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Building the foundations for AI in preclinical assessment of ATMPs: Opportunities and challenges

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About this white paper

This white paper summarises the current use of AI in ATMP preclinical assessment, outlines key challenges and limitations, and explores potential future directions to enable the meaningful integration of *in silico* and AI-based approaches into ATMP preclinical development. It also captures the key discussions, perspectives, and insights generated during the symposium "AI Applications in Preclinical Assessment of ATMPs", organised by Cell and Gene Therapy Catapult on behalf of the Centre of Excellence in Regulatory Science and Innovation for Advanced Therapies.

Introduction

- Artificial Intelligence (AI) is increasingly integrated into drug development and preclinical research
- AI offers the potential to improve efficacy and safety assessments, predict toxicity, optimise study design and reduce reliance on animal models
- However, there are challenges such as data scarcity constraints, lack of transparency in AI models, and regulatory uncertainty

AI has already demonstrated potential to transform and accelerate the development of new therapies. It has the possibility to enable more efficient and robust risk assessments, improve prediction of clinical toxicities, the evaluation of carcinogenic potential, and anticipation of adverse effects. AI also has the potential to contribute to the reduction, refinement, and replacement of *in vivo* studies by supporting model selection, enabling *in silico* experimentation, and improving predictive accuracy[1–5].

In addition, AI may help identify patient populations most likely to benefit from specific treatments, thereby increasing the success rate of clinical trials. Beyond reducing the reliance on animal studies, AI has the potential to improve development attrition rates by predicting non-clinical study outcomes, and their correlation with clinical results. This approach can help shorten development timelines and costs, limit dependence on animal testing and clinical trial modelling, and ultimately contribute to the creation of safer, more effective, and more accessible therapies[6].

As part of a Centre of Excellence in Regulatory Science and Innovation (CERSI-AT) funded project, the Cell and Gene Therapy Catapult (CGT Catapult) conducted a thorough review of the current state of AI use in Advanced Therapy Medicinal Product (ATMP) preclinical assessment. This work considered regulatory positions, companies operating in the field, and relevant databases. As part of this project, we hosted a symposium in October 2025, entitled "AI Applications in Preclinical Assessment of ATMPs". The event brought together key stakeholders from the pharmaceutical industry, academia, AI technology developers, regulatory agencies, data science, and toxicology to foster an open and collaborative dialogue focused on:

- Defining the current landscape of AI use in preclinical assessment
- Discussing engagement, expectations, and challenges from regulatory agencies
- Exploring current and emerging AI applications in preclinical development
- Highlighting the critical role of data sharing and data quality
- Identifying potential solutions to accelerate the responsible and effective integration of AI and machine learning (ML) into the preclinical assessment of ATMPs

AI and ATMP preclinical assessment survey

To gather insights on the current landscape and challenges associated with applying AI in ATMP development and non-clinical assessment, we conducted a short survey prior to the symposium. The survey aimed to assess the current use of AI in ATMP development, and perceived readiness for broader implementation.

Only 21% of respondents reported that their organisation is currently using AI for ATMP development, while 48% indicated they have a strategy to implement AI (in some cases not yet formalised). Despite this, there was strong recognition that shared data infrastructure could accelerate progress: 83% considered a non-clinical safety/toxicology database useful to support AI training, and 61% would support the creation of a database for non-clinical efficacy and safety data. Responses consistently highlighted that feasibility depends on resolving key barriers related to confidentiality, data ownership, access governance and funding, alongside ensuring data comparability and standardisation. Importantly, stakeholders cautioned that AI may remain limited in predicting novel outcomes not represented in training datasets, reinforcing the need to clearly define scope, limitations, and context of use.

Development of AI-driven methodologies in non-clinical assessment: Current capabilities

Drug development is a time-consuming, costly, and high-risk process, with fewer than 10% of clinical candidates obtaining market approval and possibly lower in the ATMPs space[7]. Preclinical efficacy and safety studies are a major contributor to these challenges: they are resource-intensive, take a significant period of time to complete, and often rely on endpoints that can be difficult to interpret and integrate across the development pipeline, limiting both reproducibility and translatability[8].

