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Second Chances for Medicines: The Promise of Drug Repurposing

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Opinion

The traditional paradigm for developing new medicinal products is increasingly unsustainable. Under typical circumstances, it requires approximately 12–15 years for a compound to progress from initial discovery to marketing authorization (1). This extended timeline and prohibitive cost structure underscore the urgent need for alternative strategies, particularly during global health crises and in the context of rare diseases. We must view drug repurposing not merely as a recycling of compounds, but as a distinct, pragmatic development pathway that leverages prior scientific investment to offer a faster, lower-risk route to therapeutic innovation (2).

Drug repurposing, also termed drug repositioning or rediscovery, involves the strategic identification of new therapeutic uses for existing drugs. By utilizing compounds that have already undergone substantial development and clinical evaluation, researchers can significantly reduce the time and capital typically required to bring therapy to patients. The concept of "new use" in this context is broad; it extends beyond targeting different diseases or mechanisms of action to include evaluation in new patient populations (e.g., pediatric use), alternative dosage forms, new routes of administration, or incorporation into novel combination regimens (3).

Although often portrayed as a modern solution, the practice is longstanding. Early instances, such as the use of mustard gas derivatives in oncology, established foundational principles for therapeutic redirection (4). However, interest has intensified as the limitations of conventional drug development, high attrition rates, and escalating costs have become pronounced. Consequently, repurposing is now recognized as a vital strategy to accelerate therapy development for diseases with unmet clinical needs (5). In parallel, computer-aided drug discovery (CADD) acts as a virtual accelerator. By streamlining candidate prioritization and predicting pharmacological effects, computational approaches improve the efficiency of matching existing compounds to new biological contexts (6).

The trajectory of sildenafil, initially developed by Pfizer in the 1980s for hypertension and angina, illustrates the power of this approach (7). As a phosphodiesterase type 5 (PDE-5) inhibitor, sildenafil was intended to relax vascular smooth muscle. While its benefits in cardiovascular indications were ambiguous in early studies, subsequent trials in the 1990s revealed consistent on-target effects in a different physiological domain. This led to its successful repositioning for erectile dysfunction (8). This case demonstrates how repurposing can convert a suboptimal development trajectory into a major therapeutic success when clinical observations align with actionable pharmacology.

The COVID-19 pandemic further highlighted the operational value of repurposing. Faced with an unprecedented global emergency, the scientific community rapidly evaluated existing therapies to identify effective treatments (9). Candidates ranging from antivirals like remdesivir and favipiravir to immunomodulatory biologics such as tocilizumab and anakinra were assessed for their roles in managing SARS-CoV-2 infection and associated inflammation (10). While outcomes varied, the broader lesson was

definitive: repurposing compresses early development timelines, enabling a faster transition to clinical testing and expanding therapeutic response capacity during crises.

Despite these advantages, drug repurposing faces persistent structural challenges. A primary barrier is the limited economic incentive for companies to invest in repurposing programs, particularly for drugs that have lost data exclusivity. Without a credible pathway to market protection, developers are reluctant to fund the expensive trials required for new indications (11). Consequently, much repurposing research is led by academic groups and nonprofits; yet, these stakeholders often lack the resources to conduct the large, definitive phase III trials needed to support regulatory decisions (12). To address this market failure, regulatory agencies should consider extending market exclusivity periods specifically for repurposed indications to make these investments viable for the industry.

To help bridge this gap, philanthropic organizations and public–private partnerships have mobilized resources. Initiatives such as the Health Innovation Challenge Fund, the Broad Institute's Drug Repurposing Hub, and the Repurposing Drugs in Oncology (ReDO) Project aim to reduce financial and logistical barriers (13). Such initiatives standardize workflows and increase the likelihood that promising repurposing signals progress to robust clinical evaluation. The potential of repurposing extends far beyond pandemic response, offering substantial promise for oncology, neurodegenerative disorders, and rare diseases. In rare diseases, repurposing is particularly impactful because it provides a viable development pathway that is often constrained by small patient populations and high uncertainty (14).

Looking ahead, advances in artificial intelligence and machine learning provide tools for extracting actionable hypotheses from large-scale datasets. In principle, these tools can identify novel drug–disease matches more rapidly than conventional approaches. However, a critical challenge remains for the biomedical engineering community: clinical utility is constrained when models are trained on biased data from well-studied diseases. To fully realize the promise of AI in this field, engineers must prioritize the generation of high-quality, unbiased datasets for underserved conditions. Coupling these predictions with experimentally testable mechanistic rationale is essential to unlock broader translational value (15).

Ultimately, drug repurposing holds promise as a route to safe, affordable, and timely therapies. Realizing this potential requires coordinated efforts to reduce financial friction, strengthen trial pathways, and incentivize the generation of high-quality evidence. Through sustained collaboration and the responsible integration of computational tools, repurposing can meaningfully reshape the therapeutic landscape—offering genuine second chances for medicines and new hope for patients worldwide.

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