Clinical Pharmacology and Drug Development

Drug Development and Discovery

Module 2 Topic 1

Pharmacology

- **Pharmacology** is a science that deals with the ***origin, nature, chemistry, effects, and uses*** of drugs
- **'Drug'** - any medicinal substance that can cure or prevent disease, relieve symptoms, and provide other benefits

Drug Discovery/Development Process

- Sources of Drugs
  - Plants
  - Animals
  - Synthetic

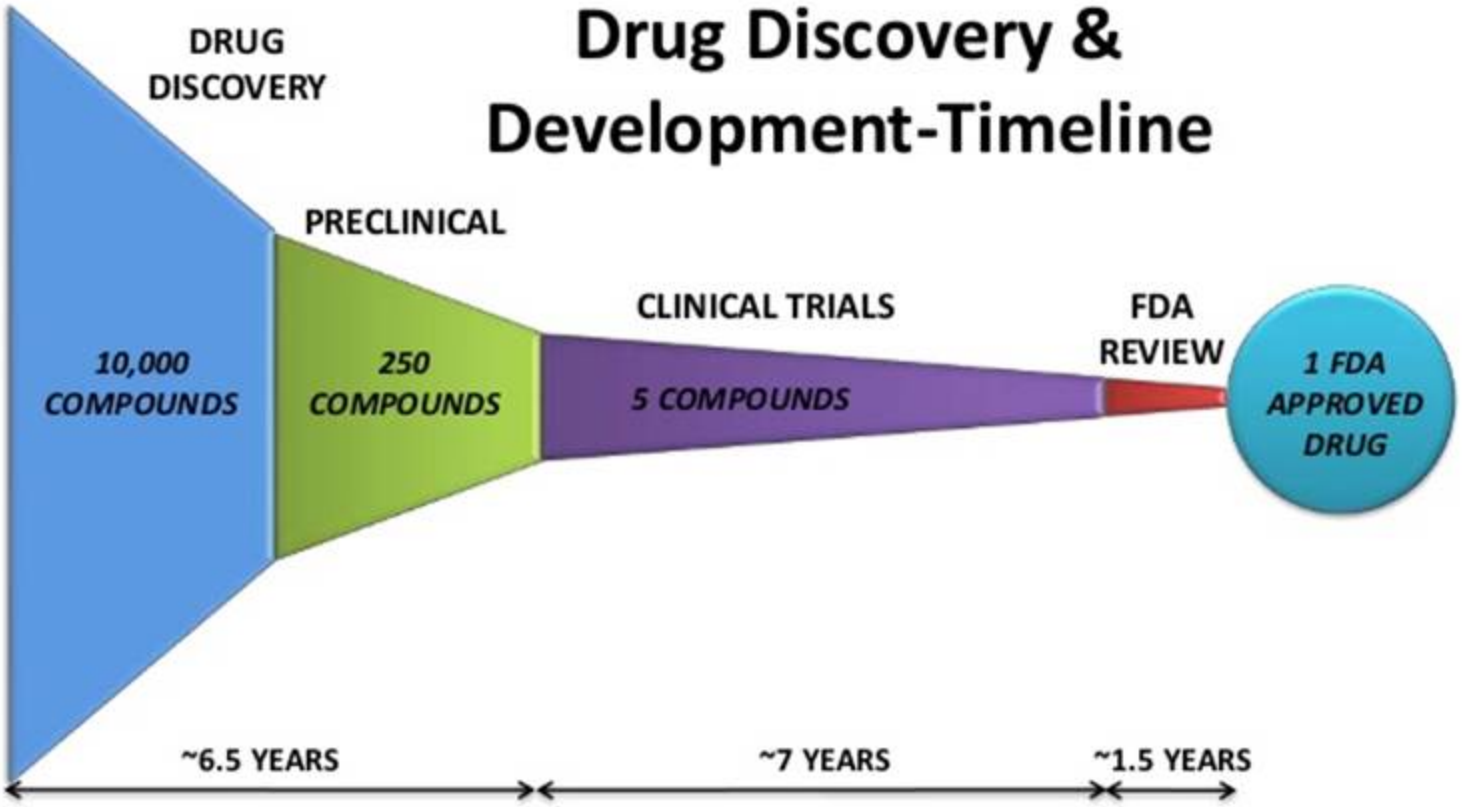
Drug Discovery/Development Process

- Discovery, refinement, chemical & biological characterization
- Safety & toxicity in animals
- Formulation development
- Volunteer studies
- Patient studies
- Regulatory approval
- Marketing
- Post marketing surveillance