Animal studies have historically been essential for developing product knowledge and ensuring patient safety. However, their predictive value for human clinical efficacy remains variable, and alongside the understandable ethical implications associated with animal studies, highlights the urgent need for innovation in this area. Despite recent updates in regulatory guidance (discussed later in this document), the use of AI in preclinical assessments is still limited, and animal studies remain the cornerstone of drug safety evaluations. At the same time, there is a growing recognition of the need to modernise safety assessment by integrating technologies that enhance efficiency, human relevance, and data integration, while reducing reliance on animal models[9–12].

There is a clear opportunity to improve the reproducibility and translational relevance of non-clinical studies through the early adoption of AI together with *in vitro* and *in vivo* studies.

This will offer the opportunity to develop:

- Deeper insights into disease pathogenesis and exposure/response relationships
- Adaptive study designs and more efficient data integration
- Virtual control groups and virtual data sets built from historical data, reducing animal use
- A foundation for *in silico* modelling and predictive simulations
- Leveraging AI/ML-driven analytics to facilitate objective, evidence-based risk assessments and enhance decision-making precision
- The generation of robust, and clinically-relevant decision-grade datasets

AI has potential applications across the entire drug development lifecycle, from discovery to post-marketing surveillance. If developed robustly, ethically, responsibly, and subsequently applied in validated ways, AI has the potential to transform both preclinical and clinical research.

Nonetheless, significant hurdles still need to be overcome for AI to become a practical tool in non-clinical assessment:

- **Data quality, format and standardisation:** Many datasets are not generated with machine learning in mind, lack consistency, or are biased toward positive results.
- **Data availability and integrity:** Access is limited for novel mechanisms of action, and proprietary restrictions hinder data sharing and can make data auditing difficult. This is particularly evident in the ATMP field, where only a few therapies have been approved, with limited training data available.
- **Model transparency and integration:** Significant challenges persist regarding algorithmic transparency, systems interoperability, and the demonstration of cross-programmatic reliability.
- **Regulatory acceptance:** While regulatory uncertainty remains, authorities are showing a growing receptivity toward AI integration as its adoption within preclinical development continues to expand.
- **Skills and expertise:** A critical workforce capability gap exists, specifically for 'AI translators' proficient in the design, validation, and interpretation of algorithmic outputs within both industry and regulatory frameworks[4,13,14].
- **Trustworthy AI:** Unlike AI models like ChatGPT which have hidden data sources and unknown parameter weights, biomedical AI models must fulfil the need to be trustworthy-by-design for community acceptance.

In the short term, AI has the potential to enhance the predictivity and reproducibility of preclinical safety studies. Longer-term, it is expected to reduce the need for *in vivo* safety studies, ultimately accelerating the delivery of safer, more effective, and more affordable therapies to patients.

Achieving this vision will be achieved by coordinated, multidisciplinary collaboration among engineers, data scientists, toxicologists, and regulators, all working to develop, validate, and integrate AI-driven tools into regulatory frameworks.

AI companies active in preclinical assessment

The number of companies leveraging AI to support safety assessments in drug development is steadily increasing. Based on our recent research, we observed that most AI-guided safety assessments in non-clinical development are focused on small molecules.

While there are fewer compared to those in the small molecule domain, several companies are actively applying AI to support the preclinical development of ATMPs. Companies such as Aganitha AI, Form Bio, and Expression Edits are using AI to enhance viral vector design, predict biodistribution across model systems, optimise gene expression, and improve manufacturing workflows.

Collectively, their platforms facilitate the identification of optimal gene therapy constructs, enable early risk assessments of production processes, and refine genetic payloads to enhance therapeutic targeting and potency without compromising the integrity of core genetic sequences.

A clear distinction must be made between AI applications that are currently feasible and increasingly acceptable within preclinical development and those that represent emerging possibilities requiring further data generation, validation, and clearer regulatory frameworks, guidance, and sustained engagement with regulatory authorities.

