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Review Article

Drug repurposing in personalized medicine: Translational pathways and recommendations

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Abstract

This review examines the integration of drug repurposing and personalized medicine as complementary approaches to transforming healthcare delivery. Drug repurposing identifies new therapeutic uses for existing medications with established safety profiles, while personalized medicine tailors treatments to individual patient characteristics. This integration offers reduced development time and costs, expanded options for rare and complex diseases, and targeted interventions based on patient-specific biomarkers. The manuscript explores translational pathways, including drug-centric, target-centric, and disease-centric approaches, as well as emerging computational and AI methodologies. Case studies in neurological disorders, oncology, and seizure disorders demonstrate successful applications. Despite promising outcomes, challenges persist across regulatory frameworks, intellectual property protection, data integration, and the management of biological variability among patients. Recommendations include strengthening regulatory support, developing robust validation pipelines, promoting open-source, collaborative models, and leveraging AI and big data technologies. Through coordinated stakeholder efforts, drug repurposing in personalized medicine can become a cornerstone of precision healthcare, providing more effective, patient-tailored treatments.

Keywords: Drug repurposing; Personalized medicine; Translational pharmacology; Precision healthcare; Biomarker-guided therapy

Introduction

Overview of drug repurposing and personalized medicine

Drug repurposing and personalized medicine are powerful, complementary approaches in modern healthcare. Drug repurposing, also known as drug repositioning, involves identifying new therapeutic uses for existing drugs [1]. This strategy leverages already available safety and efficacy data, enabling faster, more cost-effective pathways to clinical application. Traditionally, drug development is a long and costly process, often requiring over a decade and billions of dollars to bring a single new drug to market. Drug repurposing can bypass the need for early-stage trials, reducing both development time and financial burden [2]. Personalized medicine, on the other hand, focuses on tailoring treatments to each patient's individual characteristics, often based on genetic, biomolecular, and environmental factors [3,4]. By addressing patient-specific variations in disease mechanisms and responses to treatment, personalized medicine aims to optimize therapeutic efficacy and minimize adverse effects.

Combining these two approaches—repurposing existing drugs within a personalized framework- has the potential to rapidly expand therapeutic options for patients with rare, complex, or treatment-resistant diseases.

Rationale for integrating drug repurposing into personalized medicine

Integrating drug repurposing with personalized medicine offers a unique and promising solution to several unmet clinical needs. While drug repurposing expedites the introduction of treatments, personalizing these repurposed drugs allows for targeting specific mechanisms within an individual's pathology. Personalized drug repurposing is especially valuable in diseases with high interpatient variability, such as cancers, neurodegenerative diseases, and metabolic disorders, where generalized treatment approaches often fall short [5-9]. Furthermore, with the advent of high-throughput screening technologies, computational methods, and artificial intelligence, identifying viable drug repurposing candidates suited to an individual's biomolecular profile has become increasingly feasible. Together, these approaches underscore the transformative potential of repurposing in personalized medicine.

Benefits of drug repurposing in personalized medicine

Reduced development time and cost

Drug repurposing offers a significant reduction in development time and cost, key benefits that make it an attractive alternative to conventional drug development. Traditional drug discovery involves extensive preclinical studies and clinical trials, a process that can take 10-15 years and cost upwards of $2.5 billion [10]. Drug repurposing circumvents much of the early-stage development pipeline by focusing on compounds already tested in humans, enabling researchers to move directly into phase II or phase III trials. Repurposing a drug can therefore bring treatments to market in 3-12 years, often at less than a third the cost of novel drug development [9]. For personalized medicine, this shortened timeline is invaluable, as it enables the faster development of patient-specific therapies. By identifying repurposed drugs with mechanisms aligned to particular genetic, molecular, or phenotypic profiles, clinicians can rapidly provide tailored treatments to patients, particularly those with conditions that currently lack effective interventions [6]. For example, existing oncology drugs have been repurposed to target molecular pathways in non-cancer diseases, such as autoimmune disorders, where shared pathophysiological mechanisms exist [6,9]. This approach not only accelerates the availability of treatment but also makes personalized medicine more accessible to patients. To quantify these advantages, Table 1 compares typical timelines, costs, and clinical success rates for de novo discovery versus repurposed drugs.

Table 1. Development time, cost, and success metrics: de novo vs repurposed drugs.

