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Review Article

Artificial Intelligence in Drug Discovery and Development: From Target Identification to Clinical Trials

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ABSTRACT

Background: Drug discovery and development are complex, costly, and failure-prone processes that require the integration of biological, chemical, pharmacological, toxicological, and clinical evidence. Artificial intelligence (AI), including machine learning (ML), deep learning, natural language processing, generative models, and foundation models, is increasingly being applied across this pipeline.

Objective: This review examines the role of AI from target identification and validation through hit discovery, lead optimization, preclinical evaluation, clinical trial design and conduct, and regulatory oversight.

Methods: A narrative review was prepared using peer-reviewed research, major reviews, clinical trial reports, and regulatory guidance identified through biomedical literature resources and targeted searches of journal and official agency websites. Emphasis was placed on evidence published through 30 October 2026. No formal systematic screening or meta-analysis was performed.

Results: AI can integrate multi-omics and literature data for target prioritization; support structure prediction, virtual screening, molecular generation, and multi-parameter optimization; and assist toxicity prediction, trial recruitment, protocol feasibility, monitoring, and data analysis. AlphaFold 3 has expanded structural prediction to biomolecular interactions. A notable clinical example is rentosertib (formerly ISM001-055), a generative-AI-discovered TNIK inhibitor evaluated in a randomized phase 2a trial for idiopathic pulmonary fibrosis. The trial provides an important proof-of-concept but does not establish that AI alone caused clinical success or that the candidate is an approved medicine.

Conclusion: AI is becoming an enabling technology throughout pharmaceutical research and development, but it does not eliminate the need for biological reasoning, medicinal chemistry, experimental testing, rigorous clinical trials, or regulatory evaluation. Its value depends on high-quality data, prospective validation, transparent context of use, and multidisciplinary human oversight.

Keywords: Artificial intelligence; drug discovery; drug development; target identification; machine learning; generative AI; molecular docking; preclinical development; clinical trials; precision medicine.

1. Introduction

Drug discovery and development translate biological knowledge into medicines with acceptable quality, safety, and efficacy. The conventional pathway includes disease and target selection, hit identification, lead optimization, preclinical studies, clinical trials, and regulatory review. Each stage requires substantial resources, and attrition is common because promising laboratory findings may not translate into human benefit. [1,2] AI offers computational methods to analyse complex datasets, identify patterns, generate hypotheses, and prioritize experiments. Its applications now extend from target discovery and molecular design to toxicology, clinical trial operations, and post-marketing surveillance. However, the term AI covers diverse techniques with different capabilities and evidentiary requirements; it should not be treated as a single intervention or as a substitute for experimental science[2-4] This review follows the drug-development continuum, focusing on what AI can contribute, what evidence supports its use, and what scientific, ethical, operational, and regulatory safeguards are needed for responsible translation.

2. Methodology / Literature Search Strategy

A narrative literature review was developed using peer-reviewed original research, systematic and narrative reviews, clinical trial publications, and regulatory documents. Relevant publications were identified through PubMed/MEDLINE and targeted searches of journal publisher websites and official regulatory sources, including the US Food and Drug Administration (FDA) and European Medicines Agency (EMA). Search concepts included artificial intelligence, machine learning, deep learning, generative AI, target identification, target validation, AlphaFold, virtual screening, molecular docking, lead optimization, ADMET, toxicity prediction, drug development, clinical trial recruitment, clinical trial design, and regulatory science. Priority was given to publications describing validated methods, prospective applications, clinical-stage candidates, and current regulatory principles.

The literature was synthesized qualitatively according to the stage of development, AI method, data source, validation approach, and clinical relevance. This article is a narrative

review, not a systematic review: no registered protocol, exhaustive reproducible search, formal risk-of-bias assessment, or meta-analysis was conducted.

3. Background

3.1 The drug discovery and development pipeline

The pipeline is iterative rather than strictly linear. Biological insights guide target selection; target modulation informs screening; medicinal chemistry and pharmacology refine candidate molecules; and preclinical and clinical results may trigger redesign or changes in development strategy. AI can contribute at multiple points, but the value of each prediction depends on the context, training data, assay quality, and experimental confirmation.

