https://alldus.com/blog/how-ai-is-revolutionizing-drug-discovery/

THE JOURNEY OF DRUG FROM DISCOVERY TO MARKET

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INTRODUCTION:

Drug discovery is a process which aims at identifying a compound therapeutically useful in curing and treating disease. It is the process through which potential new medicines are identified. It is the process through which potential new medicines are identified. It involves a wide range of scientific disciplines, including biology, chemistry and pharmacology.

Typically, it can be divided into four main stages:

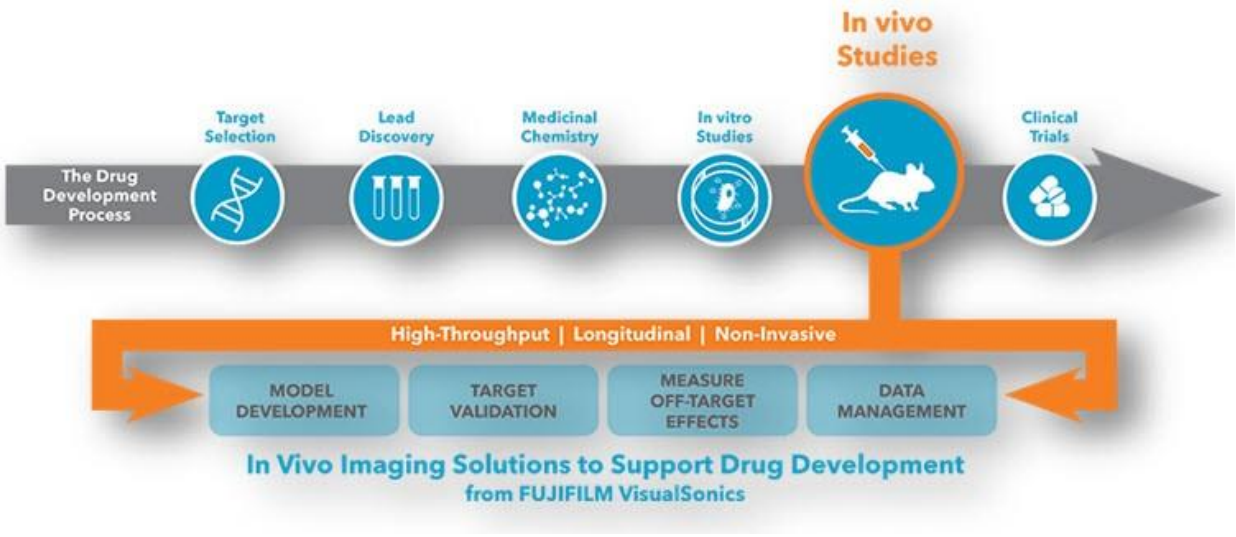
a. Early Drug Discovery

b. Pre-Clinical Phase

c. Clinical Phases

d. Regulatory Approval.

New drug development process must continue through several stages in order to make a medicine that is safe, effective, and has approved all regulatory requirements.



https://www.pharmatutor.org/articles/an-overview-of-new-drug-discovery-and-development

STAGES OF DRUG DISCOVERY AND DEVELOPMENT INCLUDE

- **Target Identification:** The first step in the discovery of a drug is identification of the biological origin of a disease, and the potential targets for intervention. Target identification starts with isolating the function of a possible therapeutic target (gene/nucleic acid/protein) and its role in the disease. Identification of the target is followed by characterization of the molecular mechanisms addressed by the target.
- **Target Validation:** Target validation is the process by which the expected molecular target – for example gene, protein or nucleic acid of a small molecule is certified. Target validation is the process of demonstrating the functional role of the identified target in the disease phenotype.
- **Identification of Lead:** A chemical lead is defined as a synthetically stable, feasible, and drug like molecule active in primary and secondary assays with acceptable specificity, affinity and selectivity for the target receptor. There are different Characteristics of a chemical lead.
- **Lead Optimization:** Lead optimization is the process by which a drug candidate is designed after an initial lead compound is identified. The process involves iterative series of synthesis and characterization of a potential drug to build up a representation of in what way chemical structure and activity are related in terms of interaction.

