Financial considerations also play a major factor in the determination of which diseases and potential drug targets are examined and which are not. Clearly, the amount of money and time available to pursue new therapeutic entities is limited, so not every target or disease state can be addressed. In the corporate world, disease state and target selection is generally driven by the ability to generate profitable products whose sale will support future research programs. On the surface, this would seem to dictate that only diseases or conditions with large numbers of patients would be of interest to corporate entities, but this is not the case. Chronic diseases such as osteoporosis, hypertension, hypercholestremia, and arthritis clearly have a large patient population that creates opportunities for corporations. Rare diseases, however, also present significant opportunities and a pathway for growth. Amyotrophic lateral sclerosis (ALS), for example, is a disease with a small, but consistent patient population with significant unmet medical needs. At any given time, there are only 20,000–30,000 ALS patients in the United States whose life expectancy is only 3–5 years, and there are no life extending therapies currently available.[63] This would appear to be a very small market that is unlikely to provide the kind of profitability required to sustain a corporation. However, it is important to realize that if a suitable treatment were available, this terminal condition would become a chronic condition wherein patients would be treated for the disease throughout the course of an otherwise normal life span. In addition, increased survival time for ALS patients would lead to a larger patient pool, providing additional revenue to a company that develops a life-extending treatment for ALS.

The selection of targets and disease states of interest sets the course for all future aspect of a research program, so the importance of this decision cannot be understated. Once the biological target is selected, the process of identifying a clinical candidate can begin.

HIT IDENTIFICATION: FINDING A STARTING POINT

Once a target of interest has been identified, the remainder of the research program is essentially a quest to identify a single compound that is suitable for use in a clinical setting. Of course, this relatively simple statement is actually a representation of an exceptionally complex and multifaceted problem. Currently, there are over 70 million compounds registered in the Chemical Abstract Service database,[64] and the total number of possible compounds to consider as drug candidates is nearly infinite, so the question of where to start the process is significant. Fortunately, there are some guidelines that have been developed in order to provide some guidance as to where one might begin to look for biologically useful molecules. Lipinski's rule of 5,[65] for example, suggests that the majority of druglike