Advanced Therapy Medicinal Products in Wallonia

Executive summary of the ATMP-PIT proposal

BIOWIN
THE HEALTH CLUSTER OF WALLONIA

1. Introduction

The expertise and excellence of the Belgian biotech valley in research, development, industrialization, and commercial manufacturing of pharma products have been internationally recognized for 50 years. Consolidating this leading position in Europe requires **efforts**, **means**, and **strategic decisions**. As part of an initiative launched by the Walloon government in April 2023, BioWin - The Health Cluster of Wallonia and the SPW Economy, Employment, Research (SPW-EER) were invited to collaborate on the development of a large-scale project to **strengthen the value chain of the biotech sector in Wallonia** and stimulate regional economic redeployment. This project targeted **advanced therapy medicinal products** (ATMPs) as an innovative therapeutic area with high economic and societal potential for the region, following an exhaustive national mapping of the different players involved in this field and the building of an ambitious action plan conducted by BioWin in 2022 ("ATMP Hub" roadmap). The present summary is intended to provide an overview of the scientific and socio-economic background underlying the emergence of this 3-year project, hereafter referred to as the **ATMP-Partenariat d'Innovation Technologique (ATMP-PIT) proposal**. It will also describe the anticipated impacts of this initiative coordinated by the BioWin competitiveness cluster on the ATMP value chain in Wallonia by unifying the expertise of different industrial and academic players within a **portfolio of collaborative work packages** designed to leverage the entrepreneurial diversity and richness of this ecosystem.

"BioWin acts as a catalyst within the highly productive and diversified ATMP ecosystem present in Wallonia. Its role as a coordinator building bridges between actors at the regional level is instrumental in promoting the development of promising therapeutic candidates that would give rise to innovative treatments for patients in need."

Hara Episkopou, Head of Discovery, **Novadip**

2. The ATMP landscape in Wallonia

2.1. What are ATMPs?

ATMPs are **next generation therapies** developed to **address unmet medical needs**. They offer groundbreaking opportunities for treating symptoms and even curing diseases for which no effective treatments (or only lifelong treatments) exist, such as genetic diseases or life-threatening cancers. For the purpose of structuring the ATMP-PIT proposal, these next generation therapies have been classified into **three main categories**: gene therapy, cell therapy, and novel therapeutic approaches based either on cell derivatives (exosomes) or bacteriophages.

Gene therapy aims to treat or prevent specific conditions by **targeting the genetic cause of the disease**. It can restore the function of a defective gene by inserting a healthy copy of this gene into the body, modulate gene expression, or modify the genetic repertoire of target cells.

Cell therapy relies on transplantation of human cells that have been manipulated to modify their biological characteristics and achieve a therapeutic intent, with the objective of **regenerating**, **repairing or replacing damaged cells**, or **modulating**

immune system. Different cellular types can be used in cell therapy (adult and embryonic stem cells, immune cells, somatic cells).

Exosomes are small extracellular vesicles naturally produced by almost all cells, and present in most tissues and body fluids. They carry biological molecules (including proteins, lipids, nucleic acids…) and play a key role in intercellular communication. They are increasingly considered for a wide range of clinical applications (biomarkers, therapeutic solutions) in regenerative medicine and oncology, owing to the therapeutic properties of their natural or artificial cargo and their unique potential as cell-free drug or gene delivery systems. Although no exosome-based medicines have reached the market yet, these products spur massive interest and efforts from fundamental research, biomanufacturing processes, preclinical and clinical studies to unveil their true therapeutic potential.

Phage therapy uses viruses naturally infecting bacteria (but unable of attacking human cells) to treat bacterial infections. This approach is viewed as a promising and sustainable alternative to broad antibiotic use to combat infections involving bacteria with evolved resistance to bactericide molecules.

2.2. The economic potential of ATMPs: global market and patient demand

Although in its nascent stages, the global economic market of ATMPs is continuously growing at an expected compound annual growth rate of more than 36% between 2019 and 2025. This market could reach a global economic value of 10 billion euros in 2025 and 80 billion euros in 2032. Around 1500 pharma and biotech companies around the world are heavily investing in the development and manufacturing of ATMPs, which are considered lucrative opportunities to gain a competitive edge in future healthcare systems. Several products have already been approved by health authorities. With more than 2200 clinical trials ongoing, the annual number of new ATMPs entering the global market could reach up to 10–20 products as of 2025[1].

