

III trial durations. The impact of phase IV studies can include alterations to labeling based on safety results, contraindication for use of the new drug in combination with other medications, or even the withdrawal of marketing approval if the findings are severe enough. The COX-2 selective non-steroidal anti-inflammatory agent Vioxx® (Rofecoxib),³⁹ for example, was removed from the market after phase IV studies indicated that it increased the risk of ischemic events in patients (Figure 1.8). In a similar fashion, Baycol® (cerivastatin),⁴⁰ a 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor marketed by Bayer AG for the treatment of high cholesterol and cardiovascular disease, was voluntarily removed from the market after reports of fatal rhabdomyolysis (Figure 1.8).

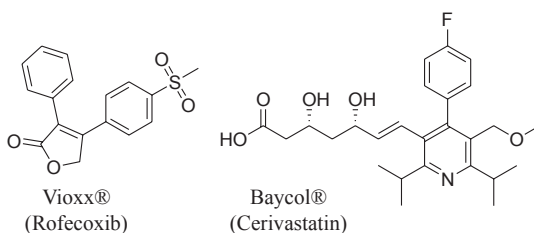


FIGURE 1.8 Vioxx® (Rofecoxib) and Baycol® (Cerivastatin) were removed from the market as a result of an increased risk of ischemic events and fatal rhabdomyolysis respectively.

It should be noted that safety studies are not the only reason for phase IV clinical trials. Companies often use the data provided in postmarketing surveillance and additional clinical studies to identify competitive advantages, new markets, and new indication for their products. There is some level of risk associated with conducting trials designed to identify clinical superiority, as the results of competitive trials are often difficult to predict. In some cases, a company's plan to demonstrate that their compound is superior to a competitor's drugs backfires, and they prove the opposite.

TARGET SELECTION: THE FIRST STEP FORWARD

The process of identifying a new drug candidate begins with identifying a disease state or condition that can be addressed or modified through the application of a suitable chemotherapeutic intervention. In theory, the most pressing medical needs would have the highest priority in order to ensure improvement of the overall quality of life for patients. In practice, however, there are many factors that contribute to the decision of which disease or condition to attempt to address through drug discovery programs. First, the pathway to develop a therapeutic intervention may not be clear for a particular disease or condition even though the medical