

From Molecular Targets to Clinical Outcomes: A Comprehensive Review of Drug Discovery and Trials

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Abstract: Drug discovery is a multifaceted process that transforms fundamental insights about molecular targets into clinically effective therapies. This review outlines the continuum from target identification and validation to preclinical optimization and subsequent clinical evaluation. We highlight advances in computational modeling, high-throughput screening, and biomarker-guided approaches that have accelerated early discovery and improved candidate selection. Key phases of clinical development—ranging from first-in-human safety studies to pivotal efficacy trials—are examined with attention to evolving regulatory frameworks and the integration of adaptive and platform trial designs. Persistent challenges, including translational gaps, variable patient responses, and late-stage attrition, are discussed alongside emerging solutions such as precision medicine and real-world evidence. By tracing the journey from molecular mechanism to patient outcomes, this review underscores the importance of collaborative innovation and rigorous evaluation in modern therapeutic development.

Keywords: Drug discovery, Molecular targets, Clinical trials, Translational medicine, Target identification

I. INTRODUCTION

The modern pharmaceutical industry represents one of humanity's most complex and expensive endeavors, transforming scientific understanding into life-saving therapeutics through an intricate pipeline spanning discovery, development, and clinical validation. Despite unprecedented advances in molecular biology, computational methods, and clinical science, the drug discovery process remains characterized by high failure rates, extended timelines, and escalating costs, with only approximately 10-15% of drug candidates successfully progressing from preclinical studies to regulatory approval⁽¹⁾. This comprehensive review examines the complete drug discovery continuum, from initial target identification through clinical outcomes, highlighting both remarkable successes and persistent challenges while exploring emerging technologies and methodologies that promise to transform this critical field.

Target Identification and Validation: The Foundation of Drug Discovery

The contemporary drug discovery process begins with target identification, a critical phase that establishes the molecular foundation for therapeutic intervention⁽²⁾. Modern target identification employs diverse methodologies, including genomic and proteomic analyses, to characterize the molecular abnormalities underlying disease states^(2,3). High-throughput screening (HTS) methodologies have revolutionized this process by enabling systematic evaluation of thousands to millions of compounds against potential targets, utilizing automated equipment to maximize reproducibility and output^(2,4).

Target validation represents a dual challenge requiring confirmation that the molecular target causes human disease and that drug molecules can effectively modulate the intended target. Genetic and genomic methodologies, including CRISPR gene editing and siRNA knockdown techniques, provide essential tools for target validation in cellular and animal models. However, significant discrepancies often exist between in vitro and in vivo systems, as well as between animal disease models and human pathophysiology. These biological discrepancies pose fundamental challenges for



first-in-class drug discovery programs, where full target validation may only be achieved upon successful drug development⁽¹⁾.

Contemporary approaches to target identification leverage computational inference methods that employ pattern recognition to analyze small-molecule effects compared to known reference compounds or genetic perturbations. Chemical similarity approaches, such as the similarity ensemble approach (SEA), quantitatively group related proteins based on chemical similarity of their ligands, often revealing unexpected biological relationships that differ from protein sequence-based classifications. Additionally, genetic interaction methods utilize the principle that gene knockdown phenotypes may recapitulate compound effects, strengthening evidence for target-compound relationships⁽⁵⁾.

The advent of artificial intelligence has significantly enhanced target identification capabilities, with machine learning algorithms capable of analyzing vast biomedical datasets to uncover hidden relationships between drugs and diseases^(6,7). AI-driven approaches can identify novel therapeutic targets by analyzing genomic, proteomic, and clinical data patterns that exceed human analytical capabilities^(7,8). However, these computational methods face challenges related to data bias, limited interpretability, and the need for robust validation in biological systems^(9,10).

Lead Discovery and Optimization: From Hits to Candidates

Following target validation, the drug discovery process transitions to hit identification and lead optimization, phases characterized by systematic structure-activity relationship (SAR) investigations. High-throughput screening remains the predominant method for identifying hit molecules, involving automated evaluation of compound libraries against drug targets or cell-based assay systems. Alternative screening approaches include focused screening using compound subsets likely to demonstrate target activity, fragment screening employing small molecular weight compounds at high concentrations, and virtual screening utilizing computational docking methods⁽³⁾.