Metric (median)	De-novo discovery	Repurposed drug (new indication)
Total development time (years)	10 – 15 years [11]	3 – 7 years [12]
Direct R & D cost (USD, billions)	≈ 1.4 B out-of-pocket; ≈ 2.6 B capitalized [11]	≈ 0.3 B [12,13]
Pre-clinical attrition (%)	45 % failure rate [14]	≤ 20 % (safety data already known)[10]
Phase II success ("go-to-III")	28 % average for novel NMEs [15]	≈ 55 % for repositioned assets [10]
Median FDA review time (months)	12 months standard NDA (505(b)(1)) [16]	6 – 13 months via 505(b)(2) pathway [16,17]

Enhanced treatment options for rare and complex diseases

Repurposing drugs expands treatment options, particularly for rare and complex diseases, where the lack of effective therapies poses a significant challenge. Diseases with low prevalence, such as rare genetic disorders, often receive limited attention in traditional drug development due to low market incentives [18]. Drug repurposing offers a viable solution to this issue by allowing the application of existing drugs with known safety profiles to new therapeutic areas.

In personalized medicine, the ability to repurpose drugs that target rare disease mechanisms enables treatments to be tailored to individual patients who may otherwise have limited options. For instance, drugs initially developed for inflammatory diseases have been repurposed for rare neuroinflammatory

disorders such as neuromyelitis optica, a severe autoimmune condition with limited treatment options [19]. In complex diseases with heterogeneous etiologies, such as Alzheimer's and Parkinson's disease, repurposing drugs offers a pathway to targeted therapies that address disease-specific molecular abnormalities.

Targeting patient-specific mechanisms and biomarkers

One of the primary goals of personalized medicine is to match patients with therapies tailored to their specific disease mechanisms, often determined by genetic or biomolecular markers. Drug repurposing aligns well with this goal, as it provides the flexibility to screen existing drugs for compatibility with patient-specific disease biomarkers. The availability of extensive drug libraries allows researchers to identify compounds that interact with unique disease targets, such as genetic mutations or dysregulated signaling pathways.

In personalized cancer therapy, for example, certain drugs initially approved for breast cancer have been successfully repurposed for tumors with similar genetic mutations in other tissues. Trastuzumab, a monoclonal antibody targeting the HER2 receptor, was originally developed for HER2-positive breast cancer but has since been repurposed for HER2-positive gastric cancer [20]. Such biomarker-driven repurposing has also been explored in neurodegenerative diseases, where drugs targeting tau or amyloid-beta aggregation pathways may provide personalized solutions for Alzheimer's patients with specific biomarker profiles.

Translational pathways for drug repurposing in personalized medicine

Drug-centric approach

The drug-centric approach to repurposing focuses on finding new applications for existing drugs based on their established pharmacological properties. This method is particularly advantageous for personalized medicine, as it allows direct testing of existing drugs against disease-specific targets without the need to design new compounds. Drugs like thalidomide, initially developed as a sedative, have been successfully repurposed for complex diseases like multiple myeloma and certain types of inflammatory disorders due to their immunomodulatory effects [21]. By employing a drug-centric approach, researchers can match available drugs to new indications based on the molecular mechanisms they modulate, thus facilitating rapid clinical translation.

Target-centric approach

In the target-centric approach, drug repurposing efforts are directed toward specific molecular targets known to play a role in the disease's pathology. This approach is particularly useful in personalized medicine, where patient-specific molecular or genetic abnormalities can be targeted precisely. For instance, the mammalian target of rapamycin (mTOR) pathway is commonly dysregulated in various cancers and neurodegenerative diseases, prompting research into repurposing mTOR inhibitors for targeted treatment [22-26]. Repurposing drugs based on shared molecular targets allows clinicians to bypass traditional pharmacodynamic screening and proceed directly to validation studies. The efficacy of mTOR inhibitors, like rapamycin and its analogs, in treating both cancer and neurodegenerative diseases illustrates the success of the target-centric approach [22]. Computational methods and omics data integration have made target-centric repurposing increasingly feasible, enabling rapid identification of drugs that can modulate key pathways linked to patient-specific biomarkers.

Disease-centric approach

The disease-centric approach to repurposing focuses on identifying drugs that target disease-modifying pathways [10,27]. This approach is particularly advantageous for conditions where disease mechanisms are not fully understood or where multiple overlapping pathways contribute to disease progression. For example, neurodegenerative diseases such as Alzheimer's and Parkinson's involve complex pathologies, including inflammation, oxidative stress, and protein aggregation. Repurposed drugs targeting these pathways can potentially alter disease trajectories and improve patient outcomes.

