

Bridging boundaries: making drug repurposing the new normal

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The potential for drug repurposing to provide faster, cost-effective ways to address unmet medical needs remains to be fully realized. Overcoming systemic challenges and promoting collaboration will be key for drug repurposing to contribute more to new treatments, especially for rare diseases.

Introduction

Drug repurposing identifies new uses for existing medicines, including approved drugs as well as investigational drugs that have demonstrated favourable pharmaceutical properties and human safety. This approach provides a compelling opportunity to develop urgently needed treatments, especially for conditions that may not otherwise attract commercial interest for de novo drug development, such as rare diseases. Together with its potential to reduce time and costs and thereby enhance the sustainability of healthcare systems, this has led to an active ecosystem engaged in drug repurposing R&D.

So why has drug repurposing not had greater impact on expanding the clinical utility of the existing pharmacopeia? We posit that this is because the ecosystem for drug repurposing has historically been fragmented, with investigators (especially those in academia) rarely able to access the full range of expertise, experience and perspectives required to take a project from the discovery stages all the way through to regulatory approval and patient access.

To address this, the International Drug Repurposing (iDR) conference series was conceived as a forum for understanding and overcoming systemic challenges to drug repurposing, and for facilitating collaborations to enable the success of individual projects, as well as of the ecosystem. Through its 2024 and 2025 editions, the iDR conference has convened over 600 thought leaders and speakers, including researchers, patients and patient advocacy groups, funders, regulators, policymakers and the biopharmaceutical sector. Here, we present insights from these conferences illuminating systemic challenges in drug repurposing and how these could be better addressed.

Unlocking the potential of drug repurposing

Patients at the centre of drug repurposing. Early, meaningful engagement of patients in setting research priorities and clinical trial design is key to ensuring the relevance and impact of repurposed therapies¹. Collaboration with patients is particularly important for rare diseases given the small populations and limited market incentives. Partnerships between academia, industry and patient organizations are critical to integrate diverse data sources and insights².

A prime example of patient-centred drug repurposing is **nitisinone**. This inhibitor of 4-hydroxyphenylpyruvate dioxygenase was first approved for hereditary tyrosinaemia type 1, in which it reduces the formation of toxic downstream metabolites such as succinylacetone. Alkaptonuria (AKU) results from deficiency of homogentisate 1,2-dioxygenase in the same pathway, leading to accumulation of homogentisic acid (HGA). By acting upstream, nitisinone reduces HGA production, providing a rationale for its use in AKU. The AKU Society helped mobilize the patient community and shape the clinical development strategy. In Europe, this effort was formalized through the **EU-funded DevelopAKUre consortium**, which brought together academic investigators, clinicians, patient organizations and industry partners to develop and support the SONIA clinical trials. These trials incorporated patient-relevant endpoints, including reduction in urinary HGA, and supported the EMA's 2020 approval of nitisinone for adult AKU. In the United States, the FDA approved nitisinone in 2025 based on a separate NIH-led study. Access in Europe continues to depend on national reimbursement decisions.

Systems-level understanding of disease pathways. Drug repurposing can leverage shared molecular targets, pathways and physiological mechanisms that link seemingly disparate conditions, as was done in the example of nitisinone for AKU. Another example is the repurposing of the kinase inhibitor alpelisib, originally approved for PIK3CA-mutated breast cancer, in treating PIK3CA-related overgrowth spectrum (PROS), which shares the same molecular target. This research led to the approval and the addition of PROS to the drug label of alpelisib (Viojo) by the **FDA in 2022**.

In addition to discrete targets and pathways, drugs that broadly modify physiological processes have also been prime candidates for repurposing. For example, sirolimus, an immunosuppressant approved to prevent transplant rejection, has been investigated for its potential to be repurposed to treat the soft-tissue sarcoma epithelioid haemangioma (EHE), based on the proinflammatory environment in tumour progression. The **EveryCure Foundation** grew out of a similar repurposing of sirolimus, in this case for Castleman's disease, which was discovered during a personalized treatment search for its founder.

Leveraging real-world data. Access to real-world data (RWD) has expanded greatly in recent years and can be a powerful approach to identify and validate drug repurposing opportunities. A notable example is the case of palbociclib, originally approved for women with metastatic breast cancer. Using RWD from multiple clinical datasets, researchers demonstrated that palbociclib exhibited comparable efficacy and safety in male patients, leading to **FDA approval** for its use in men in 2019 without the need for new clinical trials.

However, challenges remain, such as lack of standardization, privacy concerns and regulatory barriers. Improving data quality,

interoperability and incentives for data sharing are essential steps. The [European Health Data Space](#) (EHDS) aims to establish a standardized framework for secure EU-wide exchange of health data, including RWD.

Transformative change driven by AI/ML. Rapid progress in in silico methods, notably artificial intelligence/machine learning (AI/ML), is identifying drug repurposing opportunities at an unprecedented pace, complementing and boosting more traditional translational and high-throughput discovery approaches.

However, AI/ML methods are evolving so rapidly that there are concerns around how these new approaches can be most meaningfully validated. Emerging initiatives are beginning to address this gap. [REMEDI4ALL](#) contributed to systematizing the landscape through a published catalogue and review of publicly available in silico tools and databases, including resources based on RWD³. Related work from [REPO4EU](#) reinforces the importance of making AI/ML tools openly accessible, both to improve reproducibility and to support broader uptake. The growing focus on validation is further illustrated by a new programme from [Cures Within Reach](#), backed by the [Chan Zuckerberg Initiative](#), which aims to evaluate the predictive value of AI/ML drug repurposing platforms through proof-of-concept clinical trials.