Lead optimization programs systematically refine hit compounds to enhance potency, selectivity, and drug-like properties while ensuring adequate pharmacokinetic characteristics for in vivo efficacy evaluation. Structure-based drug design techniques, incorporating molecular modeling and X-ray crystallography, enable more focused optimization approaches by providing detailed insights into compound-target interactions. These methodologies can accelerate SAR development and facilitate discovery of novel binding sites on target proteins⁽³⁾.

AI methodologies have demonstrated particular promise in lead discovery and optimization, with machine learning algorithms capable of analyzing structural features, physicochemical properties, and molecular interactions to prioritize compounds with highest therapeutic efficacy likelihood^(8,11). Deep learning approaches, particularly graph neural networks, excel at molecular representation and property prediction, while generative AI models show transformative potential in molecular design⁽⁸⁾. Recent advances include tools like DiffDock, which revolutionize molecular docking within lead discovery workflows⁽⁸⁾.

The optimization process encompasses comprehensive ADMET (absorption, distribution, metabolism, excretion, and toxicity) property evaluation⁽¹¹⁾. AI-based ADMET prediction models provide increasingly accurate assessments of drug-like properties, though they require continued validation against human clinical data^(10,11). Machine learning approaches for toxicity prediction have shown particular utility, with the potential to identify toxic effects before human clinical trials, potentially reducing the estimated 30% of drug candidates discarded due to toxicity concerns⁽¹⁰⁾.

Preclinical Development: Safety and Efficacy Foundations

Preclinical development encompasses comprehensive safety and efficacy evaluation in laboratory and animal model systems before human studies. This phase typically requires 4-7 years and includes rigorous characterization of lead compounds through in vitro and in vivo experimental models that approximate human physiology as closely as possible. The primary objective involves establishing compound safety profiles through extensive toxicity testing, ensuring candidates are not harmful before proceeding to human clinical trials⁽¹²⁾.

Preclinical efficacy studies utilize disease models that recapitulate key aspects of human pathophysiology, though significant limitations exist in translating animal model results to human clinical outcomes. These translational failures



represent a major contributor to clinical trial failures, with preclinical experiments in cells, tissues, and animal models serving as imperfect representations of human disease. Small sample sizes in preclinical experiments may also generate false positive results that only become apparent during costly clinical trials⁽¹³⁾.

Current preclinical development increasingly incorporates biomarker identification and validation to support clinical trial design and patient stratification^(14,15). Biomarkers serve as measurable indicators of biological processes, pathogenic processes, or therapeutic responses, providing crucial tools for drug development decision-making. The FDA has established a structured biomarker qualification process involving Letter of Intent, Qualification Plan, and Full Qualification Package submissions⁽¹⁶⁾.

Advanced methodologies such as organoid systems and organ-on-chip technologies are emerging as potentially superior alternatives to traditional animal models. Organoid intelligence, a novel field utilizing brain organoids for biocomputation, represents a cutting-edge approach that may revolutionize pharmaceutical testing while providing new insights into brain function⁽¹⁷⁾. These technologies offer the potential for more accurate human-relevant models while addressing ethical concerns regarding animal testing.

Clinical Trial Phases: Human Validation of Therapeutic Hypotheses

Clinical development represents the most expensive and time-intensive phase of drug development, typically spanning 6-12 years with costs often exceeding \$1 billion per approved drug⁽¹⁾. The clinical trial process follows a structured progression through three main phases, each with distinct objectives and increasingly larger patient populations^(12,18).

Phase I clinical trials represent the first human studies, typically involving 20-100 healthy volunteers or patients with the target disease. The primary objectives include establishing safety profiles, determining safe dose ranges, and characterizing drug absorption and metabolism. Approximately 70% of compounds successfully complete Phase I trials and advance to Phase II studies. Phase I trials carefully monitor drug-human body interactions and adjust dosing schemes based on animal data to identify maximum tolerated doses and acute side effects⁽¹⁹⁾.