- **Product Characterization:** When any new drug molecule shows a promising therapeutic activity, then the molecule is characterized by its size, shape, strength, weakness, use, toxicity, and biological activity. Early stages of pharmacological studies are helpful to characterize the mechanism of action of the compound.
- **Formulation and Development:** Pharmaceutical formulation is a stage of drug development during which the physicochemical properties of active pharmaceutical ingredients (APIs) are characterized to produce a bioavailable, stable and optimal dosage form for a specific administration route.
- **Preclinical Testing:** Pre-clinical research in drug development process involves evaluation of drug's safety and efficacy in animal species that conclude to prospective human outcome. The regulatory authorities must ensure that trials are conducted in safe and ethical way and would give approval for only those drugs which are confirm to be safe and effective.
- **Investigational New Drug Process (IND):** Drug developers must file an Investigational New Drug application to FDA before commencement clinical research. In the IND application, developers must include Preclinical and toxicity study data, Drug manufacturing information, Clinical research protocols for studies to be conducted, Previous clinical research data (if any), Information about the investigator/ developer.
- **New Drug Application:** A New Drug Application (NDA) expresses the full story of a drug molecule. Its purpose is to verify that a drug is safe and effective for its proposed use in the people studied. A drug developer must include all about a drug starting from preclinical data to Phase 3 trial data in the NDA.

1. Proposed labeling
2. Safety updates
3. Drug abuse information
4. Patent information

CLINICAL TRIALS

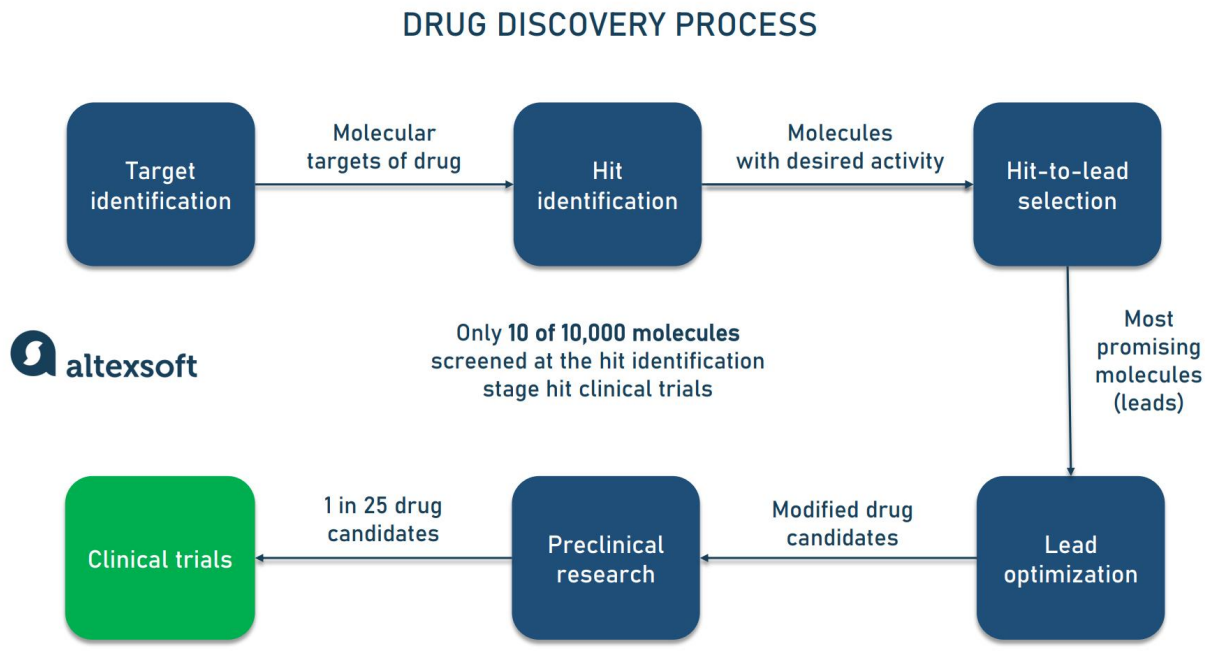
Clinical trials are conducted in people (volunteer)and intended to answer specific qu0estions about the safety and efficacy of drugs, vaccines, other therapies, or new methods of using current treatments. Clinical trials follow a specific study protocol that is designed by the researcher or investigator or manufacturer.

