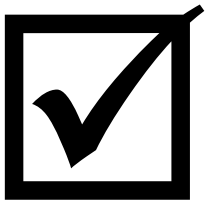
Drug Development Process

The Drug Development Process



- Each country has a drug regulatory body which governs the approval process
- US- FDA (food and drug administration)
- UK- MHRA (medical and healthcare products regulatory agency)
- European Union- EMEA (european medicines agency)
- India- CDSCO (central drugs standards and control organization)
- Sri Lanka- NMRA (national medicines regulatory authority)

- Drug must be proved to be **safe and effective**

Regulatory Agency

- Overlooks before and during various phases of product development and its marketing.
- The drug is tested:

- **Pre-clinical testing (laboratory and animals)**
- Pharmacology and toxicology

- **Clinical testing (clinical trials in humans)**
- dose regime, safety and efficacy
- consistency and reproducibility

Target Selection & Validation

- Define the unmet medical need (disease)
- Understand the molecular mechanism of the disease
- Identify a therapeutic target in that pathway (e.g gene, key enzyme, receptor, ion-channel, nuclear receptor)
- Demonstrate that target is relevant to disease mechanism using genetics, animal models, lead compounds, antibodies, RNAi, etc.

Discovery

- Develop an assay to evaluate activity of compounds on the target
  - *in vitro* (e.g. enzyme assay)
  - *in vivo* (animal model or pharmacodynamic assay)
- Identify a lead compound
  - screen collection of compounds ("compound library")
  - compound from published literature
  - screen Natural Products
  - structure-based design ("rational drug design")
- Optimize to give a "proof-of-concept" molecule—one that shows efficacy in an animal disease model
- Optimize to give drug-like properties—pharmacokinetics, metabolism, off-target activities
- Safety assessment, Preclinical Candidate!!!

What is a Clinical Trial?

The History of Clinical Trials

- First controlled clinical trial on 12 Sailors with Scurvy by James Lind
- 1747 – Lind's study comparing the use of limes and oranges in the treatment of scurvy
- What is Scurvy?
- Treatment with limes & oranges, seawater, Vinegar, Mustard-Garlic mixture, Elixir
- 2 patients each
- Two patients on limes & oranges were cured

The History of Clinical Trials

- First ***randomized*** controlled clinical trial
- 1948- First use of a randomized control group: streptomycin treatment of pulmonary tuberculosis
- Treatments: streptomycin (antibiotic) versus bed rest
- Patients received streptomycin OR just bed rest at random (randomized clinical trial)
- Outcome: streptomycin was effective

A High-Risk Undertaking

- **Time** 8-12 years from discovery to market
- **Cost** average of $500-600 million
- **Success** 1 in 4000 compounds synthesized succeed in animal studies or

  1 in 10 tested in humans reaches the market
- **Return** 1 in 3 drugs reaching the market recapture development costs

