

## The Importance of Clinical Trials in Drug Development

While preclinical research answers basic questions about a drug's safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people<sup>1,2</sup>. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process, a process they must go through before clinical research begins. The ultimate goal of drug development is to bring a new compound with proven therapeutic effect to the market. In this context, the transition from preclinical research to clinical stages marks a critical turning point, as it nears the new medicinal product to the market<sup>3,4</sup>. With the promise of marketing authorization, though far ahead in the road, hanging on the horizon, the approval of a clinical trial usually attracts investors and leads to a respectable rise of the company shares. However, everything comes at a price. Clinical trials are not without risks, and while the perspective of success is encouraging, the crude reality is that most compounds fail before reaching the market. As explained in previous entries, despite higher R&D expenditures, attrition rates are high and, what is worse, on the rise. Data collected between 1990 and 2004 show that the number of unsuccessful clinical trials has been steadily increasing during the last years: from 30% to 50% at Phase 1, from 40% to 70% at Phase 2 and from 20% to nearly 50% at Phase 3<sup>3,4</sup>. As a result, less than 10% of the drugs that enter clinical trials end up being approved by regulatory agencies. Clinical trials are only a small part of the research that goes into developing a new treatment. Drugs of the future, for example, first have to be discovered or created, purified, described, and tested in labs (in cell and animal studies) before ever reaching human clinical trials. Of all the substances that are tested in these early stages, very few are promising enough to be tested in humans. Drug development is the process of bringing a new pharmaceutical drug to the market once a lead compound has been identified through the process of drug discovery. It includes pre-clinical research on microorganisms and animals, filing for regulatory status, such as via the United States Food and Drug Administration for an investigational new drug to initiate clinical trials on humans, and may include the step of obtaining regulatory approval with a new drug application to market the drug. Indeed, of every 5,000 cancer molecules identified in the laboratory, about 250 will enter pre-clinical testing. Of this 250, fewer than 10 are tested in clinical trials and on average only one will be approved by regulatory authorities. The process of bringing a new treatment from the research stage (laboratory) to clinic is estimated to take between 10-13 years<sup>5</sup>.

### References

1. Sepanjnia K, Modabbernia A, Ashrafi M, Modabbernia MJ, Akhondzadeh S. Pioglitazone adjunctive therapy for moderate-to-severe major depressive disorder: randomized double blind placebo-controlled trial. *Neuropsychopharmacology* 2012;37(9):2093-2100.
2. Akhondzadeh S. Hippocampal synaptic plasticity and cognition. *J Clin Pharm Ther* 1999;24(4):241-248.
3. Akhondzadeh S, Malek-Hosseini M, Ghoreishi A, Raznahan M, Rezazadeh SA. Effect of ritanserin, a 5HT<sub>2A/2C</sub> antagonist, on negative symptoms of schizophrenia: a double-blind randomized placebo-controlled study. *Prog Neuropsychopharmacol Biol Psychiatry* 2008;32(8):1879-1883.
4. Amrollahi Z, Rezaei F, Salehi B, Modabbernia AH, Maroufi A, Esfandiari GR, et al. Double-blind, randomized, placebo-controlled 6-week study on the efficacy and safety of the tamoxifen adjunctive to lithium in acute bipolar mania. *J Affect Disord* 2011;129(1-3):327-331.
5. Akhondzadeh S, Ahmadi-Abhari SA, Assadi SM, Shabestari OL, Kashani AR, Farzanehgan ZM. Double-blind randomized controlled trial of baclofen vs. clonidine in the treatment of opiates withdrawal. *J Clin Pharm Ther* 2000;25(5):347-353.

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