For instance, drugs such as anti-inflammatory agents, antioxidants, and autophagy enhancers have been repurposed for Alzheimer's based on their ability to modulate disease-related pathways [28-30]. Disease-centric repurposing is particularly relevant in personalized medicine, where targeting a patient's unique disease state rather than a specific biomarker allows for a more holistic approach to treatment. Moreover, a disease-centric approach supports the development of multi-target therapies, which are often essential for managing complex, multifactorial diseases [31]. Figure 1 illustrates the three complementary translational pathways—drug-centric, target-centric, and disease-centric—that converge on clinical validation and ultimately deliver patient-specific treatment outcomes.

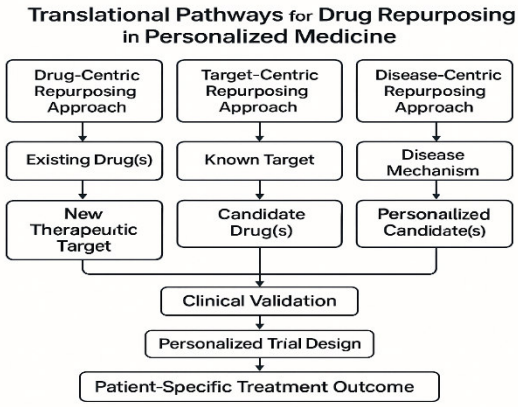

Figure 1. Translational pathways for drug repurposing in personalized medicine.

A flowchart depicting three parallel repurposing strategies-drug-centric, target-centric, and disease-centric—converging on clinical validation, personalized trial design, and ultimately patient-specific treatment

Emerging computational and AI approaches

Advances in computational biology and artificial intelligence (AI) have transformed drug repurposing by enabling the efficient screening of vast datasets to identify potential repurposing candidates [32]. AI-driven algorithms can analyze genomic, transcriptomic, and proteomic data to detect molecular similarities between diseases and predict candidate drugs that could modulate disease pathways [33]. These methods enable a more personalized approach by matching drugs to individual disease signatures or specific patient biomarker profiles. In personalized medicine, AI-based drug repurposing platforms facilitate the identification of compounds that can address patient-specific needs, thereby optimizing treatment efficacy and reducing adverse effects [34]. For example, machine learning models have been used to identify FDA-approved drugs that modulate gene expression patterns associated with neurodegenerative diseases, such as ALS and Huntington's disease [35-37]. This ability to predict drug-disease interactions based on patient-specific data accelerates the discovery of repurposing opportunities tailored to individual molecular profiles. Figure 2 illustrates how multi-omics-guided patient stratification feeds directly into adaptive and non-adaptive clinical-trial designs, forming the critical bridge from discovery to precision medicine.

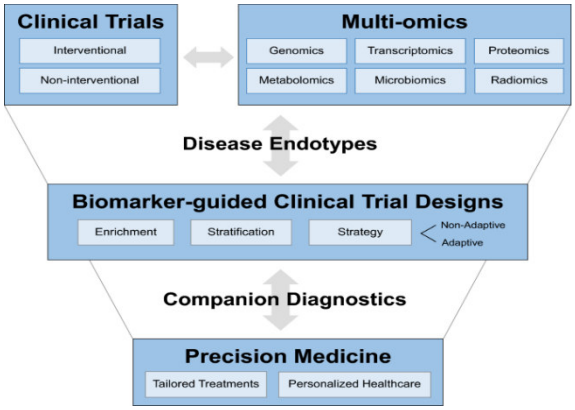

Figure 2. Flow of clinical trials—interventional or observational—integrating multi-omics profiling to delineate disease endotypes. Reproduced under CC BY 4.0 [38].

Case studies in drug repurposing and personalized medicine

Neurological disorders

The application of drug repurposing in personalized medicine has shown promising outcomes in the management of neurological disorders, which often lack effective treatments [39–42].

