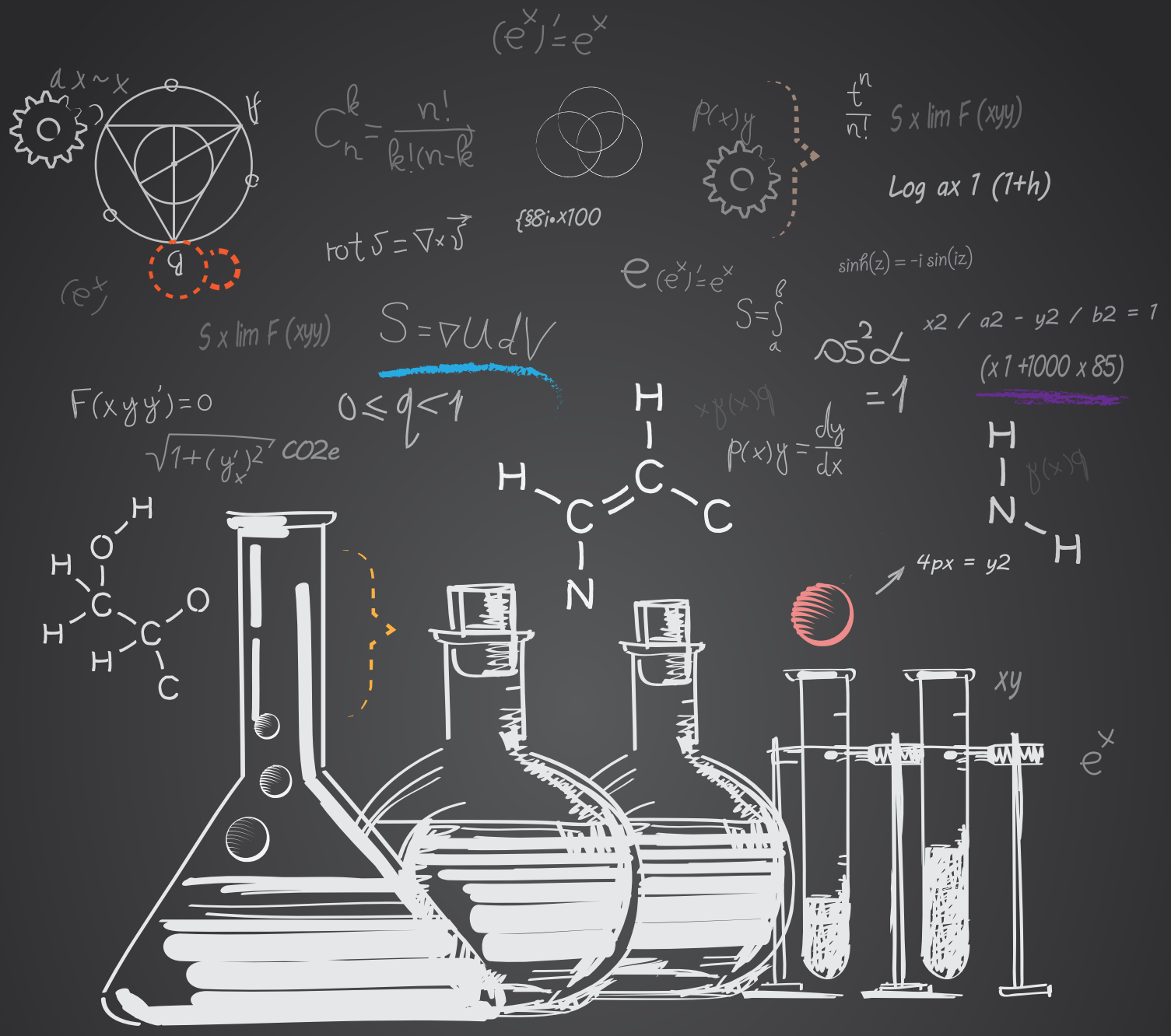

BIOSIMILARS:

a tipping point

Paula Gurz, director
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In 2005, the U.S. Food and Drug Administration (FDA) released the results of a five-year study that compared the prices of single-ingredient, brand name drugs with generic alternatives. The data demonstrated that generic competition is associated with lower drug costs. A drug with one generic competitor had slight reductions in cost, but a drug with two generic alternatives showed the greatest price reduction.[1]

