

Definition of Development Phases

Preclinical

- The drug is being tested *in vitro* (cells, test tubes) or *in vivo* (animals). The developer applies for permission to go into clinical testing.
- The procedure for applying for permission will depend on the country. For example, in the USA, an Investigational New Drug (IND) application must be granted before clinical trials can begin.
- For the purposes of using R&D Insight, the term preclinical encompasses all investigations undertaken before clinical trials are started. This includes Research Programs, from which lead compounds are selected for further development.

Phase I

Purpose: to determine safety, efficacy, and initial pharmacokinetics. These are the first trials of a new drug or therapy, usually conducted in healthy male volunteers. Patients may be evaluated instead of volunteers in phase I trials in order to treat immediately life-threatening and serious conditions for which there is no comparable or satisfactory alternative therapy available (in the US, this is called Treatment IND status). In addition, Expanded Access programs allow patients for whom standard therapy is ineffective or contraindicated, and who are ineligible to enter trials, to receive investigational drugs in parallel with controlled trials.

Phase II

- Purpose: to provide a measure of efficacy in addition to short-term tolerability.
- Phase II studies are conducted in patients who have the disease or condition that the drug is intended to treat. Other phase II study objectives include determining the minimum dose that is maximally effective, or that is sufficiently effective without undue toxicity.
 - For the purposes of using R&D Insight, phase II includes combined phase I/II trials, phase IIa pilot or feasibility trials, and phase IIb well controlled, pivotal trials.

Phase III

- Purpose: to confirm efficacy, and monitor adverse reactions from long-term use.
- In phase III studies, a drug is tested under conditions more closely resembling those under which the drug would be used if approved for marketing. The goal is to gather additional information about efficacy and tolerability that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.
 - NB. Approval/disapproval decisions are based on the results of adequate and well-controlled (pivotal) studies. To be considered pivotal, a study must meet at least the following 4 FDA-defined criteria:

Phase III (cont.)

- Be controlled using placebo or a standard therapy.
- Have a double-blinded design when such a design is practical and ethical. Be randomized.
- Be of adequate size. Study sample size is a common clinical trial design flaw.
- For the purposes of using R&D Insight, phase III includes phase II/III, phase IIIa and phase IIIb trials. Phase IIIb trials are usually those undertaken after a regulatory dossier has been submitted.

Pre-registration

All the necessary clinical trials have been completed and the drug is waiting for registration or approval for use by a governing body. For example, a New Drug Application (NDA) has been filed with the FDA in the USA. For biological drugs (e.g. proteins, antibodies, etc) R&D Insight considers the agents to be at the pre-registration stage, upon submission of the first part of a rolling Biologics License Application (BLA) irrespective of whether pivotal trials have been completed. Occasionally, rolling submission submissions are applied to NDAs.

Registered

The drug has been registered or approved for use in a particular country, or group of countries such as the European Union countries.

Launched

The drug has been launched and is now marketed in a particular country, or group of countries.

Discontinued

The company has chosen to stop development. This term is usually qualified by the phase at which development was discontinued, for example, discontinued (preclinical).

No development reported

If there has been no activity associated with a drug (no commercial information released, no recently published studies) for ≥ 2 years for indications at the clinical stage of development, and ≥ 3 years for preclinical entries, the term 'no development reported' (NDR) is assigned. NDR is an inactive status and is used until a drug is confirmed as discontinued, withdrawn or suspended, or activity is resumed.

Withdrawn

This term applies to drugs that had been launched and subsequently withdrawn from the market.

Suspended

This term is used when a company has suspended development of a drug, often in order to focus on the development of some other drug. Development has not been discontinued.

Clinical

This option is only used when the clinical phase of development is unclear.