Regulatory landscape: Current positions on AI and *in silico* methods in preclinical assessment

Regulatory bodies such as the Medicines and Healthcare products Regulatory Agency (MHRA), the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have all recently published reports acknowledging the increasing impact of AI across the medicinal product lifecycle[15–18].

In response to the UK Government's white paper published in March 2023, *A pro-innovation approach to AI regulation: government response*[15], the MHRA released a paper in April 2024 entitled *Impact of AI on the regulation of medicinal products*[18]. This policy adopts the Government's proposed framework and is structured around five cross-sector principles: safety, security and robustness; appropriate transparency and explainability; fairness; accountability and governance; and contestability and redress. The paper outlines the MHRA's intention to evaluate both the potential benefits and risks associated with the use of AI in the regulation of medicinal products.

In September 2024, the EMA published a *Reflection paper on the use of AI in the medicinal product lifecycle*[16]. This document outlines high-level principles applicable to AI and machine-learning applications across all stages of the lifecycle, from drug discovery through to post-authorisation activities. The EMA recognises the significant potential of AI/ML applications at any stage in the medicine lifecycle, from drug discovery through to the post authorisation setting, while emphasising the need for ethical, transparent, and trustworthy AI systems that are aligned with existing EU legislation and regulatory requirements.

The FDA published a draft guidance in January 2025, entitled *Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products*[17]. This guidance provides recommendations for sponsors and other stakeholders on the use of AI models throughout the drug development lifecycle. The FDA places particular emphasis on the need to establish a Model Credibility Assessment Framework, proposing a seven-step approach focused on defining the context of use, evaluating risk, planning and executing credibility activities, and documenting outcomes to support regulatory decision-making.

Interactions with stakeholders emphasised the need for appropriate regulatory incentives to support the responsible integration of AI into non-clinical assessment and enhanced model transparency to support regulatory confidence. Rapid evolution of AI approaches may outpace regulatory readiness, highlighting the need for proactive collaboration between developers and regulators to manage associated risks and opportunities.

Timely and constructive dialogue between developers and regulatory authorities has a key role in accelerating the adoption of AI-based approaches in non-clinical assessment, by reducing uncertainty, aligning expectations, and supporting efficient integration within regulatory framework compatible development pathways.

Reducing animal use in safety assessments

Regulatory bodies including the MHRA, EMA and FDA are increasingly endorsing New Approach Methodologies (NAMs), contributing to a shift away from traditional animal models. This shift is driven by both the ethical principles of the 3Rs (Replacement, Reduction, and Refinement) and recognised limitations of certain animal models in predicting human outcomes[19–21]. NAMs comprise a broad portfolio of non-animal approaches, ranging from advanced *in vitro* systems —such as human primary cell assays, 3D models, and microphysiological systems (e.g., organ-on-a-chip) — to *in silico* methods, including computational modelling supported by AI and ML. Together, these methodologies have the potential to generate data that is of greater human relevance, and enable more predictive, data-driven safety assessment[1].

Within the context of ATMPs, the adoption of NAMs represents an essential step in modernising non-clinical safety assessment. Given the complexity and modality-specific characteristics of ATMPs, reliance on conventional animal models is often scientifically suboptimal.

In this context, it is worth mentioning that the National Centre for the Replacement, Refinement and Reduction of animals in research (NC3Rs), an independent scientific organisation established by the UK Government in 2004 to accelerate the development and uptake of the 3Rs, highlighted several key enablers and challenges for reducing animal use in safety assessment.

These included:

- The critical role of data sharing in accelerating the development and regulatory acceptance of NAMs
- Key drivers and barriers to the implementation of novel animal model alternatives
- The potential for NAMs to enable faster and more cost-effective safety assessment
- The development of more predictive and human-relevant models
- Broader benefits related to sustainability and resource efficiency

In line with these perspectives, the FDA has explicitly acknowledged the limitations of certain animal studies, noting that *"the FDA recognizes the futility of many animal studies and will embrace non-animal models where possible"*, as articulated within the FDA's New Plausible Mechanism Pathway[22,19,18]. This position further underscores the growing regulatory openness to scientifically robust, animal model alternatives when supported by scientific evidence.