3.2 Core AI approaches

Table 1. Major AI approaches and representative applications

AI approach	How it works	Applications in drug R&D	Important caveat
Supervised machine learning	Learns relationships from labelled examples	Activity, toxicity, ADMET, response and risk prediction	Dependent on representative labels and external validation
Deep learning	Learns hierarchical representations from complex data	Omics, imaging, protein structure, molecular property prediction	Can be data-intensive and difficult to interpret
Graph neural networks	Represents molecules or biological networks as graphs	Molecular property prediction, interaction modelling	Performance depends on graph representation and data quality
Natural language processing / LLMs	Extracts and generates information from text	Literature mining, patent analysis, protocol and eligibility extraction	Can hallucinate; outputs require source verification
Generative models	Generate candidate molecular structures or sequences	De novo design, scaffold exploration, protein design	Generated molecules may be synthetically infeasible or biologically inactive
Reinforcement learning / active learning	Selects actions or experiments to improve an objective	Iterative design-make-test cycles and experimental prioritization	Reward functions may not reflect real developability

3.3 Data foundations

AI models may use genomic, transcriptomic, proteomic, metabolomic, imaging, structural, chemical, assay, electronic health record, and clinical trial datasets. Data integration is challenging because measurements differ in scale, assay conditions, population characteristics, annotation quality, and provenance. Data leakage, duplicate compounds across training and test sets, and non-independent validation can inflate reported performance.

4. Current Evidence

4.1 Target identification and validation

Target identification seeks to establish a disease-relevant molecule, pathway, or biological process that can be modulated therapeutically. AI can integrate genetic association data, transcriptomics, proteomics, single-cell data, pathway networks, disease ontologies, and scientific literature to rank candidate targets. Knowledge graphs and NLP can connect genes, phenotypes, pathways, drugs, and publications, helping researchers generate testable hypotheses. 3,5[3,5]

AI prioritization is not equivalent to target validation. Strong evidence requires orthogonal experimental approaches, such as genetic perturbation, biochemical assays, cellular models, disease-relevant systems, and where appropriate in vivo studies. Confounding, tissue specificity, compensatory pathways, and differences between model systems and human disease can undermine apparently plausible targets.

A 2026 review in Nature Reviews Drug Discovery discusses how AI is changing target identification and assessment, including integration of biological networks, imaging, and experimental validation. It emphasizes that target confidence ultimately depends on evidence linking modulation of the target to a therapeutic effect. 5[5]

4.2 Protein structure prediction and biological interactions

Deep-learning systems have improved prediction of protein structures and interactions. AlphaFold 2 demonstrated high accuracy in protein structure prediction, while AlphaFold 3 extended modelling to complexes involving proteins, nucleic acids, small molecules, ions, and modified residues. These tools can support structural biology, binding-site analysis, and hypothesis generation for drug design. 6,7[6,7]

Predicted structures do not automatically provide binding affinity, ligand residence time, conformational dynamics, cellular activity, selectivity, or clinical efficacy. Experimental structural biology, biophysical measurements, and functional assays remain important, especially when decisions depend on subtle conformational changes or allosteric mechanisms.

4.3 Hit discovery and virtual screening

Virtual screening uses computational methods to prioritize compounds for experimental testing. AI models can estimate molecular properties, predict drug-target interactions, classify likely active compounds, and rank large chemical libraries. Molecular docking and physics-based methods may be combined with ML to reduce the number of compounds selected for laboratory assays.

The main advantage is prioritization rather than replacement of screening. Prediction quality can deteriorate when models are applied to chemical scaffolds, targets, assay formats, or biological conditions that differ from the training data.

Prospective testing of ranked compounds is therefore more informative than retrospective benchmark performance alone.

