FORUM

The Academy of Medical Sciences

UKRI Medical Research Council

Transforming translation: innovative preclinical models

Innovative preclinical models – including advanced *in vitro*, *in silico* and *in vivo* approaches – offer the potential to improve clinical trial success rates and enhance the development of effective medicines. However, challenges in translational readiness, regulatory guidelines and targeted funding currently limit wider adoption of such models. Cross-sector collaboration, harmonised material-sharing initiatives and close working with industry and regulators will be crucial to advance the field. Attendees recognised sector needs, such as:

- Funding mechanisms that support the entire model development pathway including translational and regulatory science.
- A collaborative framework that aligns incentives for model developers, funders, industry and regulators to deliver on the potential of innovative preclinical models. This includes increased opportunities to access data, samples and compounds for model development.
- Simplification and streamlining of intellectual property and licensing agreements for samples, data and models to facilitate academic and industry collaboration on preclinical model development.
- Robust and reproducible models, incorporating the diversity of the patient population, in all areas of preclinical medical research. Advancing the most translationally ready models through validation and adoption would create exemplars of the evidence required for a model to be widely adopted and acceptable to regulators. Attendees highlighted opportunity areas where model development could create such exemplars.

> Developing innovative models is an area where the UK can have impact and leadership. But it's an area of research that only matters if we turn it into something useful in the real world.
>
> **Rosalind Campion,**
> CEO, Academy of Medical Sciences

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Background

The Academy of Medical Sciences' FORUM and the UK Research and Innovation Medical Research Council (UKRI MRC) hosted a roundtable chaired by Professor Maddy Parsons,[1] including clinicians, academics, regulators, funders, industry representatives and policymakers (see Annex 1), to explore areas where preclinical models could have the greatest impact on medicine development within five years.

Preclinical studies play a crucial role in the drug development process, assessing the safety and efficacy of a target compound before a drug is trialled in humans.[2] These studies typically use a combination of in *vitro* (cell-based assays) and *in vivo* (animal models) approaches to answer key questions about the compound's biological effects, safety, and mechanism of action, ensuring only the most promising and safe candidates advance to clinical trials in humans.[3]

However, there are challenges in reproducing the complexity of some human disease using traditional preclinical models. There is an ~90% attrition rate in drug development, in large part because models do not yet reflect molecular, genetic and phenotypic complexity in patients.[4] Inaccurate preclinical models underpin a stark lack of medicines for unmet medical needs such as pregnancy-specific conditions and chronic pain.[5,6]

Innovative preclinical models such as organoids and organ-on-a-chip systems, and *in silico* tools (computer modelling or simulation, including artificial intelligence) can help to address this problem. For example, organ-on-a-chip systems, 3D cell or tissue-like structures that mimic more complex components of tissues and organs offer the potential for more accurate prediction of tissue response prior to clinical studies. *In silico* tools – such as 'digital twins' created from matched patient-derived data and tissue/organoids – could potentially group patients based on disease characteristics to inform clinical trial selection, and to maximise chances of success.

> "Each patient is different and experiences different combinations of symptoms and speed of disease progression – if this can be encapsulated in [preclinical] studies, this would be helpful.
>
> **Parent of a child with a rare disease**

1. Professor of Cell Biology and Dean of Research Excellence Frameworks, King's College London
2. Thermo Fisher Scientific. *Preclinical studies in drug development*. **https://www.ppd.com/what-is-a-cro/preclinical-studies-in-drug-development/**
3. AMSbiopharma (2025). *Preclinical research in drug development: from toxicology to translational insights*. **https://amsbiopharma.com/preclinical-research-drug-development/**
4. Schuhmacher A, *et al*. (2025). *Benchmarking R&D success rates of leading pharmaceutical companies: an empirical analysis of FDA approvals (2006-2022)*. Drug Discov Today **30(2)**,104291.
5. Academy of Medical Sciences (2023). *Understanding pregnancy: accelerating the development of new therapies for pregnancy-specific conditions*. **https://acmedsci.ac.uk/file-download/5618046**
6. Academy of Medical Sciences (2021). *Chronic pain: experimental medicine and clinical insights*. **https://acmedsci.ac.uk/file-download/55232795**

A recent ABPI/NC3Rs review assessed the translational readiness of innovative UK preclinical models using a framework co-developed with industry. The findings indicated that most models require significant further development before they can be routinely adopted in pharmaceutical or regulatory settings.[7]

The UK Government recently announced plans to support the development, validation and uptake of alternative methods to animal models, including plans for a UK preclinical translation models hub[8] and a UK Centre for the Validation of Alternative Methods (UKCVAM).[9] A growing ecosystem of international research infrastructures – such as biobanking initiatives and disease-relevant modelling platforms – may offer further opportunities for the UK to leverage international partnerships to accelerate development and adoption of models.[10,11]

During this roundtable, participants discussed key challenges in funding, developing and translating models for use in pharmaceutical R&D, identifying opportunities to accelerate progress.