Co-developing favourable policies for drug repurposing. Policy development is also moving beyond general support for repurposing toward practical mechanisms that can enable regulatory uptake. In the UK, the NHS Medicines Repurposing Programme illustrated how incentives for industry partners can help secure label extensions, as shown by anastrozole for breast cancer prevention. Similarly, the EMA/HMA STAMP pilot programme highlights growing regulatory interest in facilitating label extensions for approved drugs for which pivotal data may already exist⁴.

These programmes highlight the need for both ‘push’ and ‘pull’ mechanisms to enable and accelerate drug repurposing through to patient access. In this context, the Spanish Ministry of Health has outlined – [and has since begun to formalize](#) – initiatives to address the challenge of single fixed reimbursement rates. These include a policy strand on repurposing medicines outside their protection periods, accelerated, conditional or provisional reimbursement pathways for new indications, and pricing reforms intended to introduce greater flexibility and, as a general rule, to avoid penalizing the reimbursement price when a medicine gains a new indication. These measures are intended to reduce the risk that repurposed indications are undervalued despite substantial investment in data generation.

Current reimbursement policies can hamper patient access to successful drug repurposing efforts. For example, the LoDoCo2 trial⁵ demonstrated that a generic, low-cost treatment for gout, colchicine, could be repurposed for cardiovascular disease. This pivotal trial was conducted through a public–private partnership involving academic researchers, public agencies and three generic drug companies. Despite positive results, government payers in Europe have been reluctant to support a pricing premium for this new medical use. In the meantime, a biotech company not involved in the LoDoCo2 trial was able to secure [US FDA approval](#) in 2023 via the 505(b)(2) route, based solely on the published trial data. This case underscores the importance of reliable regulatory and reimbursement frameworks to support both public and private initiatives and investments to bring repurposed medicines to patients.

Funders as critical enablers. As the return on investment (ROI) in drug repurposing projects often falls short compared to new drug development, it is critical that financial resources are used effectively, with clear milestones and deliverables and good alignment with regulatory and health technology assessment frameworks. In addition, funding gaps and delays can be fatal to ROI; often half or more of a project timeline can be taken up by fundraising from one milestone to the next.

As such, funders can take a more active role in ensuring that drug repurposing projects are implemented effectively, but funding for projects from multiple sources is typically not well coordinated. To help address this systemic problem, the REMEDI4ALL Funders Network at iDR24 and iDR25 brought together over 30 charities, national and European funders, commercial investors, originators and generics companies to create more collaborative and coordinated funding strategies for drug repurposing. Key outputs included a ‘funding radar’ database of active calls, a practical guide to help design joint funding calls specifically for drug repurposing, and innovative funding approaches such as ‘longitudinal’ co-funding in which multiple funders collaborate in sequential and seamless milestone-driven co-investment strategies.

Industry’s role in drug repurposing. While drug repurposing has historically been mainly initiated by academics and patients, industry collaboration is essential for bringing repurposed medicines to patients. Under current regulations in most jurisdictions, only a current manufacturer of an approved drug product has standing to apply for a label extension to include a new repurposed indication.

Successes such as the repurposing of alpelisib illustrate how collaboration between stakeholders can bring transformative treatments to market. In this case, Novartis shared existing data from its oncology trials, and funded tailored clinical trials for PROS that were critical for [FDA approval](#). Another example is a REMEDI4ALL project for which AbbVie granted access to extensive internal preclinical, clinical and drug manufacturing data to enable repurposing of an oral formulation of tazarotene for treating multiple sulfatase deficiency; tazarotene has otherwise only been approved as a topical cream for acne and psoriasis.

Drug supply for clinical trials of repurposing candidates can be challenging, particularly for medicines that are not approved or not marketed across all jurisdictions. For example, a drug repurposing effort [recently showed](#) that nitroxoline, a urinary antibacterial agent, could be used to treat *Balamuthia mandrillaris* infection, a rare and usually fatal amoebic encephalitis. However, as nitroxoline is not marketed in the US, clinicians had to locate an overseas manufacturer and obtain emergency FDA authorization to access the drug. In Europe, where nitroxoline is approved, a path to regulatory approval may be more straightforward.

In the case of generics, pharmacy substitution of equivalent drug products adds yet another disincentive to industry involvement in drug repurposing. Repurposing sirolimus for EHE illustrates such obstacles, as the rarity of the disease and minimal commercial incentives have made consistent drug supply and formal industry involvement difficult to secure.

While off-label usage can be a stopgap, regulatory approval of new indications for existing drugs is always preferable in establishing clear usage guidelines and wider and more equitable patient access and reimbursement. However, in most jurisdictions only current marketing authorization holders have the standing to submit for drug label extensions but often lack motivation to do so, especially for rare diseases and low-priced generic drugs where commercial returns may not clearly support additional investment. In the EU, ongoing pharmaceutical legislation reform could open a new pathway for repurposing authorized medicines, but its impact remains prospective. Collaboration among all stakeholders will be crucial to translate such changes into practice.

The core takeaway from iDR discussions – and the central argument here – is that breaking down silos is key to unlocking the full potential of drug repurposing, enabling it to become the ‘new normal’.

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Published online: 6 May 2026

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Acknowledgements

The REMEDi4ALL project has received funding from the European Union's Horizon Europe Research & Innovation programme under grant agreement no. 101057442. This work reflects only the authors' views and the EC is not responsible for any use that may be made of the information it contains. The authors would like to thank the iDR programming and organizing teams for their efforts in designing and delivering the conferences.

Competing interests

The authors declare no competing interests.