4.4 Generative chemistry and lead optimization

Generative models can propose new molecular structures subject to constraints such as predicted potency, selectivity, solubility, permeability, metabolic stability, and synthetic accessibility. Multi-parameter optimization is particularly relevant because improving one property can worsen another. AI-assisted design may help explore chemical space and prioritize compounds for synthesis, but medicinal chemists must assess chemical plausibility, novelty, route feasibility, and developability. 4,8[4,8]

A 2024 review by Hasselgren and Oprea notes that AI has supported compounds entering clinical development, while stressing the need for reliable ground truth, appropriate validation, and human intervention. AI-generated structures should not be equated with fully AI-designed medicines: candidate progression usually involves extensive experimental and expert-led optimization.

4.5 Preclinical ADMET and safety prediction

AI can be applied to absorption, distribution, metabolism, excretion, and toxicity (ADMET) prediction, including solubility, permeability, plasma protein binding, metabolic stability, cytochrome P450 interactions, transporter effects, cardiac ion-channel liability, hepatotoxicity, and genotoxicity. These predictions may help prioritize compounds and identify liabilities earlier.

Preclinical predictions remain imperfect because toxicity may be species-specific, dose-dependent, metabolite-mediated, or influenced by disease state and polypharmacy. In silico predictions should complement—not replace—validated in vitro assays, animal studies where required, and integrated safety assessment.

4.6 AI in clinical development

AI can support protocol feasibility, site selection, eligibility-criteria parsing, participant matching, recruitment forecasting, retention support, risk-based monitoring, endpoint extraction, imaging analysis, and statistical workflows. A 2024 scoping review mapped AI applications for recruitment and retention, while a separate review of eligibility parsing described the use of ML and NLP to convert protocol criteria into computable rules. 9,10[9,10]

These applications should be assessed according to their effect on decisions and trial quality, not only classification accuracy. Incorrect eligibility identification may affect participant safety and trial representativeness. AI-generated summaries and endpoint support require traceability to source records and human adjudication where clinically or statistically consequential.

4.7 Clinical-stage example: rentosertib

A prominent example is rentosertib (formerly ISM001-055), a small-molecule inhibitor of TNIK developed using generative AI for idiopathic pulmonary fibrosis. A randomized, double-blind, placebo-controlled phase 2a trial evaluated three dose regimens over 12 weeks. The primary endpoint was safety and tolerability; the report described broadly similar treatment-emergent adverse-event rates across active and placebo groups. An exploratory forced vital capacity signal was reported at the highest once-daily dose. The authors concluded that larger and longer trials were warranted. 11[11]

This study is an important proof-of-concept that an AI-discovered candidate can reach and be evaluated in a randomized clinical trial. It does not establish regulatory approval, definitive efficacy, long-term safety, or that AI alone caused the observed findings. Drug development remains a multidisciplinary process involving target biology, chemistry, pharmacology, toxicology, clinical operations, and independent clinical evidence.

Table 2. AI applications across the drug discovery and development continuum

Stage	AI-enabled activities	Expected contribution	Validation needed
Target identification	Multi-omics integration, knowledge graphs, literature mining	Prioritize disease-associated targets	Genetic, biochemical, cellular and disease-model validation
Target assessment	Pathway modelling, perturbation analysis, imaging analytics	Assess target relevance and context	Orthogonal experiments and causal evidence
Hit discovery	Virtual screening, docking support, activity prediction	Rank compounds for testing	Prospective biochemical and cellular assays
Lead optimization	Generative chemistry, QSAR, multi-objective optimization	Improve potency and developability	Synthesis, SAR, selectivity and functional assays
Preclinical evaluation	ADMET, toxicity and PK/PD prediction	Identify liabilities and prioritize candidates	Validated in vitro/in vivo studies and toxicology
Clinical development	Trial feasibility, eligibility parsing, recruitment, monitoring	Improve operational planning and data review	Prospective workflow and trial-level impact evaluation
Regulatory and post-market	Evidence synthesis, safety signal detection, manufacturing analytics	Support review and lifecycle monitoring	Traceability, validation, governance and human review

5. Clinical Applications

5.1 Precision target selection

AI-supported target prioritization may help identify subgroups in which a biological pathway is particularly relevant. Integration of molecular profiles with clinical phenotypes can support precision medicine hypotheses, but subgroup findings require replication and prospective testing.

