An overview of the clinical development landscape for advanced therapy medicinal products

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Key Findings

- Our study has identified a total of 749 technology included records containing 545 unique ATMPs
- Our analysis identified 909 ATMP clinical trials run by 365 unique developers.
- There is a total of 667 technology records with ATMPs identified as being currently in development.
- There is a high volume of early phase clinical trials development (phase 1/2 and phase 2).
- There are approximately 60% of ATMPs identified that are classified as gene therapies. These therapies have the potential to treat a wide range of diseases, including genetic disorders, cancer, and cardiovascular disease.
- There is a high level of ATMP development in haematological cancers and lymphomas.

Background

Advanced therapy medicinal products (ATMPs) are a group of innovative biological therapies that can be classified as gene therapies, somatic-cell therapies or tissue-engineered therapies [1, 2]. They have the potential to revolutionise patient care and offer novel approaches for the treatment of disease and injury. Many of these therapies can be curative with a one-off treatment by targeting the root cause of diseases [3]. ATMPs have shown promise in treating a wide range of diseases, including genetic disorders, certain types of cancer, autoimmune diseases, and degenerative conditions. These therapies hold the potential to provide long-term or even permanent relief for patients suffering from these conditions.

The potentially transformative nature of ATMP treatment unlocks the possibility of significant savings to the NHS and wider health systems, by reducing or removing the long-term burden of care for some patients [3]. However, they also present substantial regulatory, technical and logistical challenges, due to lengthy manufacturing processes, complex regulatory procedures and the difficulties of offering medical products with novel routes of administration [4]. As a result, the NIHR Innovation Observatory (IO) plays a crucial role in monitoring all ATMPs in clinical development that have the potential to come to market in the UK, in order to provide early awareness of these therapies before they come to market. Early awareness of these ATMPs is crucial for key stakeholders such as funders, healthcare professionals, policymakers, and the wider public. For funders, early awareness of ATMPs allows for better resource allocation and investment decisions. Healthcare professionals benefit from early awareness by staying updated on the latest advancements and potential treatment options for their patients. Policymakers can use this information to shape regulations and policies that facilitate the timely and safe introduction of ATMPs into healthcare systems. Lastly, the wider public can benefit from early awareness by having access to information about potential breakthrough treatments and being empowered to make informed decisions about their healthcare.

Aims

- Provide a comprehensive overview of the ATMP clinical development landscape
- Characterise the categories of ATMPs in clinical development
- Identify diseases and disease groups with high levels of ATMP clinical development

Methods

The IO maintains a comprehensive database of technology records (generally defined as medicinal product(s) and the indications for which they are being developed) containing ATMPs in clinical development that are currently or have previously been monitored. All ATMPs being studied in phase 2 or phase 3 clinical trials located in United Kingdom, United States, European Union, Australia, Canada, Japan and Singapore are eligible for inclusion in this database. Some ATMPs in phase 1 or phase 4 trials, or trials without applicable phases, are added on an ad-hoc

basis. An update of this database was conducted in June 2024 so that it reflects all ATMPs monitored by the IO as of the 17th of June 2024.

The research team manually updated the data utilising horizon scanning sources, including the IO's Medicines Innovation Database (MInD), trial registries (Clinicaltrials.gov[5] and the EU Clinical Trials Register[6]), developer websites and the European Medicines Agency [2]. An analysis of the updated database was undertaken in June 2024. Data was collected to identify distinct ATMPs under development, unique developers, assess their stage of development, regulatory designations, and assess areas with potential to address patient needs. In the case of technology records with multiple clinical trials, a main trial was identified based on the trial phase, size and its relevance to the record.

Results

We identified a total of 749 technology records containing at least one ATMP. In these records, we identified 585 unique ATMPs. Additionally, there were 365 unique developers considered to be leading development of an ATMP, and a total of 909 clinical trials.

As shown in figure 1, the ATMPs with the most records were talimogene laherparepvec (n=13), lisocabtagene maraleucel (n = 10), tisagenlecleucel-T (n = 8) and axicabtagene ciloleucel (n = 7) and HB-adMSCs (n = 7). The high number of records for talimogene laherparepvec and lisocabtagene maraleucel suggests that these ATMPs have garnered significant attention and interest in the research community. It may indicate that these therapies have shown promising results in clinical trials or have demonstrated potential for treating specific diseases. For example, talimogene laherparepvec, also known as T-VEC, is an oncolytic virus therapy that has shown efficacy in treating advanced melanoma[7]. Clinical trials have demonstrated that T-VEC can induce tumor regression and improve overall survival in patients with this aggressive form of skin cancer [8]. Similarly, lisocabtagene maraleucel, a chimeric antigen receptor (CAR) T-cell therapy, has shown remarkable success in treating relapsed or refractory large B-cell lymphoma, with high response rates and durable remissions observed in clinical studies[9]. These findings further support the potential of these ATMPs as promising therapies in the field of precision medicine.

