for Herceptin, 27 for Enbrel, and 35 for Rituxan. These figures are not surprising since these drugs were all blockbusters. In particular, 2013 revenues for Herceptin and Rituxan were $6.6 and $7.5 billion, respectively. Humira and Avastin were also blockbuster drugs, with 15 and 13 biosimilar developers, respectively. Patents for these five drugs are to expire between 2018 and 2028 (King, 2014).

As discussed above, not all products labeled biosimilars are truly biosimilars, but if even half of them are true biosimilars, that would still be 17 biosimilar entrants for Rituxan. As in any nascent market, it will take time for the market to adjust to a long-run equilibrium. It is highly unlikely that 17 biosimilar firms can survive in any particular biologic market. The costs of R&D as well as the other costs involved could well exceed $250 million for each biosimilar. Thus, even though the market opportunity exists, firms will presumably understand the complexity of the market and perform due diligence before they decide whether to enter the market.

There is also the issue of which markets to enter. Are there advantages for firms to develop a portfolio of biosimilars? A portfolio of four or five biosimilars will spread the risk but also entail an investment in the area of a billion dollars. Another issue is which markets to enter. Strategies for biosimilar producers involve whether to enter blockbuster or smaller revenue biological markets. There are obviously greater potential profits in blockbusters but more competition, which could result in higher discounts, potentially less profit, and possibly no return on investment. Medium-revenue markets may appear to have less potential profit, but with less entry and lower discounts, profits may actually be higher.

Thus, the issue arises as to whether biosimilars can get a return on their investment. They will face price competition not only from the originator and other biosimilars but also from biobetters, including originators developing second-generation biologics. Many firms are making huge investments to develop biosimilars, including cost of R&D, manufacturing costs, clinical trials, and other costs. How many biosimilars will enter each market is unclear, but one would expect that the mature market could only sustain four or five biosimilar competitors. The biologics market should eventually evolve to be highly competitive as biosimilars enter the market. As in the pharmaceutical market, there will be a few winners and many losers.

16.23 US SUBMISSIONS TO DATE

There have been five applications in the US for biosimilars. However, Sandoz's Zarxio is the only one that has been approved, but it has not yet entered the market because of patent issues. Sandoz submitted considerable evidence of the structure and functionality of its biosimilar. Clinical trials, along with animal studies and the experience in the EU, were provided in support of its application. One clinical trial involved breast cancer patients. Sandoz also noted that its biosimilar had been available in most of the EU, 32 other countries, and has had 7.5 million days of usage (Sandoz, 2015). Also, Sandoz was approved for all five indications of the reference product through extrapolation.

The FDA postponed the hearing on Cellitron's Remsima biosimilar application that was scheduled for March 17, 2015, as the FDA asked for more information.