> “If you’ve lived with something and you’ve experienced the negative sides of things, you’re kind of more open to your data being used [to develop alternative preclinical models] in a way to hopefully make some kind of improvement... But it’s always about hope. You just hope for the best that your data is used for the right way, for the right reasons and something good comes out of it... that glimmer of hope that it might change something for someone.
>
> **Sadia Haqnawaz,** Patient researcher with lived experience of pregnancy and baby loss

7. Association of the British Pharmaceutical Industry (2026). *From models to medicines: a landscape review of human-relevant pre-clinical model development in the UK*. https://www.abpi.org.uk/publications/from-models-to-medicines-a-landscape-review-of-human-relevant-pre-clinical-model-development-in-the-uk/
8. UK Government (2025). Policy Paper. *Life Sciences Sector Plan*. https://www.gov.uk/government/publications/life-sciences-sector-plan
9. UK Government (2025). *Replacing animals in science: a strategy to support the development, validation and uptake of alternative methods*. https://www.gov.uk/government/publications/replacing-animals-in-science-strategy/replacing-animals-in-science-a-strategy-to-support-the-development-validation-and-uptake-of-alternative-methods
10. INFRAFRONTIER. About us. https://www.infrafrontier.eu/about-us/
11. BBMRI-ERIC. About us. https://www.bbmri-eric.eu/about/

End-to-end funding for preclinical model development

Participants highlighted a need for financial support across the entire model development pathway including translational and regulatory science.

While funders often provide indirect support for preclinical model development as part of discovery research projects, there are significant funding gaps along the development pipeline for innovative preclinical models. Creation of the early version of a model should be followed by assessment of its robustness and reproducibility, and strategies to ensure broader accessibility. Sources of cells or clinical samples should be standardised and quality assured, and the model's performance and clinical relevance should be proved through validation studies that are benchmarked against clinical trial data. Developers should then prove the model's scalability and transferability to other labs.

Limited dedicated funding for preclinical models in the UK restricts the ability of developers to progress to validation and translation. The funding focus tends to be on progression of new drug development without consideration for regulatory or benchmarking stages that are critical for building confidence in models for medicine evaluation. This is, in part, due to risk aversion; investors want to fund well-defined models with a clear pathway to industry adoption. There is also a lack of consensus between sectors on what represents a 'fundable' approach to innovative preclinical model development. Moreover, pharmaceutical companies outsource model development to contract research organisations (CROs) rather than invest in in-house R&D or academic partnerships, further limiting sources of sustained funding.

The fragmented UK funding landscape for preclinical models is a barrier for developers to take models through all steps needed for model translation and validation. Participants therefore highlighted a need for UK funding that supports the entire model development pathway including translational and regulatory science. Participants also noted that the US Food and Drug Administration (FDA) has a mandate and budget for regulatory science research related to preclinical models, producing guidance and tools to be used by academia and industry. They suggested that the UK needs a comparable, sustained funding stream for regulatory science to support similar capability and impact.

> We need a concerted effort from UK funders to provide disease-agnostic, as well as any disease-specific, funding opportunities covering the entire pipeline of model development, all the way from development to translation and validation.
>
> **Professor Tony Ng FMedSci,** Senior Vice President and Head of Oncology Translational Research, GSK, and **Richard Dimbelby** Professor of Cancer Research, King's College London

Stronger collaboration to accelerate preclinical model development

A collaborative framework that aligns incentives for model developers, funders, industry and regulators is required to deliver on the potential of innovative preclinical models

One key reason for the translational readiness 'gaps' identified by the ABPI and NC3Rs report[12] is misalignment between academic and industry incentives for developing preclinical models. Academics often develop models to explore disease biology or to identify potential drug targets. By contrast, industry prioritises models that can be directly used to evaluate new medicines in drug development. CRO outsourcing further reduces the opportunities for early co-development.

Higher visibility of academic pipelines to industry (so that industry can identify alignment/opportunities) could accelerate model translation and adoption. Future initiatives, such as the UK preclinical translational models hub and the UKCVAM, will create collaborative opportunities for model development and validation. Participants noted the importance of ensuring that new investments do not become another part of a fragmented community.

Participants also highlighted a lack of access to the data, samples and compounds that academia requires to develop and validate new models. Industry expects robust validation standards while academia lacks access to usable, high-quality, standardised data and compound sets to benchmark new models. When data are shared, it is frequently non-standardised, obliquely formatted, or difficult to access, process or analyse without specialist tools. Cell and tissue supply and scale is a further barrier to academic developers. Commercial providers dominate the market and there is no coordinated system in the UK to access cells and samples at the scale needed to develop and standardise for industry.