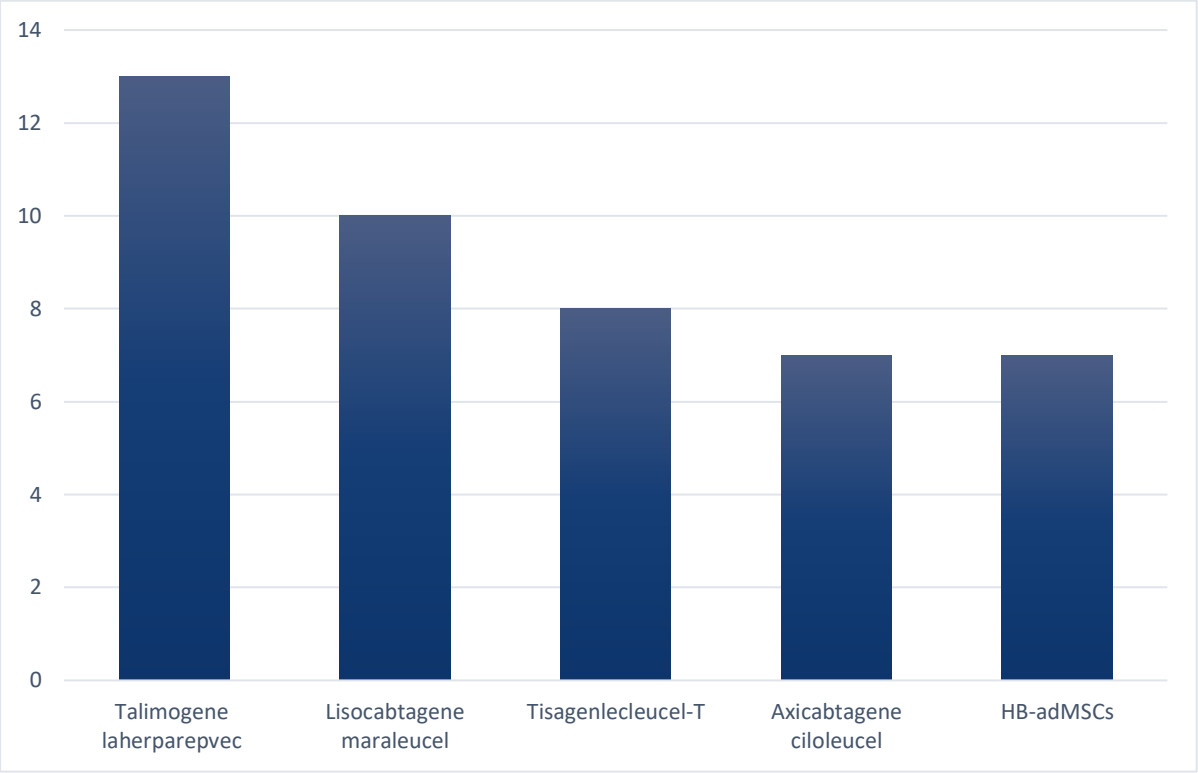

Figure 1: Number of records for the top five most commonly occurring ATMPs

Among the most active ATMP developers, Celgene Ltd (USA) had the highest number of records at 17, Mesoblast Ltd (Australia) had the second highest number at 15, followed by Amgen Ltd (UK & IE) and Iovance Biotherapeutics Inc (USA) with each having 13 records, Kite Pharma (USA) had 12 records (Figure 2). The varying number of records among the developers could be attributed to factors such as the size and resources of each company, the number of clinical trials they have conducted, and their focus on specific therapeutic areas. It is also possible that some developers have been more proactive in reporting their data or have a higher success rate in progressing their ATMPs through the development pipeline.