By providing novel therapeutic opportunities to address unmet medical requirements, ATMPs have the potential to profoundly reshape the landscape of disease treatments. Their application field is large, encompassing rare genetic illnesses, oncology, auto-immune diseases, neurological disorders, and many other clinical indications. Consequently, the patient demand for these medicines is high, especially in Europe, where the absolute unmet medical needs of an aging population increasingly affected by degenerative illnesses are growing[2]. In addition, the development and launch of ATMPs across European market could be facilitated by a robust regulatory framework, numerous funding incentives, and excellent healthcare systems providing patients with an equitable access to newly available medicines.

2.3. The value chain of ATMPs in Wallonia

Belgium, and more specifically Wallonia, has matured a specialized ATMP expertise over the last 20 years. The Walloon ATMP landscape includes 38 innovative companies (22% of the regional pool of pharma/biotech companies) operating along the value chain (15 companies in research and development, 8 in industrial production, 15 service companies). This intense industrial activity bolsters local economy and employment creation: more than 6000 jobs (2100 direct jobs) are related to the ATMP sector in Wallonia. The local ATMP industry is also supported by a network bringing the scientific and clinical expertise of academic research

[1] *Alliance for Regenerative Medicine, 2023*
[2] McKinsley & Company, 2021

centers and academic hospitals affiliated to the **5 main universities** from the Wallonia-Brussels Federation.

The Walloon industry displays a set of exceptional features resulting in a potential to develop a **rich ATMP ecosystem** and consolidate its **leading position** as one European hot spot for the development and manufacturing of these medicines. These noteworthy specificities include:

- **a regional clustering of life science players active all along the ATMP value chain**, from fundamental research to industrial manufacturing, patient access, and commercial capabilities. This dense network of academic and industrial stakeholders is unique in Europe
- **a wide range of developed skills extending to all categories of next generation therapies** (gene therapy, cell therapy, tissue-engineered products, exosomes, phage therapy)
- **a world-renowned footprint and expertise legacy** acquired through many innovations in the industrial manufacturing of vaccines and biomedicines. These innovations are strongly anchored within a **solid international ownership**.

On top of these intrinsic assets, the Walloon ATMP ecosystem benefits from various **funding opportunities** (public/private financial instruments) and **regional government actions** to support its development, notably through the "Industry of the Future" program and the BioMan initiative to accelerate the digital transformation of Walloon biomanufacturing companies. The remarkable potential of Belgium in the ATMP sector is also suggested by **favorable local factors** (central geographical location in Europe, strong logistical specialization in cold chain), and a **regulatory environment conducive to fast product launch** (the Federal Agency for Medicines and Health Products is the ATMP expert in Europe). The country is also a pioneer in the implementation of reimbursement policies for these medicines.

"Wallonia benefits from a high potential ATMP ecosystem thanks to its dense network of biotechnology players, headquarter of big pharma companies, international CDMO and other partners providing valuable tools and competencies required to be competitive in the field. This success can be explained by the availability of private and government grants/funding for R&D ATMP projects, and by the precious support that the BioWin competitiveness cluster provides to the regional consortium of partners for growth and financing, communication and talent development."

Laurent Levy, Co-founder & COO/CFO, **PDC*line**

3. The ATMP-PIT proposal: rationale and description of composition

3.1. The rationale for an ambitious sectoral project in the Walloon ATMP panorama

Despite an exceptional combination of assets and factors able to foster therapeutical innovations in Wallonia, several **challenges** and **hurdles** persist along the ATMP value chain. In the research and development phase, most challenges are encountered while gaining access to the **appropriate funding**, **material**, **and human resources** needed to translate pre-clinical and clinical research into market leadership. The number of ATMPs reaching the clinical development phase is expected to increase in the future, but here challenges exist regarding the **complexity of manufacturing processes**, their **compliance** with international guidelines and product quality standards, the **complexity of clinical trial designs** (e.g., autologous treatments) and the **difficulties in enrolling patients** for performing these trials. In the access and commercial phase, challenges mainly arise from **inconsistent policies** and **specificities** among

[1] *Alliance for Regenerative Medicine, 2023*
[2] McKinsley & Company, 2021

countries, high production costs, reimbursement uncertainty associated with rare indications and orphan designation, and the need for adequately addressing information requests from regulatory authorities. Finally, in the marketing and market growth phase, there are challenges in the production and supply chain, as medicines derived from human cells and tissues must comply with compulsory requirements for marketing authorization within the European Union.