Phase II trials evaluate drug efficacy and side effects in 100-300 patients with the specific target disease^(12,18). These studies determine therapeutic dose ranges and gather preliminary efficacy data to support Phase III trial design⁽¹²⁾. Phase II typically requires up to two years to complete and demonstrates significantly lower success rates, with approximately 28.9% of compounds advancing to Phase III⁽¹⁸⁾.

Phase III trials represent the definitive efficacy and safety evaluation, typically involving 1,000-3,000 patients across multiple clinical sites^(12,18). These studies provide regulatory evidence for market approval, with success rates of approximately 57.8%⁽¹⁸⁾. Phase III trials comprehensively document side effects and establish the risk-benefit profile that will appear in product labeling⁽¹²⁾. These studies require 1-4 years to complete and generate the primary evidence base for regulatory submissions⁽¹²⁾.

Recent innovations in clinical trial design include adaptive trial methodologies that allow protocol modifications based on accumulating data, potentially reducing development timelines and patient exposure to ineffective treatments⁽²⁰⁾. Biomarker-guided trial designs enable patient stratification and targeted therapy approaches, improving trial efficiency and success rates⁽¹⁵⁾. Real-world evidence integration is increasingly recognized as a valuable complement to traditional clinical trial data⁽²¹⁾.

Regulatory Approval: Ensuring Safety and Efficacy Standards

Regulatory approval processes ensure that marketed drugs provide benefits that outweigh their known and potential risks for intended patient populations⁽²²⁾. The FDA approval framework includes comprehensive analysis of target conditions and available treatments, assessment of clinical benefits and risks from submitted data, and implementation of risk management strategies⁽²²⁾. Generally, regulatory agencies expect results from two well-designed clinical trials to confirm findings are not due to chance or bias, though convincing evidence from single trials may suffice for rare diseases⁽²²⁾.

International regulatory harmonization efforts, led by organizations such as the International Council for Harmonisation (ICH), work to align technical requirements for pharmaceutical development and marketing^(21,23). ICH develops internationally harmonized guidelines covering Safety, Efficacy, Quality, and Multidisciplinary topics, promoting



greater efficiency in regulatory review processes and reducing unnecessary duplication of clinical trials^(21,23). The Common Technical Document (CTD) format has been widely adopted to standardize regulatory submissions globally⁽²¹⁾.

Regional regulatory approaches vary significantly, with the United States employing a single-agency system through the FDA, while Europe utilizes multiple pathways including centralized, decentralized, and mutual recognition procedures⁽²⁴⁾. The centralized procedure enables single applications for marketing authorization valid across all EU member states, while decentralized and mutual recognition procedures allow approval in multiple member states through coordinated review processes⁽²⁴⁾.

Biomarker qualification represents an increasingly important component of regulatory approval, with FDA implementing structured processes for validating biomarkers as drug development tools⁽¹⁶⁾. The 21st Century Cures Act established transparency requirements for biomarker qualification, including public posting of submission summaries and FDA determinations⁽¹⁶⁾. Qualified biomarkers may be utilized across CDER drug development programs to support regulatory approval decisions⁽¹⁶⁾.

Current Challenges and Persistent Failures

Despite decades of scientific advancement and process optimization, clinical drug development continues to exhibit failure rates exceeding 90%^(1,13). Analysis of clinical trial data from 2010-2017 identifies four primary failure categories: lack of clinical efficacy (40-50%), unmanageable toxicity (30%), poor drug-like properties (10-15%), and commercial/strategic planning issues (10%)⁽¹⁾. The persistence of such high failure rates despite extensive methodological improvements raises fundamental questions about overlooked aspects of drug development processes⁽¹⁾. True target validation remains a fundamental challenge, requiring confirmation that molecular targets cause human disease and represent appropriate therapeutic intervention points⁽¹⁾. The biological discrepancies between preclinical models and human disease often lead to false target identification, only discovered during expensive clinical trials^(1,13). Additionally, drug molecules may exert pharmacological effects through unintended molecular targets different from their presumed mechanisms of action⁽¹⁾.