5.2 Drug repurposing

Knowledge graphs, transcriptomic signatures, chemical similarity, and ML can identify existing medicines that may act on pathways implicated in another disease. Repurposing hypotheses require pharmacological plausibility, dose feasibility, safety review, and clinical testing; computational association alone does not establish therapeutic benefit.

5.3 Trial design and participant recruitment

NLP can parse inclusion and exclusion criteria and match structured or narrative patient information to trial eligibility rules. Predictive models may estimate site recruitment rates and identify barriers to enrolment. Human confirmation is essential because eligibility decisions involve clinical context, consent, and safety.

5.4 Clinical monitoring and data analysis

AI may support detection of missing data, protocol deviations, unusual laboratory patterns, imaging endpoints, and safety signals. Models can assist central monitoring and prioritization of sites for review. Statistical inference must remain prespecified and transparent; post hoc model selection or ungoverned adaptation can compromise trial validity.

5.5 Regulatory and pharmacovigilance support

AI may support structured evidence synthesis, document review, manufacturing analytics, and post-marketing signal detection. These uses require auditability, provenance, version control, and clear accountability. Regulatory decisions remain grounded in demonstrated quality, safety, and efficacy.

6. Safety & Limitations

- Data quality and representativeness: incomplete, biased, inconsistent, or assay-specific datasets can produce unreliable predictions.
- Data leakage and benchmark inflation: random splitting may place highly similar compounds or related samples in training and test sets, overstating generalizability.
- Limited external and prospective validation: strong retrospective performance may not translate to new targets, chemical space, laboratories, or patient populations.
- Interpretability and causal uncertainty: feature importance or molecular correlations do not necessarily explain biological mechanisms or establish causality.
- Generative model limitations: generated compounds may be unstable, toxic, synthetically inaccessible, non-selective, or inactive in biological systems.
- Reproducibility and intellectual property: model versions, training data, prompts, code, patents, and proprietary datasets may limit independent replication.
- Privacy and cybersecurity: omics, clinical, and trial data require secure governance, lawful use, access controls, and careful de-identification.
- Automation bias and accountability: scientists and clinicians may over-trust model outputs; responsibility for decisions must remain clearly assigned.
- Unequal access: institutions with limited computational infrastructure, data resources, and expertise may not benefit equally from AI-enabled development.

The FDA's January 2025 draft guidance proposes a risk-based credibility assessment framework for AI models used to support regulatory decision-making for drugs and biological products. In January 2026, FDA and EMA also published guiding principles of good AI practice in drug development, emphasizing human-centric design, context of use, risk management, data governance, and lifecycle oversight. These documents reinforce the need to match validation to the consequences of the model's intended use. 12,13[12,13]

7. Emerging Advances

7.1 Foundation models for biology and chemistry

Large biological and chemical foundation models are trained on extensive sequence, structure, text, or molecular datasets. They may support protein representation learning, sequence design, property prediction, and cross-modal reasoning. Their value will depend on task-specific benchmarking, uncertainty estimation, and experimental validation.

7.2 Closed-loop design-make-test-learn systems

Automated laboratories can connect AI-driven experiment selection with robotic synthesis, assay execution, and data analysis. Such systems may shorten iterative cycles and improve reproducibility when workflows are well controlled. They also require careful calibration, quality assurance, and clear handling of failed or anomalous experiments.

7.3 Digital twins and in silico trials

Computational models of biological systems or patient trajectories may support dose selection, trial simulation, and hypothesis testing. A digital twin is only as reliable as its assumptions, data, and validation domain; it should not be treated as a substitute for randomized clinical evidence.

7.4 AI-enabled biologics and protein design

Generative and structure-aware systems may aid antibody design, protein engineering, peptide optimization, and prediction of biomolecular interactions. Biological activity, immunogenicity, manufacturability, stability, and safety still require extensive experimental evaluation.

8. Pharmacist's Role

Pharmacists contribute across the translational pathway by connecting molecular design, pharmacology, clinical development, medication safety, and real-world medicine use.