This idea of competitive friction – the existence of competitors in a market that serve to put downward pressure on pricing – was largely the driving force behind the generic approval pathway set forth in the 1980s. It has contributed greatly to improved accessibility for everyday medications. It has also allowed patients to have a choice between a brand name drug and generic alternatives that contain the same ingredients at a lower cost. The biologic market is one that, until recently, has lacked that competitive friction. Finally in 2009, a pathway was provided as part of the Affordable Care Act through the Biologics Price Competition and Innovation Act (BPCI).

Since that time, U.S. regulators and industry stakeholders have struggled to agree on many aspects of creating a streamlined process to bring biosimilars to market. Unlike branded and generic drugs, biologic drugs are considerably more complex. That makes finding suitable substitutes difficult. Even so, it's critically important to moderate the costs of many cancer and other chronic disease therapies.

What Is a Biologic?

A biologic drug is a pharmaceutical derived from the proteins of living organisms. Some of these medications come from animals, such as mice, rabbits, cows, or even humans,[2] while others are extracted from plants, including tobacco and microorganisms.[3,4] Unlike small molecules that make up traditional pills, biologics are chemically complicated. They are bigger, heavier, and often, less stable than traditional drugs. Consequently, they need to be handled with particular care.[5]

Biologics are first-of-their-kind originator drugs to treat cancers, autoimmune conditions, and other serious diseases. Global sales of biologics reached $160 billion in 2012, and in 2014, six of the top 10 best-selling drugs by revenue worldwide were biologics.[6]

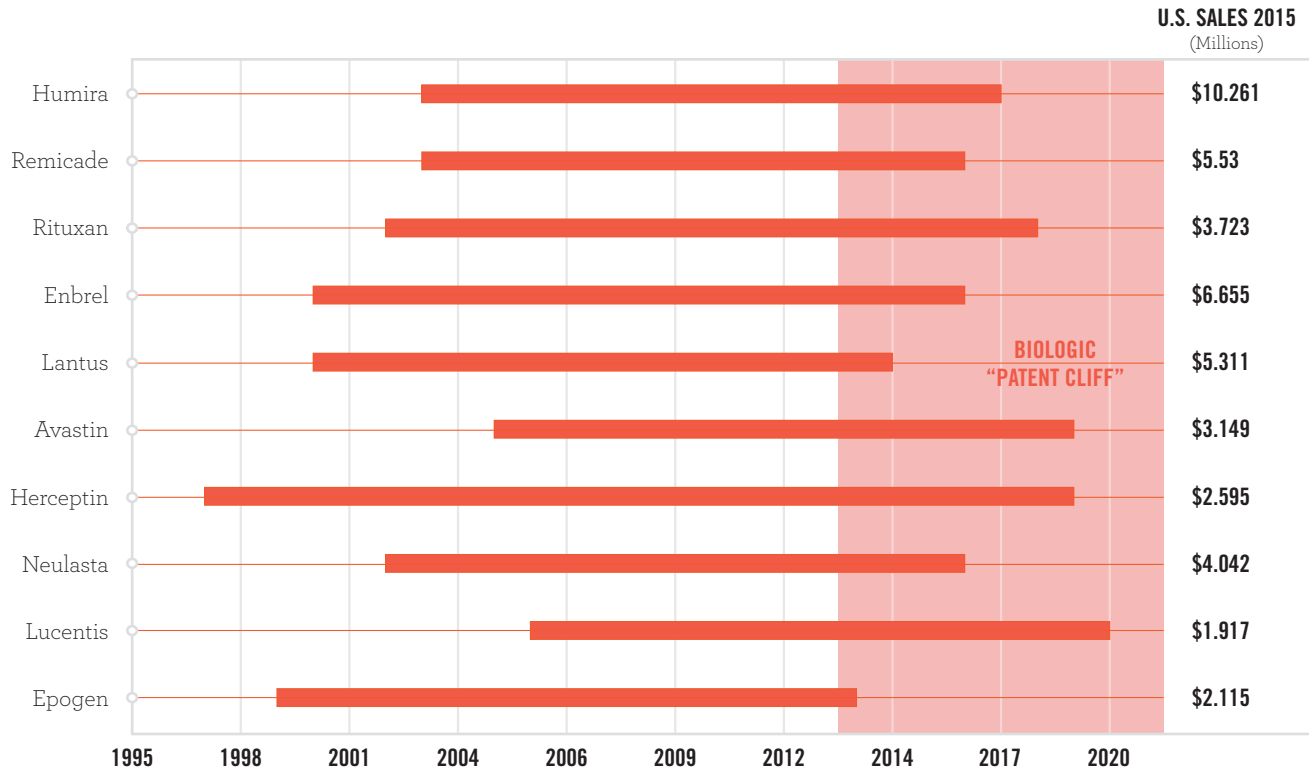
While these drugs are expected to account for 20 percent of total global pharmaceutical sales by 2017, many of the top biologic patents are expiring. This creates space for follow-on biologics to enter the market.[7]