Phase 1: Safety and dosage: Phase I trials are the first tests of a drug with a lesser number of healthy human volunteers, In most cases, 20 to 80 healthy volunteers with the disease/condition participate in Phase 1. However, if a new drug is proposed for use in diabetes patients, researchers conduct Phase 1 trials in patients with that type of diabetes.

Phase 2: Efficacy and side effects: Phase II trials are conducted on larger groups of patients (few hundreds) and are aimed to evaluate the efficacy of the drug and to endure the Phase I safety assessments. These trials aren't sufficient to confirm whether the drug will be therapeutic.

Phase 3: Efficacy and adverse drug reactions: Researchers plan Phase 3 studies to prove whether a product deals an action benefit to a specific people or not. Sometimes known as pivotal studies, these studies comprise 300 to 3,000 volunteers. Phase 3 studies deliver most of the safety data.

Phase 4: Post-Market Drug Safety Monitoring: Phase 4 trials are conducted when the drug or device has been approved by FDA. These trials are also recognized as post marketing surveillance involving pharmacovigilance and continuing technical support after approval.



https://www.altexsoft.com/blog/ai-drug-discovery-repurposing/

FDA REVIEW AND APPROVAL

- The FDA reviews information that goes on a drug's professional labeling (information on how to use the drug).
- The FDA inspects the facilities where the drug will be manufactured as part of the approval process.
- The FDA approval process can take between one week and eight months, depending on whether you self-register, submit a 510(k) application or submit a Premarket Approval (PMA) application.
- Bringing a medical device to market is not a fast process.

REVIEW PROCESS CONSISTS OF THREE PHASES

- Process mapping

Process mapping is a technique used to visually map out workflows and processes.

The purpose of process mapping is to communicate how a process works in a concise and straightforward way.

- Analysis

FDA reviewers analyze the condition or illness for which the drug is intended and evaluate the current treatment landscape, which provide the context for weighing the drug's risks and benefits.

- Redesign

FDA identifies issues or requests modifications to the product, the manufacturer may need to initiate a redesign phase.

This phase involves making necessary changes to the product, its manufacturing processes, labeling, or other elements. For short processes, you can execute all three phases simultaneously, but for practical reasons, that is usually impossible

POST-APPROVAL RESEARCH & MONITORING

- Even though clinical trials provide important information on a drug's efficacy and safety, it is impossible to have complete information about the safety of a drug at the time of approval.
- Despite the rigorous steps in the process of drug development, limitations exist.
- Therefore, the true picture of a product's safety actually evolves over the months and even years that make up a product's lifetime in the marketplace.

ADVISORY COMMITTEE REVIEW

- In some cases, the FDA may convene an advisory committee of experts to provide additional input and recommendations regarding the drug's approval.
- These committees consist of healthcare professionals, scientists, and patient representatives.

APPROVAL OR REJECTION

- Based on review, the FDA an either approve the drug for marketing or issue a complete response letter if additional information or studies are required.
- If approved, the FDA may also specify labeling, usage instructions, and post-marketing requirements.

POST-MARKETING SURVEILLANCE

- Once a drug is on the market, the FDA continues to monitor its safety and effectiveness through post-marketing surveillance and adverse event reporting.
- Regulatory actions may be taken if safety concerns arise.

POST-APPROVAL CHANGES

- Manufactures may need to submit supplements to the FDA for approval if they make significant changed to the drug's formulation, manufacturing process, or labeling after approval.
- The FDA's drug approval process is designed to balance the need timely access to new and innovative treatment with.

- It is a complex and highly regulated process that can take several years to complete, depending on the drug and the specific circumstances

REFERENCE

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(2) https://www.fda.gov/patients/drug-development-process/step-4-fda-drug-review

(3) https://ria.princeton.edu/human-research/post-approval-monitoring