Activities that build early-stage collaboration and trust between model developers, industry and regulators will be important to move the field forward. Such activities could allow stakeholders to identify opportunities for 'quick wins' – areas where collaborators could share non-commercially sensitive data, samples or provide funding and/or expertise to support standardising or scaling up a model. Some participants suggested that collaboration on diseases with high societal impact, such as dementia, could be a good starting point.

The pharmaceutical industry is also under continued pressure to routinely share clinical trial data.[13] As part of this broader conversation, participants emphasised the value that data from failed clinical trials and failed compounds could bring to academics, better enabling them to develop models that industry can have confidence in. Ideas included agreements to release a set number of datasets each year, to share 'control' arm data from clinical trials, to release a minimum set of standard compounds for benchmarking, and to share biobanked materials and data across networks.

Early engagement with regulators is required to determine the 'minimum data package' for a preclinical model – that is, the smallest set of validated, robust evidence a regulator needs to be confident that a given preclinical model is reliable enough to inform trial design, support inclusion criteria and justify progression of a medicine into human studies. Some participants highlighted that the rapid pace of preclinical model development makes it challenging for regulators to maintain the expertise required. Structured collaboration with model developers and users – such as sandboxes and regular dialogue – will be important to support effective model review.

12. Association of the British Pharmaceutical Industry (2026). *From models to medicines: a landscape review of human-relevant pre-clinical model development in the UK*. https://www.abpi.org.uk/publications/from-models-to-medicines-a-landscape-review-of-human-relevant-pre-clinical-model-development-in-the-uk/
13. Modi ND, *et al*. (2025). *The state of individual participant data sharing for the highest-revenue medicines. Clin Trials* **22(2)**,170–7

Ownership of preclinical models

Simplifying and streamlining intellectual property and licensing agreements for samples, data and models would facilitate academic and industry collaboration on preclinical model development.

The intellectual property (IP) and material-sharing agreement landscape can be challenging for the development of preclinical models. As highlighted earlier, use of proprietary technologies (e.g. commercial cell banks or proprietary software) to develop a model in academia hinders further development and translation. If not commercially sourced, ownership of materials (e.g. biobank samples and clinical data) often sits within universities, hospitals or academic biobanks that collected them, and comes with complex IP and ownership arrangements. This presents two key challenges.

First, IP negotiations between multiple parties can significantly slow down progress, creating barriers to industry engagement. For smaller companies, the cost of ongoing licensing to create a commercial product is a barrier to entry. If universities and hospitals coordinated their material-sharing processes and simplified the IP and licensing of samples and data, this could better attract industry looking to advance preclinical models.

Second, if regulators and pharmaceutical companies cannot access the original clinical data linked to a model, this creates a barrier for validation and review. Generally, these data sit with the biobanks, meaning they are the only party able to link samples used to develop patient-derived organoids back to patient information.

A concerted effort between academia, industry and regulators is needed to identify solutions to this challenge. This also relates to the need for early engagement with regulators about the minimum data package required, to understand the access they require to source data as part of their approval process.

When it comes to using and validating models, industry groups prefer newly developed models to be publicly available at first because wider scrutiny helps build consensus on what 'good' looks like from a regulatory perspective. However, once a model has commercial potential the IP position becomes more complex. In this regard, existing *in silico* models could be used as case studies for other types of preclinical models. *In silico* models are often open source but the raw data that underpins them are protected. It was suggested the same approach could be used to promote the use and validation of newly developed models.

To avoid loss of valuable research, the UK also needs to simplify the processes for biobanking of models and producing secure, futureproof systems for preserving the model materials, data and evidence underpinning them. This will create a foundation to accelerate progress and elevate the UK as a leader in preclinical model development and adoption.

Opportunity areas for preclinical model development

Attendees agreed that there was a great need for robust and reproducible models, incorporating the diversity of the patient population, in all areas of preclinical medical research. Advancing the most translationally ready models through validation and adoption would create exemplars of the evidence required for a model to be adopted and acceptable to regulators. Attendees highlighted opportunity areas where new model development could create such exemplars.