Major Stages of Drug Development

Preclinical Testing

Investigational New Drug (IND) Application

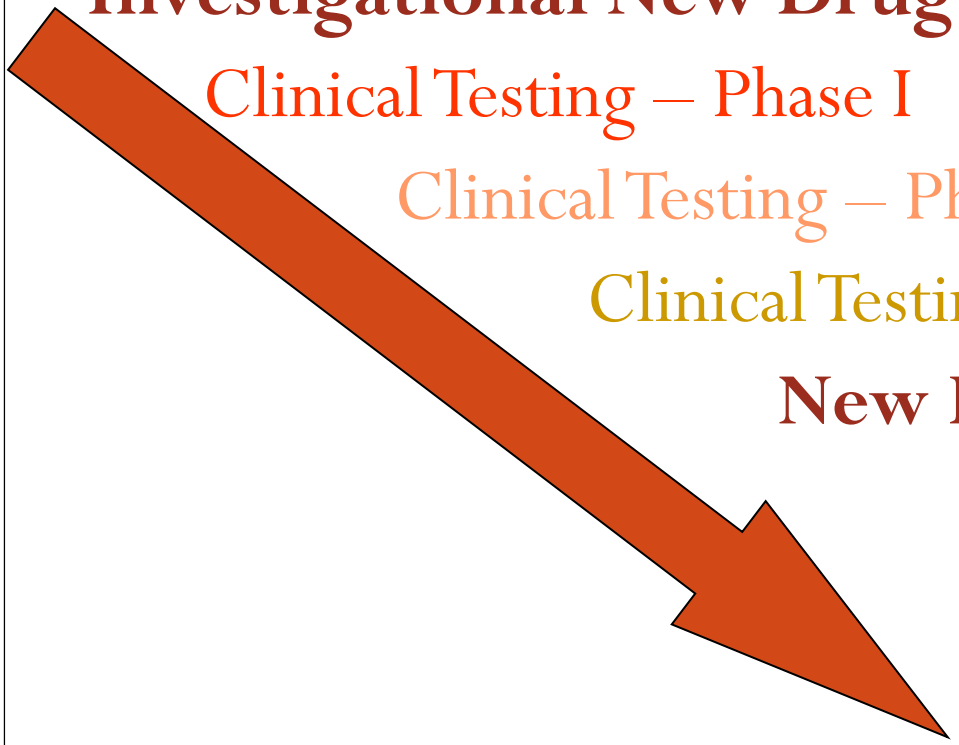
Clinical Testing – Phase I

Clinical Testing – Phase II

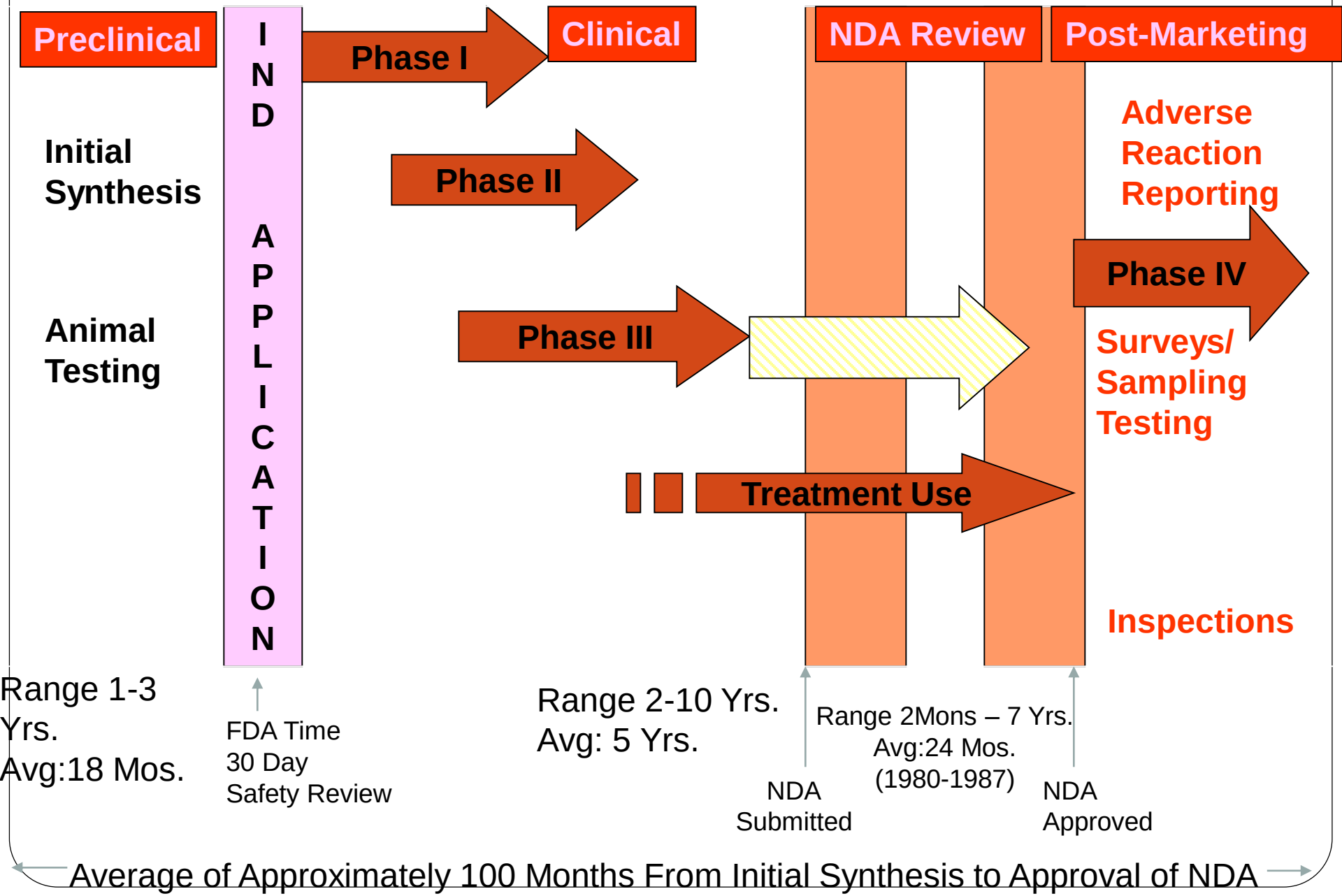
Clinical Testing – Phase III

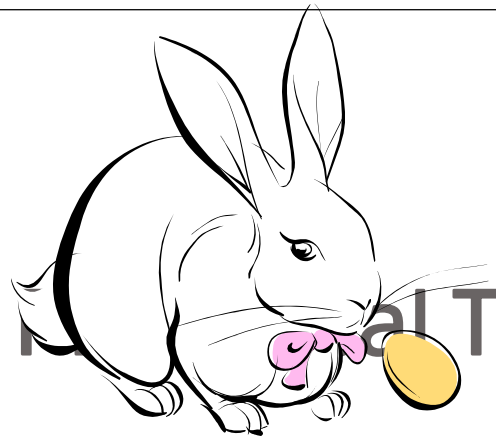
New Drug Application (NDA)

Clinical Testing–Phase IV



Drug Development Process





Testing

- Laboratory and Animal Testing is Done
- Animal models- mimic human disease
- Is compound safe(non-toxic) in living organisms ?

  Eg: Nerve Damage- Neurotoxin
- Is compound biologically active?
- If YES, file an IND Application

IND Application (Investigational New Drug)

- Report the results of preclinical testing
- Describes how the drug is synthesised
- Non-toxic
- Modus operandi

- If the FDA does not disapprove of the IND application within 30 days, then testing in humans can begin

Clinical Testing – Phase I

- Involves giving the candidate drug to a small number of healthy volunteers (free from disease being tested)
- Estimate Safety & Tolerability with single & multiple doses
- Determines the safety of the drug as well as the safe dosage range(starting with 0.1mg/kg)

- Takes a year or less to complete

Clinical Testing – Phase II

- Involves giving the drug to a large group (100-300- narrow criteria- **homogeneity** of population) of patients who have the disease that the drug is expected to treat

- Purpose is twofold….

  Does the drug work in the disease population?

  *At what dosage does **(range)** the drug demonstrate efficacy?*

- Eg: Type 2 Diabetes- brings sugar level in a desirable way
- Takes about 2 years to complete

Clinical Testing – Phase III

- Involves giving the drug to a large number of patients (1000-3000)

- Purpose is to….

  Confirms earlier efficacy results

  Identify adverse events which when drug is given to a larger population over a longer period of time

- Takes about 3 years to complete

NDA – New Drug Application

- If the results of all the previous testing is positive, then the pharmaceutical company files an NDA
- NDA contains all of the information gathered during preclinical to phase III
- NDA can be thousands of pages long
- Can take 2-3 years for FDA to review

Treatment INDs or Expanded Access Programs

- In response to the AIDS crisis in 1987, the FDA issued new regulations to speed the approval of life threatening or severely debilitating disease]
- The FDA works closely with the sponsor on promising drugs in the hopes of combining the phase II and phase III trials
- This can save 2-3 years in the approval process

Clinical Testing – Phase IV

- Once the NDA is approved and the drug is available, *post-marketing studies* are conducted to further confirm safety and efficacy during long-term use

- Can include mail-in questionnaires and personal interviews

Thank You