

Primer: The Biotechnology Industry

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Introduction

The budding biotechnology industry covers a wide range of human health biologic products and technologies that are created by way of a living system. Examples of biologic products include biologic drugs¹, blood and blood components, vaccines, pharmacogenetics², gene therapy, and genetic testing. The biotechnology industry also involves technologies developed for agriculture, animal health and environmental protection, but this primer will focus on the human health portion of the industry. Within the Food and Drug Administration (FDA), the Center for Drug Evaluation and Research (CDER) is responsible for the review and approval of biologic drugs while the Center for Biologics Evaluation and Research oversees the regulation of other biologic products.³

How Biologics Differ From Pharmaceuticals

Biologic drugs and products are more complex than most pharmaceuticals. Pharmaceutical drugs are typically produced by chemical synthesis, meaning specific reagents can be processed by chemical reactions to yield the same product every time. In contrast, biologic drugs, which are usually proteins, are made by the genetic engineering³ of an organism's cellular mechanisms to create the desired product. Small changes to the growth environment of the living organism can alter the resulting drug. Not only is the manufacturing process of biologic drugs more complex and highly variable, biologic drugs themselves are also more easily degraded in the digestive system, thus they are usually administered intravenously. The majority of drugs on the market are pharmaceuticals, but the FDA approves of new biologic drugs every year. Some examples of biologic drugs include Avastin, Enbrel, Epogen, Humira and Soliris.

Key Takeaways

Similar but different from pharmaceuticals

- Biologic drugs are made through the use of the cellular mechanisms of living organisms.
- The molecules created are much larger and more complex than chemically synthesized drugs.

Advent of biosimilars or "follow-on biologics"

- The FDA recently drafted a user fee system to review and approve of biosimilars.
- Biosimilars will compete with innovator biologics and reduce drug prices.

Acquisitions and mergers drive revenue increases

- Larger biopharmaceutical companies provide resources to smaller companies with significant research progress.

Federal deficit reduction creates murky outlook

- The stimulus package created a tax benefit for small biotechnology companies whose research produces new therapies.
- As the government is scrambling to reduce the burgeoning federal deficit, cuts to Medicare look attractive and will be damaging to biopharmaceutical companies.

¹ The specific term for a biologic drug is "therapeutic biologic product" and often is not distinguished from other drugs.

² Pharmacogenetics is the study of a drug's interaction within an individual's body based on that individual's unique genetic makeup.

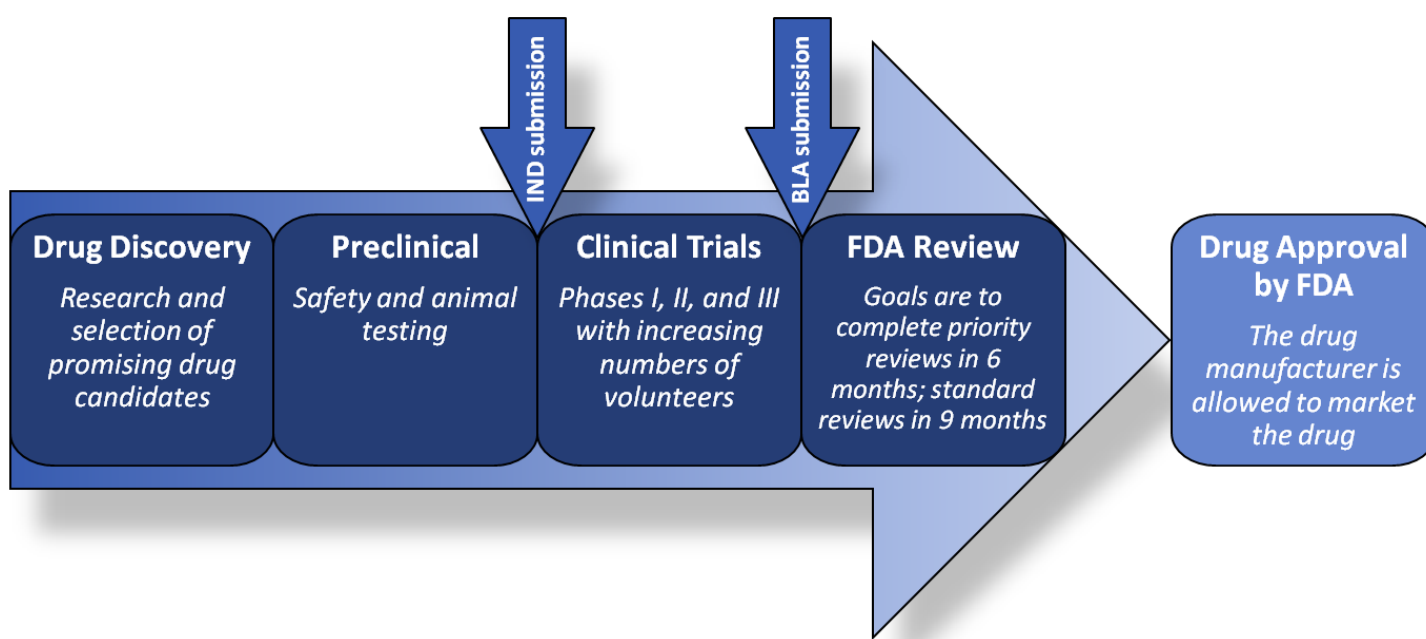
³ Genetic engineering is the modification of an organism's genetic makeup by use of various molecular biologic techniques.