At the same time, critical limitations must be addressed to enable broader adoption. These include data scarcity and lack of standardisation, which constrains the ability to train robust and generalisable AI models, as well as current challenges in capturing systemic toxicity and biodistribution using individual *in vitro* models alone. In addition, the shift toward Explainable AI (XAI) is essential for addressing the 'black box' nature of complex algorithms, which is vital for regulatory compliance and informed decision-making.

From AI potential to reality

Data sharing

Increasing access to curated, anonymised, high-quality non-clinical datasets can accelerate learning across the sector, improve the reliability of AI-driven predictions, and reduce duplication of experimental testing. By this approach, data sharing can contribute not only to improved efficiency and cost reduction, but also to enabling more clinically relevant, evidence-based approaches aligned with the 3Rs.

Perspectives from the small molecule sector reinforce that effective data sharing is not solely a technical challenge, but equally a collaborative and trust challenge. Sustainable initiatives require secure working practices, clarity on governance and access, and a shared understanding of the benefits and value exchange for data contributors. In practice, the most successful models bring together industry, regulators, and technical experts to align on expectations and enable meaningful reuse of data to support decision-making.

Data accessibility and legacy formats

Even where datasets exist, they may be difficult to mobilise due to legacy storage formats (including paper-based records), fragmented digital structures, or limited curation often leading to concerns of data integrity, resulting in uneven accessibility despite potential value.

In addition to sharing datasets, stakeholders may also choose to share models or derived knowledge generated from shared data. However, approaches vary between transparent models (where underlying evidence and outputs can be interrogated alongside the data) and less transparent models used primarily for prediction. This distinction is particularly relevant for regulatory confidence, where interpretability, traceability, and credibility of evidence may influence acceptance of AI-supported conclusions. In this context it is important to mention the FUTURE-AI Consortium, founded in 2021[23], which provides a guideline for trustworthy AI based on six guiding principles: fairness, universality, traceability, usability, robustness, and explainability[23].

Operationalising data sharing requires early planning around governance and compliance, including data provenance and ownership, copyright and contractual constraints through data stewardship, jurisdiction-specific legal frameworks, and where data will physically reside. Security is a major consideration when handling sensitive non-clinical datasets, with expectations around encryption, controlled access, and auditability. These foundations should be established upfront to ensure good practice and long-term sustainability.

Importantly, data sharing is not cost-neutral: long-term impact depends on investment in dataset curation, continued maintenance, periodic updates, and ongoing communication to ensure relevance. These efforts are essential not only to improve model performance, but also to support consistent and acceptable use of data-driven predictions in real decision-making settings.

Among European initiatives, the JOIN4ATMPs project aims to accelerate and de-risk ATMP development by mapping key obstacles, assessing real-world solutions, and defining actionable pathways to improve patient access to advanced therapies.

Initiated within the European University Hospital Alliance, JOIN4ATMPs brings together academic, clinical, and research organisations to address challenges in the ATMP development lifecycle. A dedicated work package, led by the University of Vienna, focuses on the limited predictability of preclinical safety and efficacy data. Professor Antonia Müller and Dr Nara Marella, representing JOIN4ATMPs, highlighted the importance of cross-sector collaboration in supporting the development of cell and gene therapies. They noted that challenges identified through the project included the absence of harmonised preclinical requirements across *in vitro* systems and small and large animal models. In addition, limited standardisation of source materials was reported, resulting in variability in data generation and interpretation, particularly within academic-led programmes.

As part of the initiative, a targeted survey was conducted to map hurdles in ATMP preclinical development, with a specific focus on the use of innovative *in vitro* and *in silico* approaches as alternatives to animal testing and on generating evidence-based recommendations to support their regulatory acceptance.

From a preliminary analysis of the first 174 European participants, they reported that *in vivo* studies remain a central component of ATMP preclinical packages, with 62% of respondents indicating the use of animal models. While a range of *in vitro* and alternative assays were described, the most commonly used systems were immortalised cell lines and primary human cells, whereas advanced models such as 3D organoids were used less frequently. Importantly, most respondents indicated that *in vitro* or alternative approaches did not replace animal studies, or that replacement was not applicable; only around 20% reported successful replacement.

