Determining whether or not a candidate compound is providing a benefit to the patients is measured using predefined outcome measures that are established when the trial design is approved. In some cases, the outcome may be directly tied to the disease or condition to be treated and evaluating the effect may be a simple matter of counting people. An increase in the number of patients surviving 1 year after a pancreatic cancer diagnosis when the candidate compound is added to the standard of care is a simple example of this type of outcome measure. Monitoring quantifiable attributes in patients (taking measurements) might also be used as an outcome measure. Changes in body weight in patients could be used as an outcome measure for a potential weight loss therapy, while changes in a patient's blood pressure could be used as an outcome measure for potential novel antihypertensive agents. Surrogate markers, a subset of biomarkers, such as cholesterol concentration[41] or viral load[42] can also be used as outcome measures. This type of outcome measure will be discussed in greater detail in Chapter 10.

Although a successful phase II clinical trial provides proof of principle, it is by no means a guarantee of success in phase III trials. There are many examples in the literature of candidate compound that produce a positive result in phase II that cannot be replicated in a larger, more heterogeneous patient population. A 2014 analysis of over 5800 clinical programs from 835 companies indicated that only ~60% of the compounds that produced positive results in phase II trials were also successful in phase III trials.[43] Given the expense associated with phase III clinical trials, a thorough examination of the phase II data should be undertaken to ensure that the data set is robust enough to warrant the expense of the next phase of development.

PHASE III CLINICAL TRIALS

Launching a phase III clinical trial represents a major commitment by the sponsor organization (almost always a pharmaceutical company), as the cost of this portion of the drug discovery and development process represents the largest financial commitment. In some case, as much as 90% of the costs associated with bringing a new drug to market are incurred during phase III clinical trials.[44] As a result, the successful conclusion of a phase II trial is not always enough to warrant initiating phase III studies. There are many reasons that an organization might choose to terminate a clinical program that have nothing to do with clinical trial results. A competitor drug may already be available that is more effective than the candidate compound. This would hamper the sponsor company's ability to gain market share and recoup the costs of developing a competing new therapy. The availability of a generic drug may also lead to a decision to abandon a clinical program rather than launch a phase III trial. In the absence of