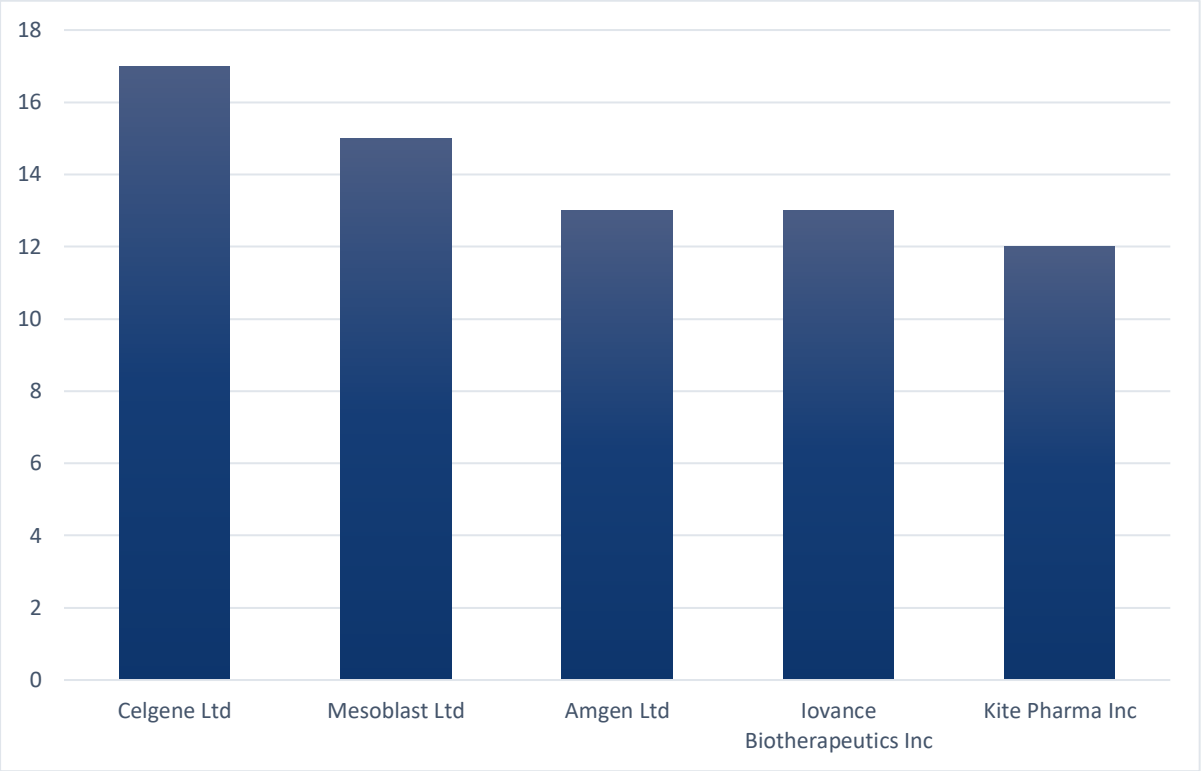

Figure 2: Number of ATMP records by top five most active developers

Figure 3 illustrates the most frequently reported therapeutic areas, which are haematological cancers and lymphomas (n = 178), musculoskeletal (n = 78), endocrine, nutritional, and metabolic disorders (n = 64), cardiovascular (n = 58), and neurology (n = 51). These findings are consistent with previous studies that highlighted that haematological cancers and lymphomas are among the most prevalent types of cancer worldwide, accounting for a significant portion of cancer diagnoses [10, 11]. According to the World Health Organization, approximately 9.7% of all new cancer cases in 2020 were haematological malignancies[10]. The treatment of haematological malignancies is often challenging due to their complex pathogenesis and difficulty in diagnosis. Advances in medical technology, such as targeted therapies and immunotherapy, have greatly improved the prognosis for haematological cancer patients [11].