Current drug optimization processes may overemphasize molecular potency and selectivity while inadequately addressing tissue exposure and selectivity profiles⁽¹⁾. The Structure-Tissue exposure/selectivity-Activity Relationship (STAR) concept suggests that optimal drug candidates require not only high potency and specificity for molecular targets but also appropriate tissue exposure patterns that maximize efficacy while minimizing toxicity⁽¹⁾. Neglecting tissue-specific exposure patterns may mislead candidate selection and compromise the delicate balance between clinical dose, efficacy, and toxicity⁽¹⁾.

Academic drug discovery faces particular challenges in transitioning from research publications to clinical development⁽²⁵⁾. Analysis of recent literature reveals that over 90% of drug discovery research articles conclude at preclinical stages, indicating a substantial gap between drug discovery and development⁽²⁵⁾. This translational deficit results from inadequate synergy between academia and industry, lack of streamlined development processes, and insufficient resources for advancing promising discoveries through clinical validation⁽²⁵⁾.

Artificial Intelligence: Transforming Drug Discovery Paradigms

Artificial intelligence is revolutionizing drug discovery by addressing traditional limitations related to high costs, lengthy timelines, and low success rates^(7,8,11). Machine learning algorithms can analyze vast chemical and biological databases to identify novel therapeutic targets, predict drug-target interactions, and optimize molecular structures with unprecedented speed and accuracy^(7,11). The global AI in drug discovery market, valued at \$1.9 billion in 2024, is projected to reach \$9.1 billion by 2030, reflecting the transformative potential of these technologies⁽²⁶⁾.

AI applications span the entire drug discovery pipeline, from target identification through clinical development^(8,27). Deep learning architectures, including convolutional neural networks and graph neural networks, excel at molecular representation and property prediction^(8,11). Natural language processing techniques facilitate literature mining and knowledge integration, while reinforcement learning approaches enable automated molecular design and



optimization⁽²⁷⁾. Recent successes include AlphaFold's protein structure prediction capabilities, which have provided structural insights for over 200 million proteins⁽⁷⁾.

Biotech companies leveraging AI have accumulated 158 small-molecule drugs in preclinical discovery, with approximately 15 already in clinical trials⁽²⁶⁾. The combined pipeline of AI-focused companies represents approximately 50% of big pharma's preclinical output, suggesting significant industry impact⁽²⁶⁾. Preliminary data suggests 80-90% success rates for AI-derived molecules in Phase I trials, declining to approximately 40% during Phase II trials⁽²⁸⁾.

However, AI implementation faces significant challenges including data quality limitations, model interpretability concerns, and potential exacerbation of healthcare disparities^(10,29,30). Biased training datasets may perpetuate existing inequities in drug development, particularly affecting underrepresented populations⁽³⁰⁾. Additionally, AI models require extensive validation in biological systems, and their predictions must be confirmed through traditional experimental approaches^(8,10).

Biomarkers and Precision Medicine: Tailoring Therapeutic Approaches

Biomarkers serve as quantifiable indicators of biological processes, pathogenic mechanisms, or therapeutic responses, providing essential tools for drug development and clinical decision-making^(15,31). The integration of biomarker strategies throughout drug development enables improved target validation, patient stratification, treatment monitoring, and safety assessment⁽¹⁴⁾. Successful biomarker implementation requires rigorous analytical and clinical validation to establish performance characteristics and clinical utility⁽¹⁵⁾.

Precision medicine approaches utilize individual genomic, environmental, and lifestyle information to guide medical management decisions^(32,33). In oncology, precision medicine has achieved notable successes through targeted therapies and immunotherapies tailored to specific molecular characteristics of tumors⁽³²⁾. Over 144 precision medicine drugs are currently available, including 107 targeted therapies and 37 immunotherapies⁽³²⁾. However, current precision medicine practices remain largely focused on biological data within biomedical frameworks, potentially neglecting broader determinants of health⁽³²⁾.