- Target and candidate appraisal: interpret pharmacological rationale, mechanism of action, selectivity, and clinical relevance of proposed targets and compounds.
- ADMET and pharmacokinetics: assess predicted absorption, metabolism, interactions, dose feasibility, organ impairment considerations, and therapeutic index.
- Preclinical-to-clinical translation: contribute to dose rationale, first-in-human considerations, formulation, stability, and risk mitigation.
- Clinical trial operations: support protocol review, investigational product handling, medication reconciliation, adherence assessment, and safety monitoring.
- Pharmacovigilance: evaluate adverse-event patterns, signal plausibility, medication errors, interactions, and benefit-risk updates.
- AI governance: participate in multidisciplinary review of model validation, data provenance, uncertainty, bias, and the intended clinical or regulatory context.
- Evidence communication: explain the difference between computational prediction, preclinical evidence, clinical efficacy, and regulatory approval.

Table 3. Pharmacist's contribution to AI-enabled drug development

Development stage	Pharmacist contribution	Key question
Target and hit selection	Mechanism and therapeutic relevance review	Is the target pharmacologically actionable?
Lead optimization	Review potency, selectivity, ADMET and interaction predictions	Does the candidate have a plausible therapeutic window?
Preclinical safety	Interpret toxicity and PK/PD findings	Are risks sufficiently characterized to justify clinical testing?
Clinical trials	Investigational product, dose, interaction and safety oversight	Is the protocol and dose rationale clinically appropriate?
Regulatory / post-market	Benefit-risk and pharmacovigilance contribution	Do accumulating data support continued use and monitoring?

9. Research Gaps

- Insufficient prospective evidence showing that AI-derived candidates outperform conventional discovery strategies across complete development programmes.
- Limited publication of negative results, failed candidates, training data, and model-development details.
- Need for standardized benchmarks that reduce chemical-series leakage and reflect prospective experimental conditions.
- Uncertain generalizability across target classes, disease areas, assay platforms, and diverse patient populations.
- Limited evidence linking AI-supported trial operations to improved recruitment, retention, trial quality, or patient outcomes.
- Need for transparent reporting of model uncertainty, calibration, provenance, version changes, and context of use.
- Limited independent assessment of cost-effectiveness, time savings, and resource requirements.
- Need for workforce training and multidisciplinary governance spanning data science, medicinal chemistry, pharmacology, clinical research, and regulation.

10. Future Perspectives

Future progress will depend less on deploying increasingly complex algorithms in isolation and more on connecting prediction to reliable experimentation. Drug-development organizations should define a clear context of use for each model, establish appropriate reference standards, test models prospectively, and record when model outputs influence decisions.

Integration of multi-omics, structural biology, chemical space exploration, automated experimentation, and clinical data may improve target-to-patient translation. Shared standards for data quality, model reporting, uncertainty, and lifecycle monitoring will be important. Regulators, academia, pharmaceutical companies, technology developers, clinicians, and pharmacists should collaborate to ensure that AI-enabled development remains transparent, safe, and scientifically credible.

For clinical trials, AI should be evaluated not only by operational efficiency but also by its effects on participant protection, representativeness, data integrity, endpoint validity, and the reliability of treatment-effect estimates. The ultimate measure of success remains the delivery of safe and effective medicines that improve patient outcomes.

11. Conclusion

Artificial intelligence is increasingly relevant across the drug discovery and development continuum, from target identification and molecular design to preclinical assessment, clinical trial operations, and post-market monitoring. Structural prediction, generative chemistry, multi-omics integration, and NLP offer powerful ways to prioritize hypotheses and experiments. Clinical-stage examples such as rentosertib demonstrate that AI-discovered candidates can progress into randomized trials, while also illustrating that clinical efficacy and safety must be established through conventional rigorous evaluation.

AI should therefore be viewed as an enabling component of evidence-based pharmaceutical research rather than an autonomous replacement for scientists, clinicians, or regulators. Data quality, experimental validation, prospective evaluation, transparency, and human oversight will determine whether computational advances translate into meaningful therapeutic progress.