Given these challenges, the favorable ATMP ecosystem present in Wallonia needs to be supported by appropriate resources and strategic decisions to fulfill its outstanding potential. Following heavy governmental investments, several ATMP initiatives have been deployed in other European countries (e.g. United Kingdom, Sweden) to accelerate new ATMP assets. In such competing settings, Belgium and Wallonia have no choice but building upon their strongest fundamentals, optimally leveraging their strengths, and capitalizing on open innovation between all players embedded in the ATMP ecosystem, a strategy that has been key in making Belgium an attractive and innovative pharma valley over the last 50 years.

To address these challenges, the ATMP-PIT proposal has been designed with the intention of federating the consortium of stakeholders active along the whole ATMP value chain within an innovative portfolio of collaborative work packages. The end goal for society is to make the most promising medicines and treatments widely available and affordable to patients in need as soon as possible. This can be achieved by incorporating key strategic decisions driving the future of the ATMP ecosystem in Wallonia. The main objective of this strategy is to consolidate the whole value chain through collaborative innovation between the players of this diversified ATMP ecosystem (biotech companies, universities, research institutes, hospitals, contract development and manufacturing organizations, service companies) bringing regional means, skills, talents, and infrastructures to the joint endeavor.

"Rooted in Wallonia, our dynamic ATMP ecosystem is a beacon of innovation and collaboration. With steadfast support from BioWin, we lead the way in pioneering breakthroughs, turning visionary ideas into advanced therapies that reshape the landscape of healthcare for the future."

José Castillo, co-founder, Quantoom CEO and Univercells

3.2. Description of the ATMP-PIT composition and portfolio of work packages

The BioWin competitiveness cluster initially contacted members of the Walloon ATMP ecosystem in the most exhaustive possible way to constitute a consortium of various stakeholders central to the ATMP-PIT proposal. This project will finally involve a close collaboration and connectivity (expertise, infrastructures, funding) within a partnership of 26 players (21 companies, 1 accredited research center, and several research units and hospitals affiliated to 4 universities from the Wallonia-Brussels Federation). The different academic and industrial entities of this impressive coalition have come to a common agreement for proactively collaborating on the development of next generation therapy medicines, manufacturing processes, associated services, and stimulation of regional employment market.

"At Quality Assistance, we recognize Belgium's vibrant ATMP ecosystem, driven by innovative academic and biotech R&D collaborations. In Wallonia, BioWin's role is pivotal in enhancing ATMP research and commercialization through strategic support, funding facilitation, and fostering key partnerships in health sector."

Arnaud Delobel, Quality Assistance

The ATMP-PIT portfolio is built on 12 work packages (collectively evaluated by BioWin and the SPW-EER) subdivided into 3 pillars, each dedicated to one category of next generation therapy (gene therapy, cell therapy, novel therapeutic approaches based either on exosomes or bacteriophages).

Within the Walloon ATMP ecosystem, several companies are investing in the development of new gene therapy medicines or providing services to this industry (production, process innovation, product characterization). These companies will be involved in several work packages of the ATMP-PIT portfolio distributed along the value chain. These work packages will notably focus on the development of novel therapies, the elaboration of analytical and characterization methods, or the implementation of digital transformation and artificial intelligence to accelerate the decentralization of ATMP production and innovate in process design and optimization.

Similarly, the field of cell therapy is another flagship of Walloon ATMP industry. The activities of companies include the development of new cell therapies and service supply (production, digital expertise and production equipment, product characterization and quality control).

Wallonia concentrates a surprisingly dense and active network of companies involved in the research and development of exosome-based medicines. A specific work package focused on exosomes will pool the expertise of 7 companies, either developing their own therapeutic products or bringing specialized skills in exosome cargo loading, development of in vitro and ex vivo models, functional characterization, analytical methods, and quality control of exosome-based products via microfluidic technology.

First geographically restricted to Eastern Europe, research and development programs in phage therapy are now expanding to other regions of the world, as they hold promise to overcome the global health issue of an emerging microbial resistance to antibiotics. The regulatory environment in Wallonia is favorable to research activities on bacteriophages and their use in clinical practice, which will be developed in a specific work package of the ATMP-PIT proposal.