What Is a Biosimilar?

Follow-on biologics, or biosimilars, produce the same clinical result as the original patented drug. But unlike generic drugs, which are exact replicas of the branded drug they compete with, biosimilars are constrained to the variation found within biologic proteins. As in the generic market, as soon as the originator biologic reaches the end of its patent (see Figure 1), the drug's formula is no longer protected, meaning that multiple companies can release a drug with a similar chemical composition, driving the cost down. This new drug is a biosimilar.

While biosimilars offer appealing possibilities, there have been a number of roadblocks in bringing them to market. Biosimilars are estimated to cost between $100 and $150 million to bring to market and are significantly more expensive than the generic version of other brand name drugs.[8] The upside, however, is that biosimilars offer a 20-30 percent discount compared to the price of their reference products.[9] While biologics may cost as much as $400,000 per patient annually, biosimilars are

Fig.1 **Top Biologic Patents Expiring 2012-2019**



Source: IPD Analytics, U.S. Food and Drug Administration

sold at a lower price, which could save $250 billion in the next decade.[10]

A second obstacle is the genetic makeup of biosimilars. Since they are created from living cells and are much more complex than small-molecule drugs, they might have slight differences in their structure that are reflected in the inactive components of the drug.[11] The FDA was concerned that these slight variations could mean the drugs would work differently in the body, causing the approval process for biosimilars to be fraught with delays.

Along with hesitation regarding the interchangeability of biosimilars with biologics, the FDA was further overwhelmed with decisions regarding the labeling and testing of new biosimilars. The FDA has offered draft guidance regarding naming, and labeling of biosimilars, but has yet to offer guidance on interchangeability. It recommended biosimilar labels incorporate information from the FDA-approved labeling for the reference product, along with any modifications specific to the biosimilar drug.[12] The FDA also proposed a naming scheme that closely aligns with the WHO's final guidance.[13]

Recent Progress in The Market

In 2015, the FDA approved the first biosimilar for use in the United States.[14] Zarxio™ is used to prevent infections in cancer patients receiving chemotherapy, and it is expected to save the U.S. healthcare industry $5.7 billion over the next 10 years. It was followed in April 2016 by the approval of Inflectra™, which is expected to double those savings.[15]

More recently, the FDA debated the approval of Amgen's version of AbbVie's Humira arthritis drug. In July 2016, the FDA Arthritis Advisory Committee concluded that Amgen's version of Humira is "highly similar" to the original and should be approved.[16] A second drug, Sandoz's biosimilar of Amgen's blockbuster Enbrel, received a unanimous vote in favor of drug approval for all indications. It is expected to be approved for sale in the United States, but the timing for market entry for both of these biosimilars has yet to be determined.[17]

These recent approvals are just the tip of the biosimilar iceberg, as there is much more deliberation ahead. Premier has been vocal on the importance of market competition and greater drug availability. We are also working with manufacturers to help bring new biosimilar products to market.

The FDA's rulings not only will speed the approval process for upcoming biosimilars but will also reassure providers that biosimilars are measured accurately, have names that are easily identified, and are equipped with tracking and tracing measures. Patents on biologics are expiring each year, and the U.S. healthcare industry has a remarkable opportunity to make lifesaving and disease-altering drugs more accessible and more affordable.

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