12. Declarations

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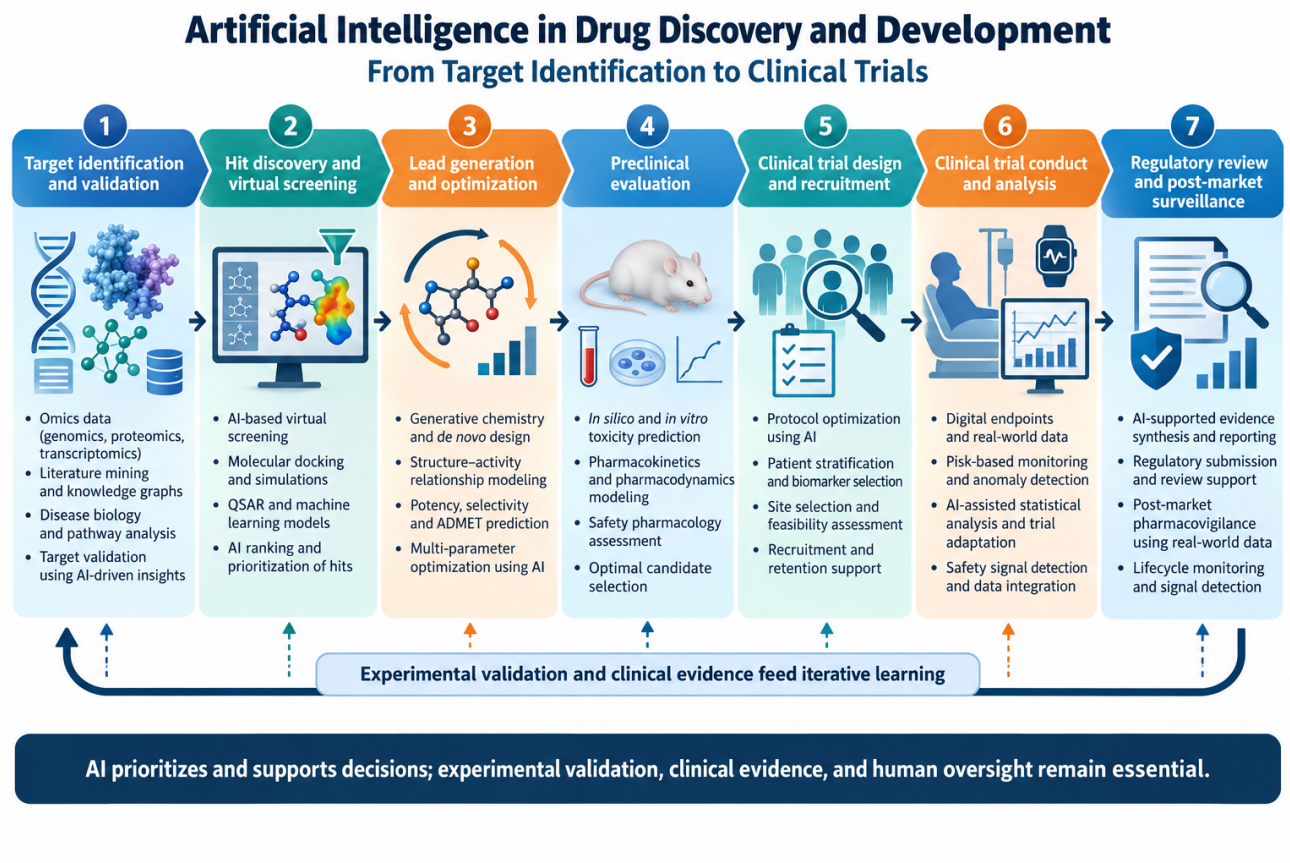
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14. Tables & Figures

Figure 1. AI-enabled drug discovery and development pipeline, from target identification to clinical trials and regulatory review.



Note: Conceptual overview. AI outputs prioritize hypotheses and decisions; experimental validation, clinical evidence, and human oversight remain essential.