The main barriers identified included concerns regarding the suitability of these models for both safety and efficacy assessment and the lack of sufficient scientific evidence to support their broader use in regulatory decision-making.

Incentives for data sharing

CGT Catapult have sought views on AI and *in silico* approaches that could help reduce reliance on animal studies for non-clinical evidence generation in ATMP development. In light of these perspectives, it is clear that meaningful progress will depend on establishing the right foundations, including access to high-quality data, robust validation approaches, sufficient cross-disciplinary expertise, and incentives to enable safe and interoperable data sharing and the importance of validating AI models within a clearly defined context of use, in line with the principles highlighted in the FDA draft guidance on AI (January 2025)[17].

This ensures that model credibility is assessed against the specific scientific question and intended decision-making purpose. A key barrier remains the limited availability of trainable datasets, alongside challenges in standardisation and validation. It has been proposed that developing a consensus on a minimum dataset and common data formats for ATMPs, ideally tailored by therapy type and indication, would be an important step towards implementation. Defining shared baseline measurements and testing conditions could improve comparability across programmes and support the development of more robust and generalisable *in silico* models. Structured focus groups and community discussions, with outputs published as best-practice guidance, were suggested as practical mechanisms to achieve this. In addition, iterative benchmarking initiatives (e.g., recurring "challenge" exercises) may support continuous refinement as complexity increases.

While data sharing was recognised as essential, it also raises concerns around governance, anonymisation, intellectual property, data integrity and safe access. The importance of secure technical infrastructure, controlled access mechanisms, and trusted governance frameworks to enable responsible use of sensitive datasets are clearly central to this.

Finally, participants noted that coordinated incentives and international alignment will be required to make these approaches sustainable. It has been suggested that the UK is potentially well positioned to pilot such frameworks, while global harmonisation will remain critical for broad adoption. Overall, it has been concluded that reducing reliance on animal studies through *in silico* approaches (such as AI and ML) is feasible but requires coordinated action to build shared standards and confidence in AI-derived evidence.

Possible next steps

Priorities and proposed next steps to be taken to allow the UK infrastructure to improve the use of AI in this space

Short-term (0-12 months)

- Strengthen workforce capability by ensuring access to professionals trained in both experimental and computational technologies.
- Promote AI validation approaches linked to a defined context of use, aligned to the question of interest and intended decision-making purpose.
- Initiate multi-stakeholder focus groups to define what a minimum non-clinical dataset for ATMPs (or specific ATMP subtypes) should include, including baseline measurements and testing conditions. This should take into account regulatory gaps where no current alternative evidence exists, enabling targeted use of AI and *in silico* approaches to fill these voids.
- Identify practical requirements for data sharing including safe access to data, considerations around anonymisation, IP, and keeping datasets secure and up to date. These efforts will also support cross-sector collaboration, helping to bridge communication gaps between laboratory scientists, regulators, and translational teams, and enabling more efficient, risk-informed use of *in silico* methods.

Medium-term (1-3 years)

- Publish best-practice guidance on minimum datasets to support comparability across programmes and enable more robust model development while addressing regulatory gaps and fostering confidence in AI-supported approaches.
- Encourage the adoption of Common Data Models (CDMs) to harmonise disparate datasets, enabling a decentralised collaboration hub where academics and regulators can co-validate evidence alongside industry partners and patient representatives.
- Support regulatory engagement and capability-building to ensure regulators have the expertise and confidence to assess AI-supported approaches, helping bridge the gap between technology adoption and regulatory readiness.
- Establish iterative benchmarking approaches (e.g., recurring "challenge" initiatives) to refine minimum standards over time as complexity increases.
- Encourage the curation of high-fidelity longitudinal health records into machine-readable formats; by leveraging this data to establish baseline population variance, developers can better contextualise therapy-specific evidence and refine safety thresholds.