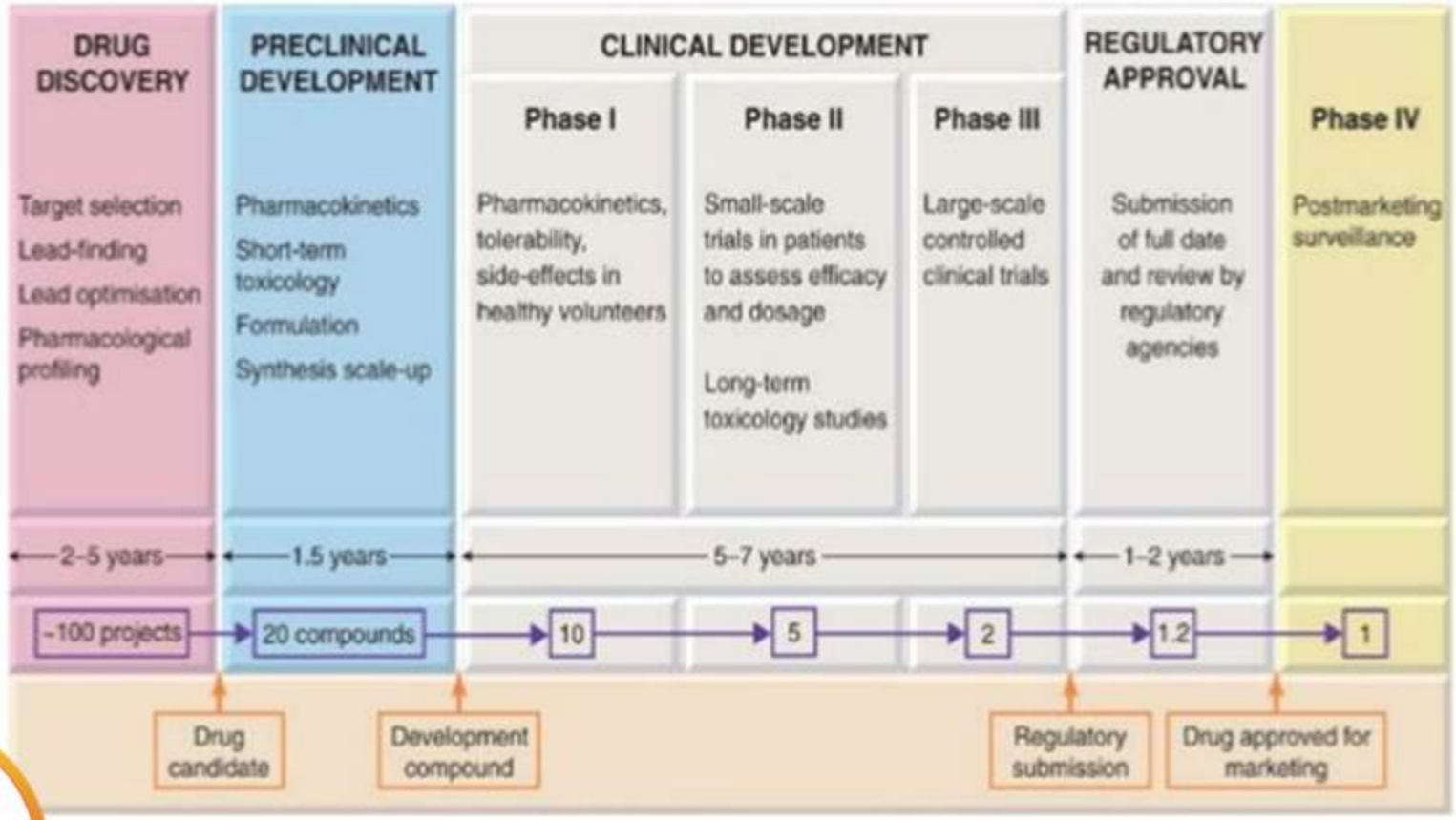
Drug Discovery/Development Process

- The average time span for a new drug development
  - About six-and-a-half years of discovery, preclinical testing, and toxicity studies
  - One-and-a- half years in Phase I trials to assess safety in healthy volunteers
  - Two years in Phase II trials with a few hundred patients to evaluate the drug's effectiveness and side effects
  - Three- and-a-half years in Phase III trials involving thousands of patients and scores of research centers to confirm effectiveness and evaluate long-term effects
  - One-and-a- half years of Drug Authority's review of all the clinical trial data

Drug Discovery/Development Process



Drug Discovery/Development Process



Drug Discovery/Development Process

Preclinical stage:

Evaluation of drug's pharmacological and toxic effects through in vitro and in vivo laboratory animal testing

- **Pharmacological Evaluation**
  - Effects of the drug i.e. Pharmacodynamics
  - Pharmacokinetics i.e. absorption/ distribution/ metabolism/ excretion (ADME); identification of metabolites, bioavailability, principal route of admin and excretion
- **Toxicological Evaluation**
  - Acute toxicity studies
  - Subacute toxicity studies
  - Chronic toxicity studies

Drug Discovery/Development Process

Clinical trials:

- Set of procedures in medical research and drug development to study the safety and efficacy of new drug
- Essential to get marketing approval from regulatory authorities
- May require up to 7 years

Drug Discovery/Development Process

Clinical Stages

- **Phase 0** - Microdosing
- **Phase I** - Human Pharmacology
  (Healthy volunteers - 20 to 50 subjects)
- **Phase II** - Therapeutic Exploration
  (patients - 50 to 400)
- **Phase III** – Therapeutic Confirmation
  (large scale multi-center; 250-1000)
- **Phase IV** - Therapeutic Use
  (post-marketing surveillance)

Drug Discovery/Development Process

Phase 0

- Recently designated
- Purpose - to expedite early phase 1 studies to make drug development process more efficient
- No therapeutic benefit involved