To inform activities of the UK ecosystem towards accelerating the development and use of preclinical models, participants highlighted disease areas where innovative preclinical models had the opportunity to transform medicine development in five years (Table 1). These opportunity areas were highlighted by participants for one or more reasons: (1) potential benefit to research across diseases; (2) unmet need; and/or (3) the relative scientific readiness of the existing preclinical models; and/or (4) availability of materials/tools to develop new models. In addition to those in Table 1, other disease areas that were highlighted include kidney disease, chronic obstructive pulmonary disease, endometriosis, and mental health. Endometriosis, for example, affects 10% of women but the disease mechanism is unknown and few models exist. Reproducing clinically relevant endpoints of mental health conditions in current animal models is difficult, and models rarely incorporate consideration of drug interactions or crosstalk.

There is also a lack of models for healthy physiological systems such as the microbiome, vasculature, brain, retina, blood–brain barrier and placenta. This makes it very challenging to study aspects of medicine development such as drug penetration across the blood–brain barrier or the placenta, or phenotypes such as vascular stiffness. A model of the microbiome that can reproduce the interplay between gut and liver function was also considered important.

Development of models that better reproduce the diversity of patient populations is a major unmet need, particularly as some diseases are more prevalent in certain ethnic populations. Recruitment of people from minority ethnic groups into clinical trials can be difficult, resulting in a lack of the clinical samples and data required to develop models. As a result, preclinical models are often less representative of these populations, meaning that approved medicines are less effective in real-world settings.

Some participants suggested a focus on the regulatory science (i.e. validation, standardisation, performance and scaling) that needs to happen to build the case for different model types (e.g. organoid, lab-on-a-chip). It was argued that funding should be disease-agnostic, and instead focus on technology advancement; prioritising one disease over another may fragment available expertise.

Table 1. Opportunities and challenges in highlighted disease areas

Disease area	Need	Challenges	Opportunity
Inflammation and autoimmunity	These processes are important drivers or features of many prevalent diseases. There are currently few preclinical models of these pathophysiological systems.	Defining how the immune system is interacting with a particular organ/system.	Immune involvement is currently being incorporated into diverse disease models, presenting many opportunities for shared learnings.
Metabolic liver diseases and liver cancer	Obesity-driven liver disease is becoming more prevalent.	Fibrosis models do not recapitulate complexity or evolution of patient disease. *In vivo* models of diet-induced diabetes and liver disease exist but are not standardised. Models of metabolic liver disease are not representative enough of human disease.	Data from the initiatives such as Human Liver Cell Atlas (HLiCA)[14] and the Billion Cell Atlas[15] are freely available for data mining, and are motivating 'digital twin' opportunities.
Neurodegenerative diseases	Neurodegeneration is increasingly prevalent in the ageing population.	Current human preclinical models rely on post-mortem patient samples and do not reproduce early-stage disease where disease-modifying therapies might be most effective.	Alzheimer's disease was identified as a key opportunity because of the abundance of longitudinal clinical data and the UK having one of the world's biggest brain banks. Data from longitudinal trials are beginning to be fed back to *in vitro* models.

14. Human Cell Atlas Data Portal. *Liver Network*. https://data.humancellatlas.org/hca-bio-networks/liver
15. Illumina. *The Illumina Billion Cell Atlas is here*. https://www.illumina.com/areas-of-interest/genomics-in-drug-development/cell-atlas.html

Disease area	Need	Challenges	Opportunity
Pregnancy and gestational diseases	Preclinical models of pregnancy-related and gestation conditions is an area of significant unmet need. Being born preterm affects health for life and is the costliest unmet medical need. There is little charity funding. Regulators support models to evaluate medicines for pregnancy and lactating women.	Risk appetite is low: companies generally do not want to use drugs until the end of the first trimester. Modelling the mother, placenta and foetus in combination brings additional complexity. First trimester and full-term models are required. Rodent and rabbit gestation does not map well to humans, and primates could be a more relevant model. Need to understand the relationship between efficacy and risk appetite – e.g. would a patient accept a lower efficacy if the drug were safer?	Opportunities to use *in silico* models and digital twins. Challenge studies in volunteers and research in non-pregnant women could inform models.
Children's cancers	Accuracy of preclinical models is a challenge, and there is a need to align clinical trials to models used to develop therapies.	Biology of late-stage tumours is very different to early-stage tumours. Children entering trials have usually been treated for a long time, so the samples used in models rarely reflect early-stage disease.	Good scientific readiness of some models of leukaemia and brain tumours.
Rare diseases	An area of high unmet need. Although rare diseases are rare for individual diseases, they are common if considered all together.	Lack of data due to small population sizes. Less investment from industry due to small potential reach.	Monogenic rare diseases can be more amenable to deriving stem cells for model development, and could be used as exemplar, where there is enough data to develop robust *in silico* and *in vitro* models. Rare diseases often have well-established patient advocacy groups and multinational research efforts. However, some are better networked than others. The smaller population numbers means less competitive space.

Annex 1

Chair: Professor Maddy Parsons FMedSci,
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Participants

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