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Regulation of Biologics

As mentioned earlier, CDER regulates biologic drugs while CBER regulates all other biologic products. Although regulation is segregated into two branches of the FDA, the approval for a biologic product the same procedure regardless of the oversight authority. FDA approval is required at two steps: for clinical trials and for final approval for market (Figure 1). An Investigational New Drug Application (IND) submission is required for the drug to be allowed for human clinical trials. After clinical trials⁴, the drug manufacturer is required to submit a Biologic License Application (BLA) containing all preclinical and clinical data for the FDA to review and determine whether the new drug is safe and effective. From drug discovery to FDA approval, the process is estimated to 10 and 15 years and cost companies \$1.2 billion.ⁱⁱ

Figure 1: The Biologic Drug Development Processⁱⁱⁱ



Biosimilars: The Generic Biologic

A biosimilar, also known as a follow-on biologic, is a copycat version of an innovator biologic. Because the production process of a biologic drug is complex and involves the extraction of a molecule from a living organism, it is nearly impossible to create a generic version that is identical to the original. Much like how generic drugs provide steep discounts to brand name pharmaceutical drugs, biosimilars would provide a cheaper alternative to innovator biologics. Until President Obama signed the Patient Protection and Affordable Care Act (PPACA) in March of 2010, there was no FDA approval process for biosimilars. Under the Biologics Price and Innovation Act of 2009 (BPIA) provision within the PPACA, a 12 year patient protection period was established for biologics.^{iv} This helps the originator biologic company recoup the estimated \$1.2 billion in research and development (R&D) to bring a biologic drug to market.^v In efforts to implement the BPIA, FDA and industry stakeholders have been conducting meetings to develop a user fee system for the review of biosimilars and interchangeable products for fiscal years 2013 to 2017, to be named the 351(k) program.

⁴ Clinical trials are typically the most expensive and time-consuming part of drug development.

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Major Markets and Determinants Driving Demand

The major markets of the human health biotechnology industry overlap with that of the pharmaceutical industry, which are healthcare providers including hospitals and doctors. As many blockbuster drugs are losing patent protection in the next two years, pharmaceutical companies are looking to develop their own biologic drugs as well as acquire smaller biotechnology companies to spur growth. Similar to the medical device and the pharmaceutical industries, public health drives demand for biologic drugs. As the number of Medicare enrollees grows, more Americans will be covered, increasing demand for biologic drugs.

Reimbursement policy of both private and public health insurance payers will largely determine the profitability of each biologic. Several factors affect the willingness and amount insurers will pay for a biologic drug (Figure 2).