Neurodegenerative diseases like Alzheimer's, Parkinson's, and amyotrophic lateral sclerosis (ALS) involve multifaceted pathologies, including protein aggregation, mitochondrial dysfunction, oxidative stress, and inflammation. Repurposed drugs targeting these pathways can provide tailored treatments for patients based on specific disease mechanisms. For example, fingolimod, a drug initially approved for multiple sclerosis, has shown potential in targeting TDP-43 pathology associated with ALS [43]. TDP-43 proteinopathy, characterized by the accumulation of TAR DNA-binding protein-43, is present in various neurodegenerative diseases, including ALS and frontotemporal dementia. Using Drosophila models, researchers have demonstrated that fingolimod alleviates symptoms associated with TDP-43 toxicity [44,45], suggesting it as a candidate for ALS treatment. Similarly, the use of calcineurin inhibitors like cyclosporine A has been investigated in Alzheimer's disease, where neuroinflammation and calcium dysregulation contribute to cognitive decline [46-48]. Repurposing cyclosporine, which modulates calcineurin activity, could help slow disease progression in patients with specific biomarkers of calcineurin dysregulation [49].

Repurposing drugs for personalized neurodegenerative treatment allows clinicians to select therapies based on patient-specific markers, such as genetic mutations or proteinopathies, increasing the likelihood of therapeutic success. By stratifying patients based on biomarkers like TDP-43 or tau, drug repurposing offers a more targeted approach to managing these challenging diseases [50].

Oncology

Oncology has been a major beneficiary of drug repurposing, with numerous examples of repurposed drugs finding new applications in targeted cancer therapies. Cancer is a highly heterogeneous disease, with different mutations and pathways activated in different patients [51]. Repurposing drugs based on tumor-specific genetic alterations aligns well with the principles of personalized medicine, enabling targeting of specific oncogenic pathways or mutations. A well-known example is the use of non-cancer drugs, such as metformin, in oncology. Initially developed to treat type 2 diabetes, metformin has shown anticancer potential in specific patient subsets [52]. Studies indicate that metformin activates AMPK (adenosine monophosphate-activated protein kinase) and inhibits mTOR, a pathway implicated in cancer cell proliferation. This effect is especially beneficial in tumors with mutations in the PI3K-AKT-mTOR pathway. For patients with metabolic profiles that make their cancer cells more dependent on glycolysis, metformin serves as an effective adjunct to traditional chemotherapy, demonstrating the synergy between repurposing and personalization [52]. Another notable example is the repurposing of PARP (poly ADP ribose polymerase) inhibitors, initially designed for treating BRCA-mutated breast and ovarian cancers. These inhibitors have now been expanded to target cancers with homologous recombination repair deficiencies beyond BRCA mutations, such as those with PALB2 or RAD51 mutations [53]. In this way, repurposing PARP inhibitors for patients with broader mutation profiles has personalized cancer therapy options, expanding the reach of precision oncology.

Status epilepticus and seizure disorders

Status epilepticus, a prolonged seizure state with high morbidity and mortality, poses unique treatment challenges, particularly because drug resistance often develops over the course of the seizure [54]. Repurposed drugs targeting specific molecular mechanisms implicated in status epilepticus have shown promise as personalized treatments. Drug repurposing is especially valuable in this context due to the urgency of treatment and the limitations of current options. Benzodiazepine resistance, a common issue in refractory status epilepticus, has prompted the repurposing of drugs like ketamine and tacrolimus, both of which target NMDA receptors involved in excitotoxicity [55]. Additionally, AI and computational models have been used to identify potential repurposed candidates based on gene expression changes observed in seizure disorders [56,57]. For instance, recent studies have identified metformin as a potential neuroprotective agent for status epilepticus, due to its effects on mitochondrial

function and oxidative stress, pathways relevant to seizure-induced neuronal damage [58,59]. Such targeted repurposing provides an opportunity to address the specific mechanisms underlying seizure pathology, leading to better outcomes for patients with treatment-resistant forms of epilepsy.

Challenges and limitations of drug repurposing in personalized medicine

Regulatory and intellectual property challenges

One of the primary challenges in drug repurposing lies within regulatory and intellectual property barriers [60]. Regulatory agencies such as the FDA and EMA have stringent requirements for drug approval, and repurposed drugs, despite their prior approval for other indications, often require extensive clinical trials for new applications. Repurposed drugs can move through the regulatory pathway faster, but they must still undergo testing for efficacy and safety in the new context. This is particularly challenging for diseases with limited patient populations, as conducting large-scale trials may not be feasible. Intellectual property (IP) issues further complicate repurposing efforts. Once a drug loses patent protection, pharmaceutical companies have less incentive to invest in expensive clinical trials needed for repurposing, as generic competitors may benefit without bearing the development costs. This issue is especially prominent in personalized medicine, where therapies are designed for smaller patient populations. Policy changes, such as extended exclusivity periods or financial incentives, are needed to encourage drug repurposing in personalized medicine and make these investments more appealing to pharmaceutical companies.