Pharmacogenomics represents a rapidly advancing component of precision medicine, utilizing genetic variations to predict drug responses and optimize therapeutic selection⁽³⁴⁾. Next-generation sequencing (NGS) technologies enable comprehensive genomic profiling to identify variants that influence drug metabolism, efficacy, and toxicity⁽³⁴⁾. The FDA has developed flexible regulatory approaches to accommodate NGS test validation while leveraging consensus standards and open-source computing technologies⁽³⁴⁾.

Biomarker-driven clinical trial designs demonstrate improved efficiency and success rates by enabling patient stratification and treatment selection based on molecular characteristics. Examples include the FDA approval of pembrolizumab for microsatellite instability-high tumors across multiple cancer types, representing the first tissue-agnostic approval based on biomarker status. Such approaches require coordination between drug development and companion diagnostic development to ensure appropriate patient identification⁽¹⁵⁾.

Global Access and Pharmaceutical Pricing: Equity Challenges

Pharmaceutical pricing represents a critical determinant of global health equity, with significant disparities in drug access across socioeconomic and geographic boundaries^(35,36,37). High-income countries often achieve lower drug prices through sophisticated negotiation mechanisms and purchasing power, while low- and middle-income countries may lack infrastructure for similar arrangements⁽³⁶⁾. These disparities create scenarios where life-saving medications remain accessible in wealthy nations while being unavailable in resource-limited settings⁽³⁶⁾.

Drug pricing policies must balance affordability for patients with incentives for pharmaceutical innovation, ensuring healthcare system sustainability⁽³⁸⁾. Value-based pricing models link drug costs to demonstrated clinical and economic benefits, while reference pricing systems establish benchmark prices for therapeutically equivalent medications^(37,38). International reference pricing approaches utilize price comparisons across countries to inform local pricing decisions, though implementation in large markets like the United States may impact global innovation incentives⁽³⁹⁾.



The orphan drug market presents unique pricing challenges, with specialized treatments for rare diseases commanding high prices due to limited patient populations and extensive development costs^(40,41). Despite regulatory incentives including tax credits, grants, and market exclusivity periods, over 7,000 rare diseases continue to lack approved treatments⁽⁴¹⁾. The global orphan drug market, valued at \$200 billion in 2020, is projected to reach \$400 billion by 2030, reflecting growing investment in rare disease therapeutics⁽⁴¹⁾.

Medicine shortages represent an increasingly critical global challenge, affecting access to essential treatments and placing additional pressure on healthcare systems⁽⁴²⁾. Causes include manufacturing problems, pricing policies, and parallel export practices that disrupt supply chains⁽⁴²⁾. Effective collaboration between stakeholders including manufacturers, distributors, regulators, and healthcare providers is essential for addressing shortage issues⁽⁴²⁾.

Recent Innovations and Success Stories

The past decade has witnessed remarkable advances in therapeutic modalities, with cell and gene therapies achieving significant clinical successes^(43,44). Forty-three cell and gene therapy products have received FDA approval to date, with seven new approvals in 2024 alone^(43,44). CAR-T cell therapies represent the largest single category with seven approved products, while umbilical cord blood derivatives account for nine approvals⁽⁴³⁾. Recent milestones include the first tumor-infiltrating lymphocyte therapy (Amtagvi) for solid tumors and the first T-cell receptor therapy (Tecelra) for synovial sarcoma⁽⁴⁴⁾.

Immune checkpoint inhibitors have revolutionized cancer treatment, with monoclonal antibodies targeting CTLA-4, PD-1, and PD-L1 demonstrating unprecedented clinical efficacy across multiple cancer types^(45,46). The first approved immune checkpoint inhibitor, ipilimumab, improved survival in metastatic melanoma patients and opened the gate for subsequent PD-1 and PD-L1 inhibitor development^(45,46). Alternative approaches including small-molecule checkpoint inhibitors, aptamers, and bispecific agents are emerging to address limitations of current monoclonal antibody therapies⁽⁴⁶⁾.