Major Companies (Table 1)

Amgen Inc. and Genentech Inc. are the two largest biotechnology companies with a combined 42% of the human health biotechnology market share. Amgen is independently owned and is the developer of Enbrel and Epogen. Genentech, often considered to be the founder of the biotechnology industry is owned by global healthcare company, Hoffman-La Roche. Cancer drugs Avastin and Rituxin are the top two revenue-generators for Genentech. Although Avastin recently ran into FDA roadblocks in the treatment of late-stage breast cancer, it is still approved for other cancers. Genzyme Inc. and Baxter International are the next two largest human health biotechnology companies, but only control 5.2% and 4.6% of market share, respectively.

Figure 2: Factors Influencing Payer Reimbursement Policy^{vi}



Figure 3: Major Biotechnology Companies by U.S. Market Share^{vii}

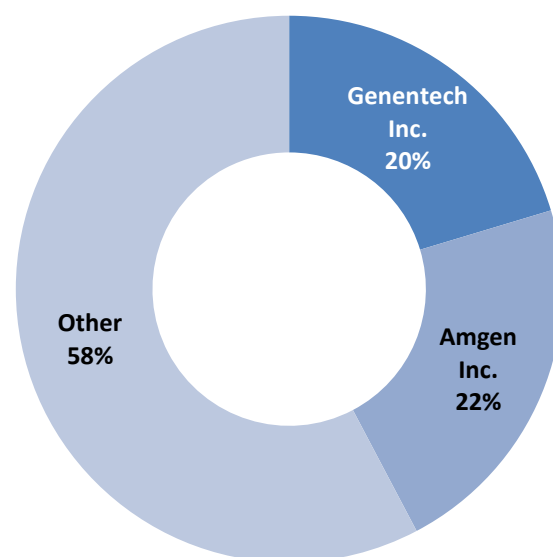


Table 1: 2011 Estimated US Statistics for the Top Two Biotechnology Companies^{viii}

Company	Revenue		Operating Income	
	(\$ million)	% change from previous year	Operating income (\$ million)	% change from previous year
Amgen Inc.	11,592	+1.9	4,504	+4.7
Genentech Inc.	10,684	-5.5	3,975	-5.0

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Industry Prospects

The biotechnology industry was profitable for the first time in 2009. The trend of mergers and acquisitions between biotechnology companies will drive profit margins more so than R&D in the next five years even as several biologic drugs are nearing market approval.^{ix} Looming expirations of many blockbuster drug patents has prompted larger pharmaceutical companies to sign deals with smaller biotechnology companies to accelerate drug development. Larger companies give the smaller ones the resources to research and distribute the drug in return for a share of the revenue.

In recognition of the innovative technologies and jobs created by the biotechnology industry, several pieces of legislation have been passed in attempts to help the industry. The Obama administration will increase the National Institute for Health (NIH) budget by \$1 billion to promote basic and applied sciences in 2012. The Patient Protection and Affordable Care Act also contains the Qualified Therapeutic Discovery Project Program, which provides a 50% tax credit to an individual's investment in research that results in new therapies. Only companies with fewer than 250 employees are eligible for this credit, which again promotes basic research by smaller companies, which are then acquired by industry giants.

Medicare spending will be a target for the recently formed super committee, which will look to reduce the federal deficit by at least \$1.2 trillion over the next 10 years. One popular idea has been to require drug manufacturers to pay rebates to drugs reimbursed under Medicare Part D similar to the rebates paid in Medicaid. However, this only shifts the costs of the drug to either private insurers or to seniors in the form of increased premiums.^x Another bill, drafted by Congressman Peter Welch, proposes that the Secretary of Health and Human Services (HHS) negotiate drug prices under Medicare Part D.^{xi} If passed, this would effectively be price-fixing by the government, and would be detrimental to the industry. Due to deficit reduction plans, future of the human health biotechnology industry is cloudy, but if federally-aided research results in blockbuster biologic drugs, immense strides could be made in both industry and public health.

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- ^{iv} 111th Cong. H.R. 3590. Section 7002.
- ^v Op cit. DiMasi and Brabowski.
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- ^{ix} Ibid.
- ^x Holtz-Eakin D & Ramlet M. "Cost Shifting Debt Reduction to America's Seniors." July 2011.
- ^{xi} H.R.2248. *Medicare Prescription Drug Price Negotiation Act of 2011*. <http://thomas.loc.gov/cgi-bin/query/z?c112:H.R.2248.IH>. June 21, 2011.