Data integration and interoperability

Data integration and interoperability represent significant challenges in both drug repurposing and personalized medicine. Comprehensive repurposing efforts rely on diverse datasets, including genetic information, pharmacological profiles, electronic health records, and omics data [61]. However, consolidating and analyzing this data to identify suitable repurposing candidates is challenging due to the lack of standardized data formats and the limitations of current data-sharing frameworks. In personalized medicine, integrating patient-specific data from multiple sources, such as genomics, proteomics, and metabolomics, can help identify potential repurposing targets aligned with individual disease mechanisms [61,62]. Unfortunately, interoperability issues between data platforms, hospitals, and research institutions impede effective data integration. Overcoming these challenges requires developing universal data standards, interoperable systems, and secure platforms for data sharing. Open data initiatives and public-private collaborations could facilitate the data exchange necessary to drive repurposing efforts in personalized medicine.

Biological and patient variability

The success of drug repurposing in personalized medicine is often limited by the inherent variability in patient responses to treatment. Factors such as genetic background, epigenetics, environmental influences, and lifestyle all contribute to this variability, impacting the efficacy and safety of repurposed drugs. For example, while a drug may demonstrate efficacy in one subset of patients with a specific genetic profile, it may have limited or adverse effects in others [3,63]. Furthermore, many diseases exhibit considerable heterogeneity, meaning that what works for one individual may not work for another, even within the same disease classification. For instance, Alzheimer's disease patients may present with different biomarker profiles, indicating varied underlying mechanisms [64]. Thus, a repurposed drug targeting amyloid-beta accumulation may not be effective for patients whose pathology is primarily driven by tau protein abnormalities. Personalized approaches to repurposing require advanced biomarker screening and patient stratification to ensure that treatments are appropriately matched to individual needs.

Recommendations for advancing drug repurposing in personalized medicine

Enhancing regulatory support and incentives

To overcome the regulatory and intellectual property challenges, there is a need for enhanced support from regulatory agencies, including streamlined approval processes and incentives for drug repurposing [65]. One approach could be to create a specific pathway for repurposed drugs with established safety profiles, enabling expedited approvals when unmet clinical needs exist. Additionally, extending market exclusivity for repurposed drugs or providing tax credits could incentivize pharmaceutical companies to invest in repurposing efforts. A regulatory framework that allows for partial exclusivity—covering only the repurposed indication—would also help reduce market competition, ensuring that companies recover the costs of additional clinical trials. In cases where data on repurposed drugs are collected through public research funding, government programs could provide supplementary grants to support their clinical translation. Enhanced collaboration between regulatory agencies and research organizations would facilitate a smoother path to market for repurposed drugs, ultimately making personalized treatments more accessible [2,66].

Developing robust translational and validation pipelines

Advancing drug repurposing in personalized medicine requires robust translational and validation pipelines that enable rapid movement from discovery to clinical application. Preclinical studies using patient-derived models, such as organoids or iPSC-based systems, can help validate drug efficacy in a personalized context before moving to clinical trials [67]. Additionally, integrating translational research with clinical data collection enables researchers to rapidly identify drugs that perform well in real-world settings. To strengthen these pipelines, research institutions, pharmaceutical companies, and regulatory agencies must collaborate in designing validation frameworks that prioritize repurposed drugs for high-impact diseases. Real-world evidence, collected from electronic health records and patient registries, can serve as a valuable resource for validating the clinical effectiveness of repurposed drugs. Developing these pipelines ensures a continuous flow of candidates from discovery through clinical implementation, especially in areas of high unmet medical need.

