WHITEPAPER

Decentralized Manufacturing: Improving Access to Cell and Gene Therapies and Removing Barriers to Global Markets

By Erika Francoeur B.Sc., Domhnall McGowan M.Sc. and Enayat Mohammad Gul B.SC., PMP

Abstract

Over the past decade, Advanced Therapeutic Medicinal Products (ATMPs), including Cell and Gene Therapies (CGTs), have revolutionized treatment options, particularly for patients with blood cancers. Despite their therapeutic success and substantial market growth, the current Centralized Manufacturing Model (CMM) poses accessibility challenges, especially for non-urban patients. Many patients face long waits or extensive travel for treatment, with some not surviving long enough to receive treatment because of manufacturing shortages. The Decentralized Manufacturing Model (DMM) is a promising alternative to expanding manufacturing capabilities, offering more localized production and reducing travel requirements for patients. Early implementations, like Point of Care (PoC) manufacturing in select institutions, demonstrate the viability of this approach.

Introduction

The field of Cell and Gene Therapies (CGTs), also known as Advanced Therapeutic Medicinal Products (ATMPs), has seen significant growth. The first autologous CGT was approved in 2017 for

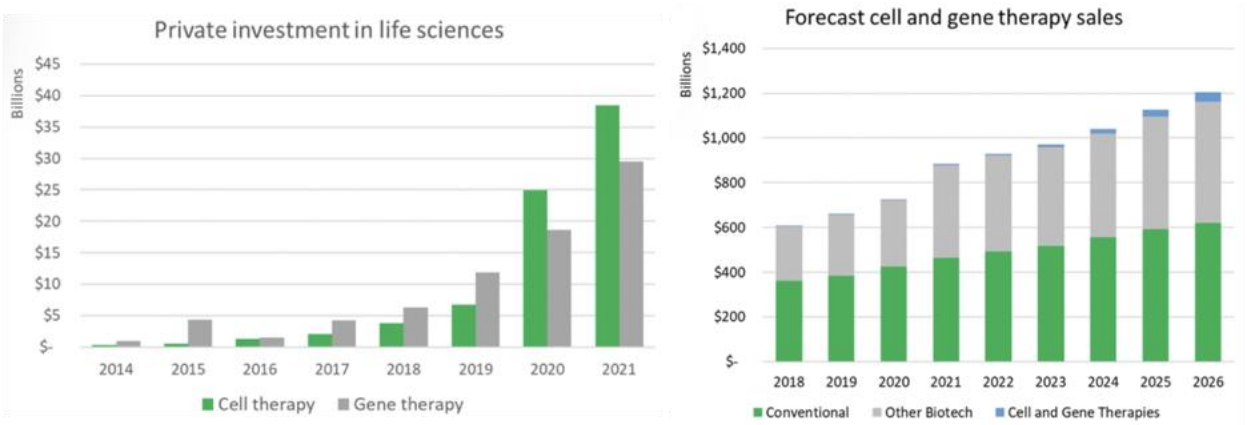

Figure 1. ATMPs are growing in market presence and gaining interest from private investors. ATMPs account for about a third of all private investment in the life sciences. Source: CipherBio

the treatment of blood cancers, and subsequent ATMPs, such as CAR-T, have emerged as transformative treatment options for patients previously reliant on chemotherapy or those without alternative treatment options [2]. Owing to their therapeutic efficacy and market success, ATMPs now constitute nearly one third of private investments in life sciences, as depicted in Figure 1 [1]. As of 2022, CGTs comprise 7% of the 340 FDA-approved biologics, and projections indicate that the global ATMP market could surpass $9B by 2027 [6].

Despite the increasing demand and effectiveness of ATMPs, the prevailing Centralized Manufacturing Model (CMM) for producing autologous therapies has inadvertently introduced accessibility issues for many deserving patients [2]. Studies reveal that one in five eligible cancer

patients do not survive long enough to receive a manufacturing slot for their autologous cells [3]. Most of the facilities essential for ATMP production are concentrated around major urban areas. This centralization makes it logistically challenging to treat patients outside these regions due to stringent timelines, transportation costs, and specialized packaging requirements [2]. However, the Decentralized Manufacturing Model (DMM) offers a promising alternative to the CMM. By allowing for localized, miniaturized, and even mobile manufacturing setups, the DMM significantly reduces accessibility and cost barriers [2]. Evidence suggests that rural cancer patients often face more obstacles in accessing specialized care, resulting in potentially poorer outcomes compared to their urban counterpart [9]. Recognizing these challenges, 58% of large-scale companies (with valuations exceeding $5B) have already begun outsourcing ATMP production to broaden their reach, with outsourcing predicted to grow by 42% over the next five years [5].

