and adapting curriculums in response to emerging technologies.

The ATMP sector is a recent and fast-evolving field, which means that most companies have limited experience. The pipeline to patients is long, and SMEs lack the resources to have such knowledge in-house. Europe urgently needs an accessible, expert ecosystem, allowing for better-informed decisions that deliver products to patients.

Recommendations

Promote ATMP academic and professional development

To address the skills gap with both current and future demands, SMEs need more significant support from governmental authorities and academic and professional institutions to prepare the next generation of ATMP professionals in the most critical and urgent domains, including manufacturing, regulatory, clinical practice and digitalisation.

Foster partnerships with larger companies and strategic sectors

Europe must strengthen its knowledge-sharing platforms and mechanisms, including public-private partnerships and SME/large company interaction facilitation. In addition, it is also essential to foster better cooperation with other innovative and strategic sectors, including digital technologies.

> *There is a growing demand for bio-processing skills in Europe, especially for cell and gene therapy professionals. Considering the scale of growth, it is anticipated that there will be not enough highly skilled individuals in the future to perceive the demand.*

Vivian Tseveleki,
PhD, Chief Operating Officer at Theracell

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The Life Science Cluster
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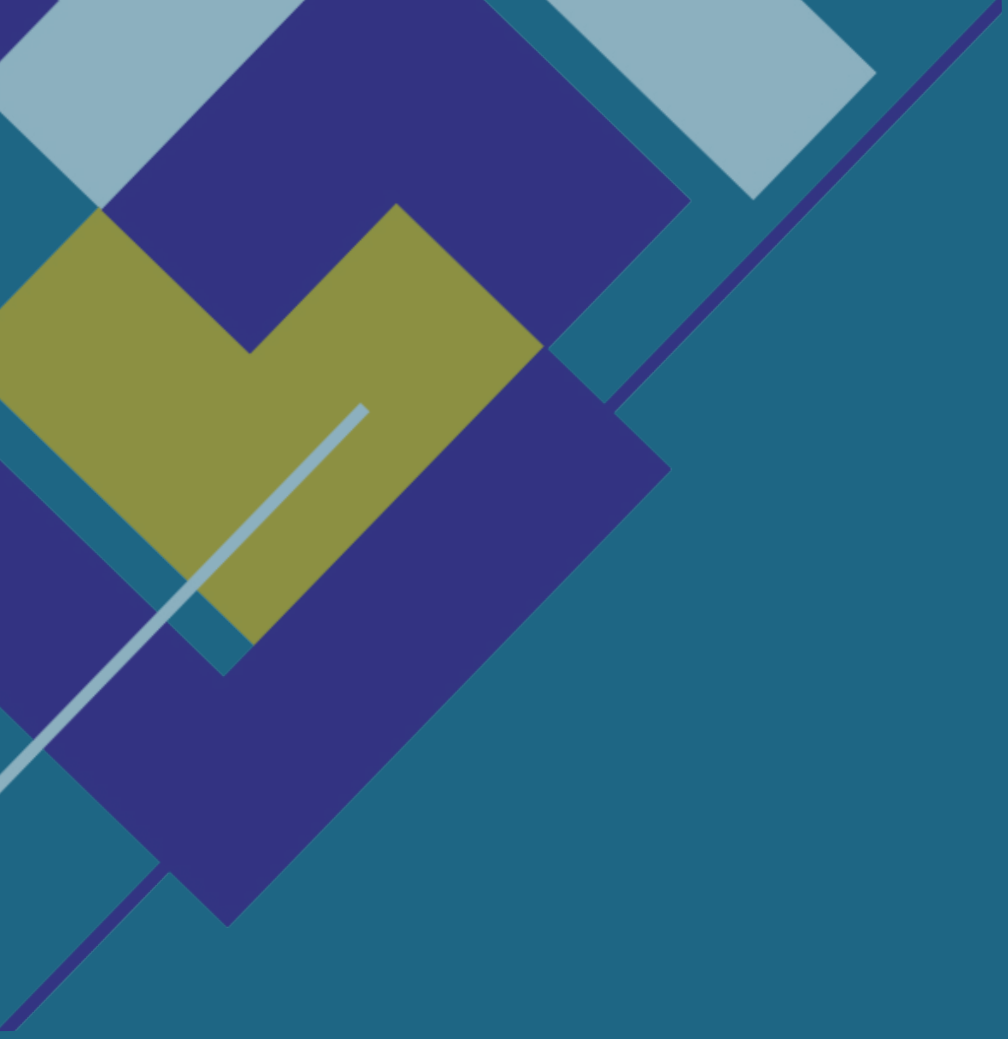
Notes



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