Collaborative and open-source models

Collaboration is crucial for advancing drug repurposing, particularly within the scope of personalized medicine. An open-source model in which pharmaceutical companies, academic institutions, and government agencies collaborate and share data could accelerate repurposing initiatives. By sharing clinical trial data, drug libraries, and patient health information (in compliance with privacy standards), these stakeholders can collectively overcome the limitations of individual drug discovery efforts [68]. Public-private partnerships are also essential in pooling resources and expertise to tackle complex, multifactorial diseases that require personalized approaches. For instance, the NIH's Accelerating Medicines Partnership (AMP) program collaborates with biopharmaceutical companies, patient organizations, and government agencies to develop more effective therapies through open science [69,70]. In personalized medicine, such partnerships could focus on generating shared databases of patient-specific responses to repurposed drugs, enabling more efficient identification of candidates tailored to individual disease mechanisms. An open-source model also facilitates the use of large, diverse datasets to support AI-driven drug repurposing algorithms [71]. By granting access to extensive pharmacological and clinical data, stakeholders can improve the accuracy of predictive models, enabling faster, more precise identification and validation of repurposed drugs. Open-access databases like Drug Bank, which compile detailed information on drugs and their targets, are valuable resources that could be expanded through collaborative contributions, driving forward both drug repurposing and personalized treatment initiatives.

Leveraging AI and big data for personalized repurposing

Artificial intelligence and big data analytics are transformative tools in the drug repurposing field, enabling the rapid analysis of vast datasets to match drugs with new therapeutic uses based on patient-specific variables [72]. AI algorithms, such as machine learning and deep learning, can analyze complex datasets from genomics, transcriptomics, proteomics, and electronic health records to identify patterns and predict drug-disease interactions [33,73,74]. In personalized medicine, these algorithms help match patients to therapies that align with their molecular profiles, thereby optimizing treatment efficacy and minimizing adverse reactions. For example, AI-driven platforms can predict how drugs will interact with specific genetic mutations, aiding in the identification of repurposing candidates for genetically stratified patient groups[74]. By leveraging data from sources like the Genomics England dataset or the Cancer Genome Atlas, AI can help researchers identify drugs that might modulate pathways implicated in a patient's disease. Additionally, algorithms that analyze real-world evidence can determine which repurposed drugs show efficacy in practice, offering insights that clinical trials alone may not reveal.

Integrating big data with AI in drug repurposing could also benefit rare disease research. In cases where limited patient numbers make clinical trials challenging, AI can analyze historical data to suggest potential treatments, allowing clinicians to make more informed choices based on similar patient profiles. As AI continues to evolve, incorporating predictive modeling into drug repurposing strategies will be critical in scaling personalized medicine, ensuring that patients receive therapies aligned with their unique health profiles [72].

Conclusion

This review demonstrates that drug repurposing, when coupled with emerging computational platforms and biomarker-led clinical designs, can compress discovery timelines, reduce development costs, and increase the probability of regulatory success while advancing the goals of personalized medicine. By analysing time-and-cost benchmarks, we showed that repositioned compounds routinely move from concept to market in fewer than seven years, less than half the time required for de-novo chemical entities, and at a fraction of the out-of-pocket spend. Case studies such as dexamethasone and baricitinib highlight how rapid in silico triage, followed by targeted experimental validation, can accelerate the journey from bench signal to a positive randomized-controlled-trial outcome.

Our survey of regulatory frameworks revealed that adaptive pathways—505(b)(2) in the United States, orphan-drug incentives in multiple jurisdictions, and collaborative pre-qualification schemes further streamline approvals while providing additional exclusivity, thereby lowering commercial barriers and encouraging industry participation [17]. Equally important, the integration of multi-omics data sets with machine-learning algorithms now enables drug–disease signature matching at unprecedented scale [61,73]. These tools refine candidate selection, inform mechanism-of-action hypotheses, and, when paired with basket or umbrella trial designs, make it feasible to align repurposed drugs with molecularly defined patient sub-groups. Despite these advances, challenges remain. Data interoperability, access to high-quality real-world evidence, and equitable availability of biomarker diagnostics are uneven across health-care systems. In addition, AI-driven predictions still require rigorous prospective validation to avoid false-positive leads and to mitigate bias.

Future priorities should therefore include: (i) establishing open, standardized data commons that continuously feed and benchmark AI pipelines; (ii) expanding biomarker-guided master-protocol trials to validate repurposed agents rapidly across multiple endotypes; (iii) harmonizing global regulatory guidance to balance speed with safety; and (iv) ensuring that biomarker testing and repurposed therapies are affordable and accessible in both high- and low-resource settings. Implementing these measures will transform drug repurposing from an opportunistic strategy into a reproducible pillar of precision medicine, delivering timely, cost-effective, and patient-tailored treatments worldwide.

Ethics approval and consent to participate

Not applicable. This study is a review article and does not involve human subjects or animal experiments.

Consent for publication

Not applicable

Availability of data and materials

All data analyzed in this review were obtained from publicly available sources cited in the references.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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