Long-term (>3-5 years)

- Work towards international harmonisation around a minimum dataset standard that is globally meaningful while avoiding excessive burden for developers. This should include guidance on data embargo periods and the inclusion of negative or discontinued programme data to improve AI model training.
- Explore incentives and regulatory mechanisms to support availability of essential datasets, promote international alignment, and strengthen regulatory confidence in AI-supported approaches.
- Support healthcare-system incentives for improved data completeness and return, recognising that key population and system datasets are often held outside industry.
- A central question concerned ownership, governance, and stewardship of such a repository, as well as the current stance of regulatory authorities. From a regulatory perspective, a centralised, regulatory-grade data platform would not only support developers but could also significantly benefit regulators by improving contextualisation of preclinical evidence and enabling more robust benefit–risk assessment.

There is a consensus in the field that the importance of data sharing is pivotal to reducing reliance on animal studies for non-clinical evidence generation. It can be emphasised that the MHRA is receptive to engaging in open discussions on the creation of a data repository, including how it might be governed and operationalised. The importance of a coordinated position was underlined, not only at the national level but across the international regulatory community to ensure consistency, credibility, and long-term sustainability.

There is a need for active engagement within industry and academia. An open dialogue is required to understand what incentives or safeguards would encourage companies and academic developers to contribute data.

At present, regulatory agencies face a limited internal capacity for data science and data curation, which represents a practical constraint on their ability to host or directly manage large-scale datasets.

From an international perspective, Antonia Müller highlighted that, in the United States, the National Institutes of Health (NIH) could represent a natural institutional home for such a repository. This raised parallel questions for Europe regarding which organisation(s) could credibly assume a similar role.

Building on these ideas, two additional considerations were identified as critical for any future data-sharing framework, particularly in ensuring that AI-enabled approaches are feasible and sustainable:

- **Data embargo periods:** the management of data release through "data embargo periods", which define how long data remain restricted before broader sharing. Careful design of embargo periods is essential to balance intellectual property protection with timely access for scientific research and model development. Long embargoes of 10–15 years are incompatible with the rapid evolution of ATMP development. A more realistic model may involve embargoes aligned with market access or development milestones, balancing intellectual property protection with scientific value.
- **Inclusion of negative and failed programme data:** Data from products that never reach the market are often lost, yet these datasets are essential for training and validating AI models. The systematic capture of such "negative data" is particularly valuable for improving predictive performance and avoiding repetition of unsuccessful development paths.

Collectively, these discussions highlight that while technical solutions for data repositories exist, governance, incentives, and international alignment remain the key challenges to be addressed before AI-enabled data sharing can be fully realised in the ATMP preclinical space.

Conclusions

In silico approaches such as AI/ML have the potential to transform preclinical assessment for ATMPs by improving efficiency, reducing animal use, and enhancing predictive accuracy.

In order to achieve this potential, progress will require access to transparent, high-quality and well-structured data, combined with collaborative data-sharing efforts and clear regulatory alignment on expectations for AI-generated evidence.

Early and sustained engagement among industry, academia, and regulators will be key to building a robust and trusted AI ecosystem, enabling shared standards, consistent validation approaches, and wider adoption of AI-supported decision-making.

Key enablers for responsible and scalable integration of AI tools include:

- **Collaborative initiatives** to align stakeholders, share best practices, and develop reusable evidence frameworks.
- **Early-stage data sharing** to inform study design and programme strategy, with safeguards for confidential and proprietary information.
- **Anonymised datasets**, where feasible, to increase accessibility and reuse while reducing intellectual property (IP) and commercial barriers.
- **Data standardisation**, including harmonised metadata and reporting conventions, to enable evidence pooling, support robust model validation, and strengthen regulatory confidence.

Research methods

All data, suggestions and ideas presented in this manuscript originate from research conducted in 2025 by the CGT Catapult. Additional insights were obtained from presentations and discussions during the symposium “AI Applications in Preclinical Assessment of ATMPs,” organised by the CGT Catapult on behalf of the CERSI-AT.

We acknowledge the contributions of the symposium speakers and panellists, listed here in alphabetical order:

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