Decentralized vs. Centralized Manufacturing Models

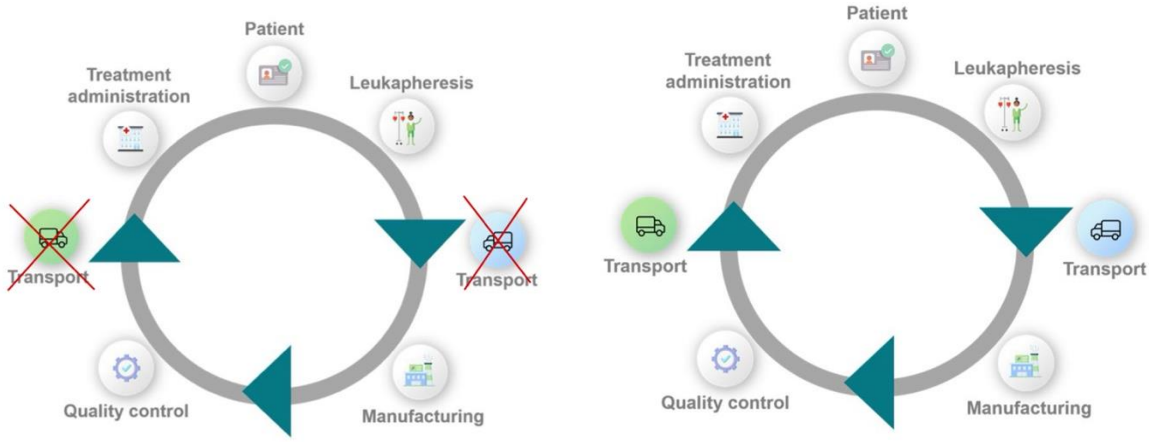

Figure 2: A Decentralized Manufacturing Model (left) eliminates complex transportation logistics associated with the Centralized Manufacturing Model (right) that may include cryogenic shipping and storage. Source: A digital platform for the design of patient.

The Centralized Manufacturing Model (CMM) is known for its reliability in producing autologous cell therapies. However, it often means that patients must travel to receive treatment. Even with support for logistics, there may be risks for both the patient and the product if there are delays or mistakes in handling. In contrast, the Decentralized Manufacturing Model (DMM) uses smaller facilities that can be adjusted for regional needs, eliminates transport logistics and risk of mishandling, and may eliminate need for cryogenic shipping and storage [2].

Case Study: Pioneers in Decentralized Manufacturing

Several hospitals and clinics in North America and Europe have started using Point of Care (PoC) manufacturing for autologous cell therapies as an early example of the DMM. With PoC, small labs

are set up close to where patients get treated, and they produce therapies like CAR-Ts for blood cancers. Institutions like the Medical College of Wisconsin and Hospital Clinic de Barcelona have finished Phase I clinical trials using PoC manufacturing for CAR-Ts, demonstrating that the DMM could be an alternative model supporting the distribution of ATMPs [7, 8]. While PoC does address the problem of waiting times in centralized manufacturing, it is not currently being implemented with the intentions to resolve the issue of reaching patients in rural areas who often face a more challenging experience of accessing specialized care.

The Future of ATMP Manufacturing

REALM Bio is actively working to establish a comprehensive DMM clinical platform. Our primary objective is to offer all-encompassing outreach and manufacturing services for companies currently in the clinical phase. This initiative aims to streamline the process, allowing for seamless patient registration and treatment, irrespective of their geographical location. In December 2021, while still operating as Boston Labs, researchers laid the groundwork for the future of REALM Bio with a successful proof-of-concept study in collaboration with Germfree Laboratories. This study showcased the practicality of the DMM platform within a mobile lab setting, adhering to GMP standards. With these advancements, the foundation is being laid for ATMPs to be readily available to patients everywhere, ensuring no one is left behind because of the region they live.

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