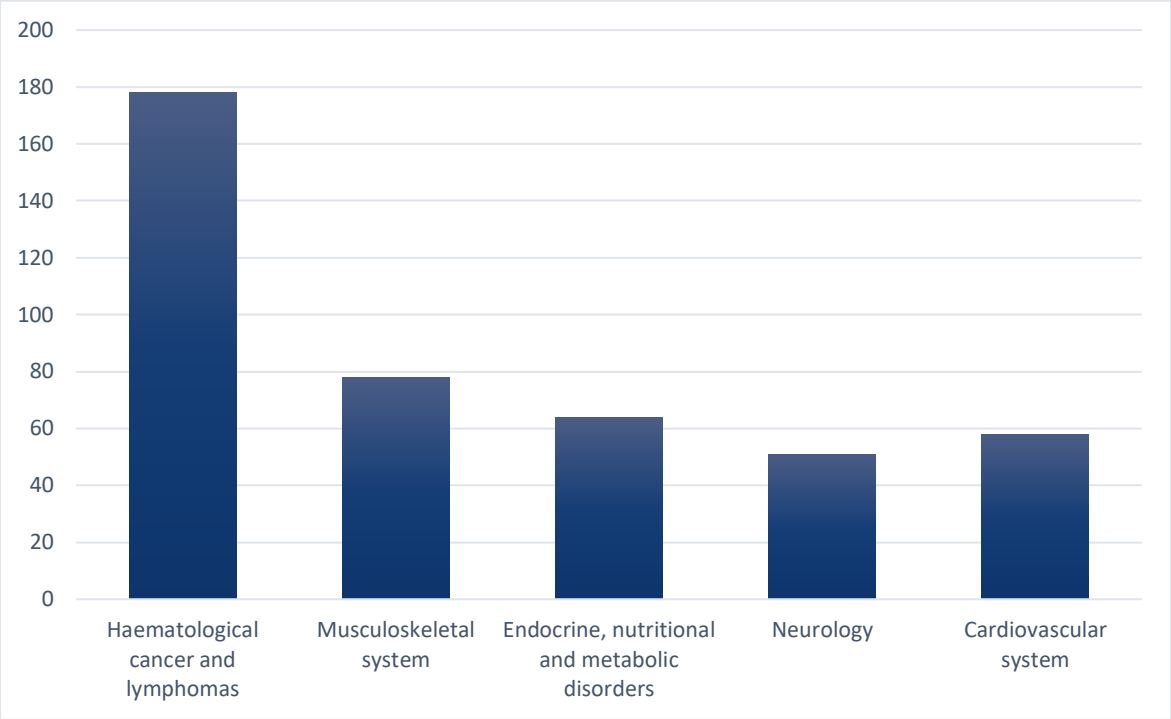

Figure 3 - Top five most common therapeutic areas

Clinical development status

The analysis in Figure 4 revealed that the majority of ATMP records were still in clinical development (n = 667). Only 50 ATMPs already had a UK and EU licence. There were 2 ATMPs with only an EU license. Lastly, 2 ATMPs were in the pre-registration stage and 1 was withdrawn. The limited number of ATMPs with UK and EU licenses can be attributed to the stringent regulatory requirements and extensive testing that these therapies must undergo before receiving approval. Additionally, the process of obtaining licenses can be time-consuming and costly, which may deter some companies from pursuing them. Nonetheless, the high number of ATMPs in clinical development indicates a strong commitment to advancing these therapies and holds promise for future regulatory approvals.

Figure 4: Clinical development status of ATMP records

749 main clinical trials were identified for technology records. The majority of main trials were currently or previously being conducted at earlier phases, such as phase 1/2 (n = 320, 43%) and phase 2 (n = 213, 28%). 98 (13%) trials were also identified at phase 3 (Figure 5). The distribution of trials across different phases indicates that the majority of the main trials took place in earlier phases, specifically phase 1/2 and phase 2, accounting for 71% of the total trials. This suggests that a significant focus was placed on assessing safety and efficacy in the earlier stages of the research process.