- All drug candidates may NOT be appropriate for phase 0 testing
- Helps reduce the time and resources needed to distinguish between potential candidates that hold promise and those that do not

Drug Discovery/Development Process

Phase 0 (contd)

- Selecting a candidate with most favourable properties for further clinical testing and eliminating 'bad' candidates early in clinical development due to bad Pharmacodynamics (PD) or Pharmacokinetics (PK), such as lack of proper effect, poor bioavailability, rapid clearance etc.
- Confirm whether mechanism of action defined in pre-clinical models can be observed in humans and provide human PD/PK data before definitive phase I/ II studies

Drug Discovery/Development Process

Phase 0 (contd)

- Micro-dosing phase 0 studies use sub-pharmacological doses to obtain basic PK data such as volume of distribution, clearance, half-life etc. subject to availability of ultrasensitive analytical methods

Drug Discovery/Development Process

Phase I

- Small no of healthy volunteers, – usually 20 to 100
- Purpose - identify metabolic and pharmacological effects of drug in humans
  - Determine the side effects associated with increasing doses
  - Gain early evidence on effectiveness
- Mainly determine safety profile

Drug Discovery/Development Process

Phase II

- Early controlled clinical studies in a small number of patients
- To obtain preliminary data on the effectiveness of the drug for a particular indication in patients determine the common short-term side effects and risks

Drug Discovery/Development Process

Phase III

- Performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase II
- Intended to gather additional information about effectiveness and safety needed to assess the risk-benefit ratio of the drug
- Phase III studies include several hundred to several thousand people

Drug Discovery/Development Process

Phase IV

- Also known as Post Marketing Surveillance
- Carried out once the drug is approved and marketed
- Aim of Phase IV study is to find out safety profile in large patient pool across the world