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## Drug Innovation and Development Cycle

Nagashree Kotturi\*, Phani kummar Kotturi

Department of Clinical Research, Nizam's institute of medical sciences, Hyderabad, India

### Commentary

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#### \*For Correspondence

Nagashree K, Department of Clinical research, Nizam's institute of medical sciences, Hyderabad, India;

E-mail: nagashreekotturi@yahoo.com

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#### ABSTRACT

Drug discovery and development initiates with identification of lead molecules targeted for a treating a particular disease. The identified lead compound which is termed a new chemical entity is subjected to drug development process. Drug development process involves different stages like

- 1) Pre-Clinical Testing
- 2) Phase I Clinical Trials
- 3) Phase II Clinical Trials
- 4) Phase III Clinical Trials
- 5) New Drug Application (NDA) / Biologics License Application (BLA)
- 6) Phase IV or post marketing surveillance.

### INTRODUCTION

Drug discovery and development [1-3] is complex and time consuming process, which involves experts from different departments like research, development, manufacturing, medical, regulatory, marketing and business management to jointly collaborate for successful synthesis, and marketing the novel medication or drug.

Drug discovery [4-7] follows with the drug development process, in which the drug passes various development stages necessary to get approval, by regulatory authorities for marketing of the drug.

### Process of Drug Discovery and Development

#### Preclinical testing

Pharmaceutical companies examine thousands of compounds with therapeutic value [8] targeting specific disease. The entire process for preclinical testing involves near to about 6 to 7 years, which involves synthesis, purification of the drug with limited animal testing. Out of various compounds subjected for testing, five would be favorable for the company to file IND application (Investigational new drug application). The manufacturer can proceed with the first phase of development, once IND is approved by FDA.

#### Phase I clinical trials

The investigational new drug consists of three phases, phase I, phase II and phase III. Phase I clinical trials are conducted in healthy volunteers in order to identify the drug properties and safety profile in human beings. Phase I clinical trials are conducted in 20-100 volunteers. Various drug properties like safety, pharmacokinetics [9-13] and pharmacodynamics are being determined. This phase I clinical trials usually take several months to complete. The patients are segregated into smaller groups known as cohorts. Each cohort is treated with an increased dose of new therapy. Thus, the highest dose with an acceptable level of side effects is considered to be appropriate for further testing.

## Phase II clinical trials

Phase II clinical trials are considered as exploratory trials. In phase II, efficacy trials begin as the drug is administered to patients with target population. Controlled Phase II trials are conducted in population ranging from 100-300. Phase II clinical trials are conducted to identify the efficacy of the drug, and to assess the dosing requirements. This phase lasts from several months to two years. Phase II studies are usually conducted in randomized manner, in which one group of patients receives experimental drug, and second “control” group receives standard treatment or placebo. These studies are not conducted in “blinded” manner, in which patients nor do the scientists know who has received the experimental drug. Thus the investigators provide the comparative information about safety and effectiveness of the new drug to the pharmaceutical company and FDA. Mostly one-third of experimental drugs successfully complete phase I and phase II studies. At the end of phase II clinical trials, the manufacturer is responsible for discussing with FDA officials regarding the development process continued human testing, and the protocols for phase III clinical trials, which is the most extensive and expensive process of drug development.

## Phase III clinical trials

Phase III clinical trials are considered as confirmatory trials, which involves randomized and blind testing in several hundred to thousand patients. This phase of study usually lasts for several years, in which the extensive understanding, the effectiveness of the drug is been provided to pharmaceutical company and FDA. After completion of phase III clinical trials, pharmaceutical company gets the approval <sup>[13-15]</sup> from FDA for marketing the drug. Mostly 70-90% of drugs that enters phase III studies successfully completes phase III testing.

## New drug application (NDA)/Biologics license application (BLA)

Before marketing the drug, sponsor submits the NDA (new drug application) to FDA for approval. NDA includes all the drug <sup>[16-20]</sup> related information including the human, animal data. Once the NDA <sup>[21-25]</sup> is filed, FDA has 60 days to decide whether to file it, so that it can be reviewed. FDA declines the application in case if it is found to be incomplete, in case of any missing drug data related to studies.

## Phase IV clinical trials

Phase IV clinical trials are known as post marketing surveillance, in which studies are being conducted after the drug is being marketed. Phase IV studies involves comparison of drug with other marketed drugs, the long term drug effectiveness and its impact on patients quality of life, and cost-effectiveness of drug in comparison to other traditional or new drug. In case of any discrepancy found in post marketing surveillance, the product may be “called off” or withdrawn from the market or use of the drug may be restricted in case of any study findings during phase IV trials.

Thus the drug discovery and development process may take several years to complete, to make the product fit into the market for treating the particular disease.

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