Gene therapy achievements include notable successes in inherited disorders, with recent approvals for hemophilia B (Beqvez), aromatic L-amino acid decarboxylase deficiency (Kebilidi), and sickle cell disease (Casgevy)^(43,44). These approvals demonstrate the maturation of gene therapy platforms and their potential for treating previously intractable genetic conditions⁽⁴⁴⁾. Additionally, the first gene editing therapy (Casgevy) represents a watershed moment for CRISPR-based therapeutic applications⁽⁴⁴⁾.

Drug repurposing initiatives have achieved significant successes by identifying new therapeutic applications for existing medications⁽⁴⁷⁾. This approach offers dramatically reduced development costs and timelines compared to de novo drug discovery, making it particularly attractive for addressing unmet medical needs⁽⁴⁷⁾. Examples include colchicine for cardiovascular disease, methotrexate for inflammatory conditions, and various approaches for COVID-19 treatment^(47,48).

Future Directions and Emerging Technologies

The future of drug discovery will likely be characterized by increased integration of AI technologies, advanced biological models, and precision medicine approaches^(7,8,29). Quantum computing applications in drug discovery show particular promise for analyzing complex biological systems and optimizing molecular interactions at unprecedented scales^(28,49). Companies like Kvantify and Qubit Pharmaceuticals are developing quantum software specifically for drug discovery applications⁽²⁸⁾.

Organoid intelligence and brain-computer interfaces represent frontier technologies that may revolutionize pharmaceutical testing and provide novel insights into human biology⁽²⁷⁾. These biocomputing systems combining biological tissues with digital interfaces offer the potential for more accurate human-relevant models while raising important ethical considerations regarding consciousness and rights of biological systems⁽²⁷⁾.

Advanced delivery systems including lipid nanoparticles, antibody-drug conjugates, and protein degraders represent emerging therapeutic modalities with significant potential⁽⁵⁰⁾. The success of mRNA vaccines has highlighted the versatility of lipid nanoparticle delivery systems, while proteolysis-targeting chimeras (PROTACs) offer novel approaches for targeting previously undruggable proteins^(46,50).



Real-world evidence integration will likely play an increasingly important role in drug development and regulatory decision-making⁽²¹⁾. ICH has developed guidance for harmonizing real-world evidence terminology and reporting standards, facilitating global acceptance of these data sources⁽²¹⁾. The integration of electronic health records, wearable device data, and patient-reported outcomes promises to provide comprehensive insights into drug performance in clinical practice⁽²¹⁾.

II. CONCLUSION

The journey from molecular targets to clinical outcomes represents one of the most challenging and expensive endeavors in modern science, requiring unprecedented integration of diverse scientific disciplines, technological capabilities, and regulatory frameworks. Despite remarkable advances in our understanding of disease mechanisms, molecular biology, and clinical investigation methods, drug development continues to be characterized by high failure rates and extended timelines that limit patient access to new therapeutic options.

Current challenges in drug discovery stem from fundamental limitations in translating preclinical findings to human clinical outcomes, inadequate target validation methodologies, and suboptimal balance between drug potency and tissue-specific exposure profiles. The persistent 90% failure rate in clinical development highlights the need for innovative approaches that address these underlying limitations rather than simply optimizing individual components of the discovery process.

Artificial intelligence and machine learning technologies offer transformative potential for addressing traditional drug discovery challenges, with early evidence suggesting improved success rates for AI-derived compounds. However, these technologies must be implemented thoughtfully to avoid perpetuating existing biases and inequities in healthcare. The integration of precision medicine approaches, biomarker-guided development, and real-world evidence collection promises to enable more targeted and efficient therapeutic development.

Global health equity considerations demand continued attention to drug pricing policies, access mechanisms, and international collaboration to ensure that scientific advances benefit all populations regardless of geographic or socioeconomic circumstances. The success of cell and gene therapies, immune checkpoint inhibitors, and drug repurposing initiatives demonstrates that breakthrough innovations can emerge from diverse approaches and sustained research investment.