"BioWin's support was pivotal in the creation of this unique consortium bringing together the main Walloon players in the field of exosome production, loading and therapeutic use; and promoting a collaborative approach pooling technological resources with a view to accelerating clinical development."

Hugues Wallemacq, CEO, EXO Biologics

4. Expected outcomes and associated risks of the ATMP-PIT proposal

The ATMP industry is a promising sector with the potential of generating **significant economic and societal impacts** in the future. Therefore, it is forecasted that the ATMP-PIT initiative will yield **major beneficial outcomes** throughout the whole ATMP value chain.

From an economic viewpoint, the ATMP-PIT proposal is expected to enable Belgium and Wallonia to keep their position as both a **market leader** and a **center of excellence** within the European landscape in terms of research, clinical development, and industrial manufacturing of ATMPs. This should translate into an increase in added value for companies, export growth, and new opportunities for job creation (including positions requiring various levels of qualification: maintenance and production staff, logisticians, engineers, PhDs). Assuming that the ATMP-PIT proposal will help maintaining employment growth rate at levels observed over the last 17 years (4.5% per year), this project could contribute to the creation of **more than 1800 additional jobs** in the upcoming 5 years, 600 of which being directly related to the ATMP sector. Another major economic outcome of this project is to **promote talent attraction and formation** at the regional level, which will also need to be supported by concrete and proactive governmental actions.

From a societal viewpoint, the groundbreaking therapeutic and curative solutions provided by ATMPs could **transform modern medicine** and benefit patients suffering from diseases for which major progress or prospect for cure are currently limited by ineffective treatments. By directly and precisely targeting the underlying cause of the disease, ATMP-based treatments should meet high clinical standards in terms of **effectiveness**, **improvement of patient's quality of life**, and **safety** (mitigation of undesirable side effects). As potentially life-saving treatments, they should offer **new hope perspectives** for patients affected by so far untreatable pathologies and for whom no other alternative interventions or only therapeutic solutions with limited effectiveness are currently available. Furthermore, ATMPs are highly sophisticated and tunable medicines: they can be finely designed to adapt to the unique set of biological and genetic characteristics of each patient, thereby opening new avenues for the development of **more personalized**, **patient-tailored medicines** to maximize clinical effectiveness. Finally, despite their high initial production costs, ATMPs can generate **important economic savings for society over the long term** by reducing the healthcare expenditures related to the clinical management of chronic diseases and their associated complications.

The ATMP-PIT initiative should also result in **positive environmental outcomes** by comparison with other pharma and biotech manufacturing processes. The ATMP production system can be perfectly integrated within an environmental, social and governance framework. Since ATMPs are medicines from biological origin, their industrial production is less dependent on chemical processes involving harmful substances, which should subsequently contribute to **simplifying waste management** and **reducing environmental footprint**. In this regard, ATMPs should constitute relevant alternatives to chemotherapeutic treatments, which rely on extremely active and noxious molecules associated with a high risk for aquatic ecosystems, even at low dose of environmental contamination. Another convincing example entails phage therapy as an alternative to antibiotics, whose excessive and inappropriate use has resulted in the evolution of massive bacterial resistance now recognized as a serious public health concern.

Finally, it is important noting that the ATMP-PIT proposal is not a risk-free investment, but risk mitigation efforts can be shared between participating stakeholders, many having a strong and well-established experience in the development and manufacturing of ATMP products.

"Driven by the ambition to improve patient lives, UCB applauds the strategic foresight and dedication to the biopharma and life sciences exhibited at both the Belgium federal and Walloon regional levels. With the support of BioWin, the Walloon Region is actively strengthening and promoting the local ATMP ecosystem through relevant and focused incentives impacting different stakeholders across the value chain and driving transversal collaboration."

Jiri Keirsse, Head of Innovation Strategy and Public Private Partnerships, **UCB**

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About BioWin

BioWin is the health cluster in Wallonia, Belgium, the regional reference for all stakeholders in health, biotech and medtech research, and innovation projects. It includes 250 members from the private, public, and academic sectors.

BioWin's mission is to accelerate innovation to meet tomorrow's public health challenges and develop the knowledge, employment, and competitiveness of all players in the health sector ecosystem. By bringing together all the innovation players in Wallonia's life sciences field, BioWin aims to stimulate regional economic redeployment. The cluster is also involved in implementing the sector's industrial policy (industrial innovation and research, training, support for business growth), to develop and anchor skills, knowledge, and jobs.