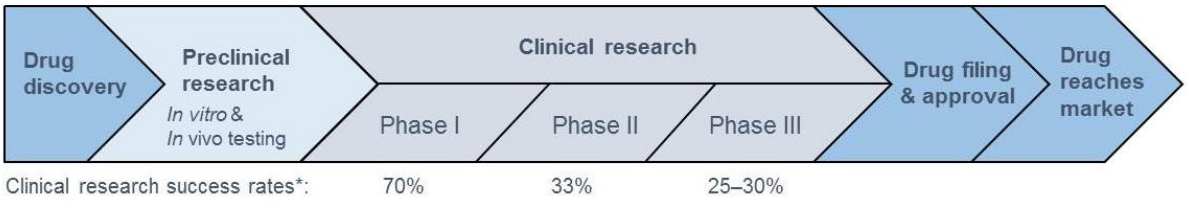
RETINA INTERNATIONAL Seeking A Cure For Retinitis Pigmentosa, Macular Degeneration, Usher Syndrome and Allied Retinal Dystrophies

Understanding Drug Development

A new therapy must undergo extensive testing and meet strict regulatory requirements before it can be approved and made available to patients.[1]

Overview of the drug development process



*Source: US Food and Drug Administration. The Drug Development Process - Information for Patients (https://www.fda.gov/forpatients/approvals/drugs/default.htm).

Step 1: Discovery and development

The development process typically begins in the laboratory, where researchers characterise the specific processes and pathways involved in the development of the disease being studied. Insights from this work allow researchers to develop or identify targets and associated therapies that may be able stop or slow the progression of a disease.

Step 2: Preclinical research

Before testing a new therapy in people, researchers must perform preclinical studies to evaluate its safety and potential toxicity. The results of preclinical research can be used to decide whether a therapy should be tested in humans.

Preclinical research experiments can either be:

- *in vitro* ("in glass"; in a test tube) experiments that are performed in a plastic or glass vessel in the laboratory; or
- *in vivo* ("in the living organism") experiments that are done in the body of a living organism.

Step 3: Clinical research

"Clinical research" is the term used to describe studies or clinical trials performed in people. Clinical trials are performed in a succession of different phases:

- Phase I clinical trials which are performed in small numbers (20–100) of healthy volunteers or people with the disease over a short time period (i.e. several months). The primary purpose is to evaluate safety and dosage (the amount of therapy that can be given before side effects become intolerable or dangerous).

[1] The Therapy Development Process - Information for Patients (https://www.fda.gov/forpatients/approvals/therapies/default.htm). US Food and Therapy Administration. Accessed September 2017.

Understanding Drug Development

- Phase II clinical trials are performed in larger numbers of people with the disease or condition (100–300 volunteers) over a longer time period (several months to 2 years). The primary purpose is to evaluate efficacy and side effects. Only around one-third of new therapies proceed from Phase II studies to the next Phase of clinical testing

- Phase III clinical trials are performed in a larger numbers of people with the disease (300–3000 volunteers) and can last several years. The purpose of these studies is to determine whether the new therapy offers a clinical benefit in a population of people it is intended to treat. Phase III trials compare the effectiveness and safety of the new therapy against the current standard treatment or a placebo (dummy treatment). If the Phase III trial is successful, the company can apply for marketing authorisation to make the therapy available for public use

- Phase IV clinical trials (also called 'post-marketing surveillance trials') are sometimes performed once the new therapy has received marketing authorisation. The purpose of these studies is to monitor the safety of new therapies in a larger population of people (up to several thousand) with the disease over a longer period of time.

Challenges with therapy development

The process for bringing a new therapy to market is time-consuming, complex and expensive, and is also associated with a high rate of failure:

- Overall, the average time from the discovery of a new therapy until it reaches the marketplace is 12 years.[2]

- The clinical research process for a new therapy (i.e. Phase I, II and III trials) typically takes an average of 6 to 7 years.[3]

- Clinical development success rates (i.e. the likelihood that a new therapy entering clinical testing will eventually be approved for the treatment of patients) are estimated to be less than 12%.[4]

- Marketing authorisation (regulatory approval) does not guarantee access to the therapy for all patients. Individual payers (governments, insurers, etc.) each set their own criteria for paying for a new therapy and require health economic assessments to be conducted based upon their individual cost environments.

[2] Van Norman G. Therapies, Devices, and the FDA: Part 1: An Overview of Approval Processes for Therapies. JACC: Basic to Translational Research. 2016;1(3): 170-179.
[3] Biopharmaceutical Research & Development: The Process Behind New Medicines. Pharmaceutical Research and Manufacturers of America (PhRMA), 2016.
[4] Clinical Development Success Rates 2006-2015. BIO, Biomedtracker, Amplion., 2016.

Understanding Drug Development

- Developing a new therapy is also associated with significant financial costs. Cost estimates vary considerably between studies. A US study published in 2016 calculated the average cost to develop and gain marketing approval of a new therapy to be $2.558 billion (based on 2013 dollars).[5]

[5] DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of health economics. 2016;47: 20-33.