Looking forward, the convergence of AI technologies, advanced biological models, quantum computing, and precision medicine approaches will likely reshape drug discovery paradigms over the coming decades. Success will require continued collaboration between academia, industry, regulatory agencies, and global health organizations to address the complex challenges of developing safe, effective, and accessible therapeutics for human disease. The ultimate measure of success will be the translation of scientific discoveries into improved health outcomes for patients worldwide, making the journey from molecular targets to clinical outcomes not just scientifically rigorous but also equitably accessible to those who need these advances most.

REFERENCES

- [1]. Lifesciences Danaher. Drug Discovery Pipeline. Danaher Life Sciences. 2025.
- [2]. Principles of early drug discovery. PMC. 2010. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3058157/>
- [3]. Prioritization of molecular targets for antimalarial drug discovery. ACS Infect Dis. 2021;7(9):2547–2556.
- [4]. Target identification and mechanism of action in chemical biology and drug discovery. Nat Rev D Drug Discovery. 2003;2:507–515
- [5]. Yao Y, et al. AI-guided pipeline for protein–protein interaction drug discovery identifies a SARS-CoV-2 inhibitor. EMBO Rep. 2024 Mar;25(3):e543320
- [6]. Biostock. Drug development – The four phases. 2025. <https://biostock.se/en/2023/01/drug-development-the-four-phases>
- [7]. /Supercomputer-based ensemble docking drug discovery pipeline with application to Covid-19. J Chem Inf Model. 2020;60(8):3621-3633.



- [8]. FDA. Step 3: Clinical Research. 2018. <https://www.fda.gov/patients/drug-development-process/step-3-clinical-research>
- [9]. Challenges in Alzheimer's disease drug discovery and development: The role of modeling, simulation, and open data. Clin Pharmacol Ther. 2020;108(1):54-66.
- [10]. Why 90% of clinical drug development fails and how to improve it. PMC. 2022. <https://pmc.ncbi.nlm.nih.gov/articles/PMC9293739/>
- [11]. About Biomarkers and Qualification. FDA. 2021. <https://www.fda.gov/drugs/biomarker-qualification-program/about-biomarkers-and-qualification>
- [12]. Machine learning in drug discovery: A review. Artif Intell Rev. 2021;54:2559–2599.
- [13]. Drug repurposing in cardiovascular inflammation: Successes, failures, and future opportunities. Front Pharmacol. 2022;13:1046406.
- [14]. Artificial intelligence in drug discovery and development. Front Pharmacol. 2020;11:579981.
- [15]. Precision and personalized medicine: What their current definitions say and do not say. PMC. 2023. <https://pmc.ncbi.nlm.nih.gov/articles/PMC9989160/>
- [16]. Precision Medicine. FDA. 2018. <https://www.fda.gov/medical-devices/in-vitro-diagnostics/precision-medicine>
- [17]. The changing scenario of drug discovery using AI to deep learning: Recent advancement, success stories, collaborations, and challenges. J Pharm Anal. 2024;14(7):652-663.
- [18]. ISCT Global. From the Editors: Cell & Gene Therapy Approvals in 2024. 2025.
- [19]. Clinical development of immune checkpoint inhibitors. Cancer Chemother Pharmacol. 2010;66(6):1067-1079.
- [20]. Immune checkpoint inhibitors in cancer therapy. Cancer Med. 2025;14(6):2155-2167.
- [21]. Cambridge. Global health challenges in the pharmaceutical world. Eur J Public Health. 2008;18(6):584–588.
- [22]. WHO. Medicines Affordability and Pricing. 2024. <https://www.who.int/teams/health-product-and-policy-standards/medicines-selection-ip-and-affordability/affordability-pricing>
- [23]. ICH Guidelines Decoded. Biotech.com. 2023. <https://biotech.com/2023/10/05/ich-guidelines-decoded-2/>
- [24]. International Council for Harmonisation. EMA. 2024. <https://www.ema.europa.eu/en/partners-networks/international-activities/multilateral-coalitions-initiatives/international-council-harmonisation-technical-requirements-registration-pharmaceuticals-human-use-ich>
- [25]. PMC. Development of orphan drugs for rare diseases. 2023. <https://pmc.ncbi.nlm.nih.gov/articles/PMC11222908/>
- [26]. Banerjee S, Chakrabarty S. “A Comprehensive Review of the Advancement in Omic Technologies in the Field of Drug Discovery and Development.” Current Drug Discovery Technologies. 2024;21(1):30-46.
- [27]. Shao Y, Zhang L, et al. “A comprehensive review on recent advancements in drug delivery via selenium nanoparticles.” Expert Opinion on Therapeutic Patents. 2024;34(10):855-874.
- [28]. Sharma S, Kumar N. “Indole Derivatives: A Versatile Scaffold in Modern Drug Discovery—An Updated Review on Their Multifaceted Therapeutic Applications (2020–2024).” Molecules. 2024;29(19):4770.
- [29]. Wang H, Li Z. “A review on graph neural networks for predicting synergistic drug combinations.” Artificial Intelligence Review. 2024;57(3):2407-2435.
- [30]. Khojasteh C, et al. “Metabolism of new drug modalities research advances – 2023 year in review.” Drug Metabolism Reviews. 2024;56(2):133-163.
- [31]. Hu H, Sun R. “From understanding diseases to drug design: can artificial intelligence bridge the gap?” Artificial Intelligence Review. 2024;57(2): 1137-1159.
- [32]. Ferreira FJN, Carneiro AS. “AI-Driven Drug Discovery: A Comprehensive Review.” PMC. 2025 Jun 5.
- [33]. Li Y, Song J. “Advances in drug design and discovery.” GSC Biological and Pharmaceutical Sciences. 2025.
- [34]. Bai YR, et al. “A comprehensive review of small molecule drugs approved in 2024.” Chinese Chemical Letters. 2025.