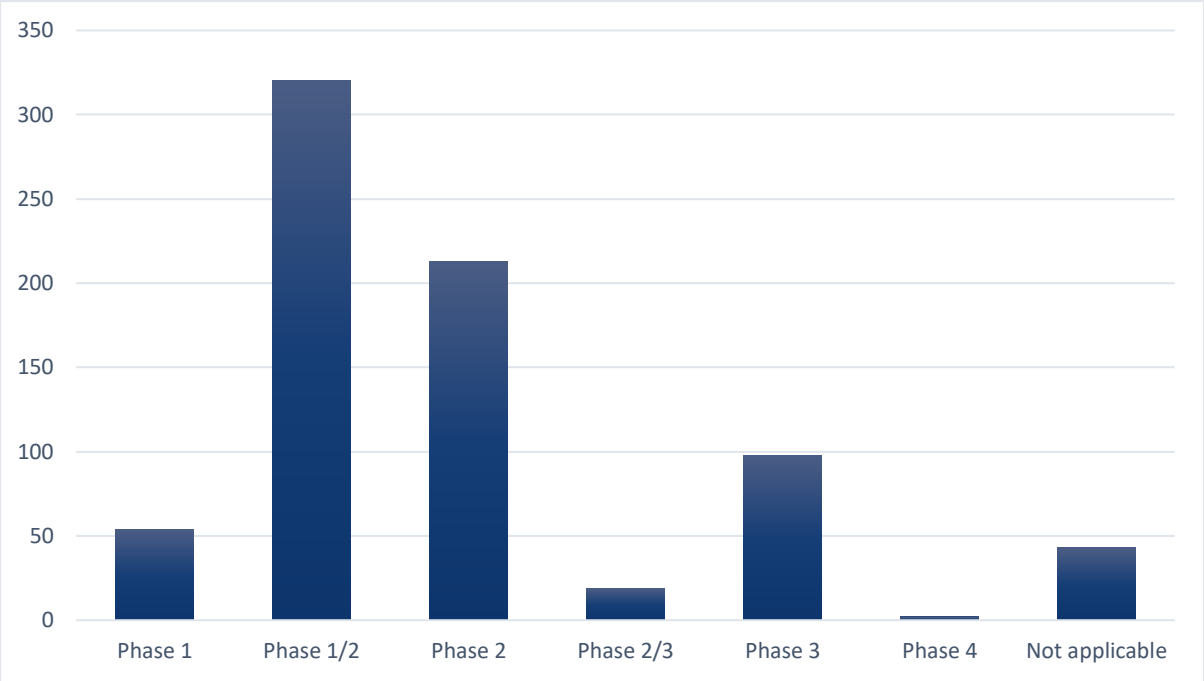

Figure 5 - Main clinical trial phases for technology records

EMA ATMP classifications

The most common classification of product based on the EMA ATMP classification system was gene therapy making up 59% (n = 445) of the records, followed by somatic cell therapies at 25% (n = 183), and tissue-engineered therapies making up 15% (n = 111). 1% (n = 10) of recorded ATMPs were identified as combined therapies, consisting of 2 or more classes of ATMP (Figure 6). The high percentage of gene therapy products can be attributed to the significant advancements in genetic research and technology. Gene therapy holds immense potential in treating a wide range of genetic disorders by introducing functional genes into the patient's cells. This approach offers promising solutions for previously untreatable conditions, leading to its dominant representation in the EMA ATMP classification system.

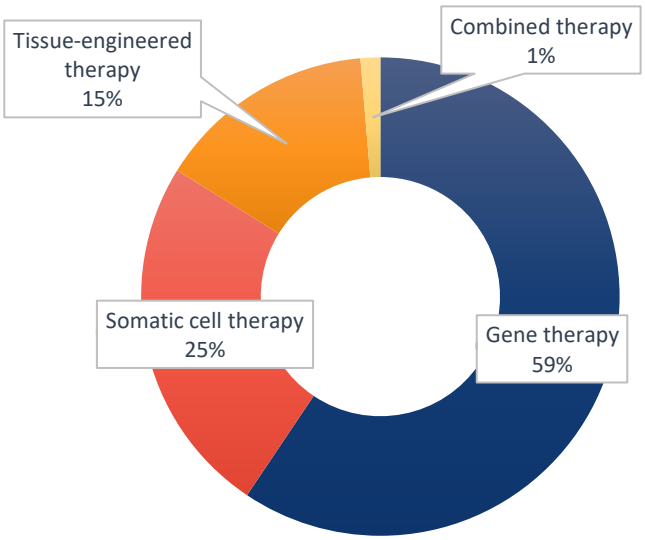

Figure 6: Distribution of EMA ATMP classes found

EMA regulatory designations

A total of 165 ATMP records had an EMA designation (Figure 7). Of these records, 79% were EMA Orphan designations (n = 131), followed by 13% (n = 21) as EMA ATMP and 8% (n = 13) as EMA PRIME.

Figure 7: Distribution of EMA regulatory designations

ATMP technology record classifications

623 (83%) technology records contained a single ATMP being tested as a monotherapy and 126 (17%) records were testing an ATMP in combination with other medicinal products (Figure 8). Of the total ATMP records, 45% (n = 334) were being studied in non-rare disease indications, with 55% (n = 415) indicated for a rare disease (Figure 9). ATMPs were being studied in cancer indications in 47% (n = 349) of records, with the remaining 53% (n = 400) being studied in non-cancer indications (Figure 10).

