

can be delivered as safe and effective therapeutic agents? How does one determine which of the nearly infinite possibilities are useful and which ones are not? Of the useful compounds, which ones will be of interest to the companies that manufacture drugs and which ones will not? These issues are exceptionally complex, and become even more so, when the health issue is something other than an invading organism. In considering chronic pain management, for example, a drug provided to a patient should alleviate the chronic pain without interfering with the pain associated with protective instincts, such as withdrawing one's hand from a hot stove. This added complexity is a common feature of the vast majority of disease states and must be addressed in order to successfully develop any new medication.

Given the large number of complex issues associated with drug design and development, it should be abundantly clear that no one individual could possibly conquer all of the tasks required to discover, develop, and successfully bring to market a new therapeutic entity. The process is a multidimensional one and as such requires the coordinated effort of individuals with a wide array of expertise such as medicinal chemistry, *in vitro* biology, drug metabolism, animal pharmacology, formulations science, process chemistry, clinical research, intellectual property, and many other fields. Enabling technologies, such as high throughput screening, molecular modeling, pharmaceutical profiling, and biomarker studies, also play key roles in modern drug research. It is critical that anyone interested in pursuing a career in the development of pharmaceutically useful agents, whether in an industry setting or an academic institution, must be willing and able to participate in collaborative research effort over a significant period of time. In addition, it is important that any participant in this field understands the magnitude of the costs associated with the pursuit of new drugs. The rewards for those who are successful can be substantial, as indicated by the success of compounds such as Lipitor<sup>®</sup> (Atorvastatin), which had peak annual sales of over \$13 billion,<sup>34</sup> Prozac<sup>®</sup> (Fluoxetine, peak sales \$2.8 billion),<sup>35</sup> and Singulair<sup>®</sup> (Montelukast, 2011 sales \$5.5 billion),<sup>36</sup> but the cost in time and resources is substantial (Figure 1.5). As indicated in Figure 1.6, it has been estimated that the identification of a single marketed drug can require an initial examination of over 100,000 candidate compounds, hundreds of preclinical animal studies, and numerous clinical trials involving thousands of patients. A recent analysis of clinical trial success rates has indicated that only 1 out of every 10 clinical candidates will successfully traverse clinical trials and reach the market. This represents a success rate of less than 0.001% if measured by the number of compounds examined at the outset of the process. If measured according to the number of programs required to advance a single drug to market, program attrition rates indicate that only 1 in 24 programs is successful.

The cost associated with the identification of useful and marketable therapeutic entities is also staggering. As of 2011, it is estimated that a