superiority over the cheaper drug (e.g., better efficacy, improved safety profile), market penetration for a new drug may be difficult to achieve. The expense of producing the candidate compound or formulation requirements may also be too high to warrant the cost of advancement. It is also possible that the length of time required for phase III clinical trials is too long relative to the remaining patent life for the candidate compound. Generic competition might be able to enter the market before the originating company would be able to recoup the cost of developing the candidate compound. There are many non-scientific reason why a candidate compound might be abandoned before a phase III trial is initiated. The decision to move forward or stop should be weighed carefully, given the enormous financial risk of moving forward.

If the decision is made to move forward, the nature of the phase III trial is heavily dependent on the purpose of the candidate compound. There are, however, some overarching goals that must be met in order for a phase III program to reach a successful conclusion (e.g., provide support for marketing the candidate compound). First and foremost, the phase III clinical trials, often referred to as pivotal studies, must confirm the efficacy and safety of the candidate compound in the broad patient population. This process generally requires 1000–3000 patients, possibly more, multiple clinical sites, an institutional review board (IRB) and they can last from 2.5 years to 5 years, depending on the nature of the disease and the patient population. In order to be considered a success, a phase III clinical program must produce at least two "adequate and well-controlled studies" that demonstrate both the safety and efficacy of the candidate compound. In other words, the studies must be robust enough that the end results can be extrapolated to the general population and the resulting information can be provided to the health care providers (e.g., physicians, nurses, pharmacists, etc.) in the form of a package insert.

In theory, a sponsor company could develop the data necessary to support a request for market approval (licensure) by conducting only two phase III clinical trials. In practice, however, many companies choose to run a third study. While this will add significant cost to the overall program, it is often viewed as a worthwhile investment. If two trials are conducted and it is determined that one of the two was not sufficiently supportive of the compound candidate's efficacy or safety, then a third trial would be required in order to develop the data necessary for marketing approval. There could also be procedural problems such as patient monitoring inconsistencies or data collection issues that result in a regulatory agency excluding a clinical trial from a New Drug Application (NDA) package. If only two studies are run, the sponsor organization would not have enough data to support licensure. A third trial would be necessary and would create a substantial delay in obtaining marketing authorization. This would reduce the time available to recoup the significant investment required to reach the market. In a sense, a third trial is an insurance policy against the unexpected.