- [35]. Singh R, Patel M. "Comprehensive Review on Drug Discovery and Development Process." JCHR. 2024 Jun 15.
- [36]. Nature Reviews Drug Discovery. "Nature Reviews Drug Discovery." Nature. 2024 Nov 3.
- [37]. FDA. "Novel Drug Approvals for 2024." U.S. Food & Drug Administration. 2025.
- [38]. Hartung T. "Leveraging biomarkers and translational medicine for safety assessment without animal testing." ALTEX. 2023;40(4):511-523.
- [39]. Chen J. "Advancing pharmaceutical research: A comprehensive review." Progress in Drug Research. 2024;79(1):88-113.
- [40]. EMA. "Human medicines in 2024." European Medicines Agency. 2025 Jan 15.
- [41]. ASCB. "Biomarkers 2024." American Society for Cell Biology. 2024.
- [42]. Zhou J, Xu Y. "Fragment-based approaches to discover ligands for tumor-specific E3 ligases." Expert Opinion on Drug Discovery. 2024;19(10): 959-971.
- [43]. Sahu SK, Das S. "Advances in chalcone-based anticancer therapy: mechanisms, preclinical advances, and future perspectives." Expert Opinion on Drug Delivery. 2024 Nov 30.
- [44]. Cancer Res. "Abstract 902: Explainable AI: Graph machine learning for response prediction and biomarker discovery." Cancer Research. 2024 Mar 21.
- [45]. IEEE. "A Critical Analysis and Classification of Breast Cancer Using Histopathology Images." IEEE Transactions on Medical Imaging. 2024 Apr 17.
- [46]. Springer. "Paradigms and Success Stories of Natural Products in Drug Discovery Against Neurodegenerative Disorders (NDDs)." Neurodegener Dis Manag. 2023;13(1):25-38.
- [47]. Kluwer Law Online. "Fair Access to Drugs and the Relationship Between Big Pharma and Public Authorities in Global Health Governance." European Public Law. 2023;29(2):223-241.
- [48]. MDPI. "Analysis of Drug Pricing Trends of Antiretroviral Therapies in the Management HIV/AIDS." Int J Recent Pharm Res. 2025;6(4):112-128.
- [49]. ScienceDirect. "Advancing pharmaceutical research: A comprehensive review." ScienceDirect. 2024.
- [50]. Taylor & Francis. "Drug approval trends and perspectives in regulatory science." Expert Opinion on Drug Metabolism & Toxicology. 2024;20(3): 227-241.