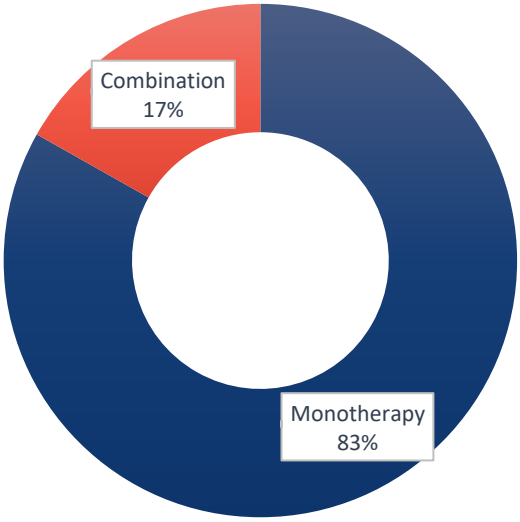

Figure 8: ATMPs being used as monotherapies and as part of combinations

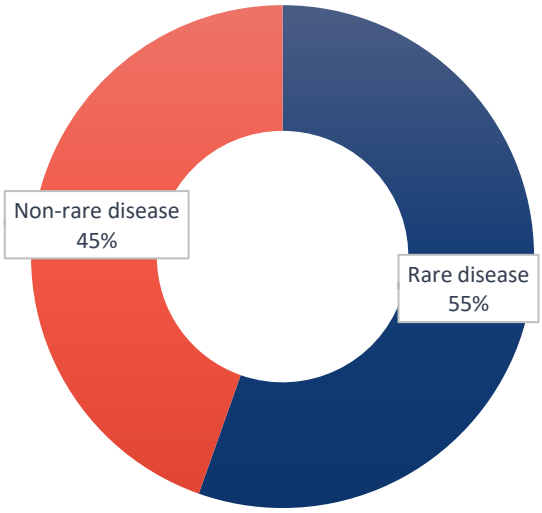

Figure 9: ATMP records with rare and non-rare disease indications

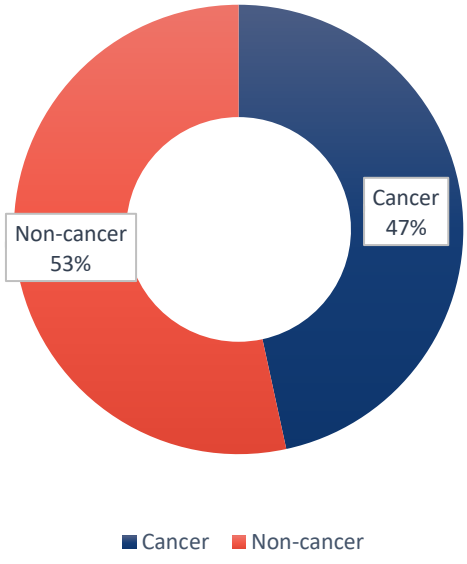

Figure 10: ATMP records with cancer and non-cancer indications

Conclusion

We identified a total of 749 technology records containing at least one ATMP. These unique ATMPs are characterized by their novel approaches to treating diseases, often providing options for conditions that were previously untreatable or inadequately managed with conventional therapies. The findings of this study clearly show that the most frequently reported therapeutic areas, which are haematological cancers and lymphomas (n = 178), musculoskeletal (n = 78), endocrine, nutritional, and metabolic disorders (n = 64), cardiovascular (n = 58), and neurology (n = 51). One explanation why haematological cancers and lymphomas are the most frequently reported may be attributed to the fact that they are among the most prevalent cancer types worldwide, accounting for a significant portion of cancer diagnoses.

The majority of the main trials took place in earlier phases, i.e., phase 1/2 (n = 320, 43%) and phase 2 (n = 213, 28%). One possible reason for the higher number of trials in phase 1/2 could be that these phases involve testing the safety and efficacy of a new intervention or treatment. As a result, more preliminary studies may be conducted to gather sufficient data before progressing to phase 3, where larger-scale trials are conducted to further evaluate the intervention's effectiveness.

Our analysis showed that approximately 60% of identified ATMPs were classified as gene therapies. One potential reason for the high percentage of gene therapy products could be the significant advancements in genetic engineering and gene editing technologies. These advancements have paved the way for more targeted and effective treatments for genetic disorders, leading to an increased focus on gene therapy as a viable treatment option. Additionally, the potential for personalised medicine and the ability to tailor treatments to an individual's specific genetic makeup may have contributed to the popularity of gene therapy.

The development and application of these therapies require careful consideration of regulatory, manufacturing, and clinical challenges to ensure their safety, efficacy, and accessibility to patients. The development of these ATMPs has significantly impacted the biotech industry, as seen by the competition among the most active companies such as Celgene, Mesoblast, Amgen, and Iovance Biotherapeutics. This race to innovate and produce ATMPs highlights the growing importance of these therapies in revolutionising medical treatments and shaping the future of biotechnology.

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