Overview

The biotechnology (biotech) industry has experienced tremendous growth over the last several decades. In recent years, investors' enthusiasm has grown as advances in medicine have led to an increasing number of new and exciting discoveries. We believe it is important for investors to understand the risks associated with the industry and how best to gain exposure to innovation in medicine, while minimizing risk.

The Biotech Explosion

Biotechnology stocks have received a lot of attention from investors in recent years due to an increasing number of new discoveries and commercial success through advances in understanding human genetics. This enthusiasm is reflected in the tremendous flows of investment dollars into the industry. The launch of several new exchange traded funds (ETFs) and a booming biotech initial public offering (IPO) market reflects the seemingly insatiable demand. In addition, numerous mergers and acquisitions have occurred in the sector over the last several years that have aided in the strong performance and investor interest.

New innovation in drug development can be beneficial to both patients and investors. However, at times, enthusiasm can lead to high stock prices. This can be especially pronounced when a small company has one innovative drug generating a lot of excitement. We believe investors should avoid companies that are not yet profitable or are heavily reliant on the success of one particular product.

How to Invest

We believe that investors interested in gaining exposure to new, innovative drugs should look to companies with strong fundamentals that are profitable, diversified and have a successful track record.

Biopharmaceutical recommendations - Over time, the line between traditional pharmaceutical (pharma) companies and biotech companies has blurred. We classify the entire drug-development industry as biopharmaceuticals. In our view, the best way to gain exposure to innovation in drug development is through our Buy-rated biopharmaceutical stocks. We believe these companies are well-positioned to take advantage of innovations in drug development, have strong fundamentals, and attractive valuations.

Buy-rated biopharmaceutical companies mentioned in this report:
Allergan (AGN - $250.36)
Bristol-Myers Squibb (BMY - $55.50)
Johnson & Johnson (JNJ - $133.35)
Merck (MRK - $63.52)
Novartis (NVS - $84.87)
Pfizer (PFE - $33.43)

Prices and opinion ratings are as of market close on 8/1/17 and subject to change. Source: Reuters.
What Is Biotechnology?

The History of Biotechnology - Biotechnology describes the process of using biology, rather than chemistry, to develop medicines. As a result, biologic products are developed through the use of living cells and organisms, and they are typically injected or infused by needle. By contrast, traditional drugs are chemical mixtures that are usually packaged in pill form and taken orally.

The biotech industry began in the 1970s, and the first biologic product to receive approval by the U.S. Food and Drug Administration (FDA) was human insulin (for diabetic patients) in 1982. Since then, hundreds of biologic drugs and vaccines have been approved to treat conditions such as rheumatoid arthritis, anemia, cancer, multiple sclerosis, and HIV/AIDS.

Benefits of biologic drugs - Through the use of living cells, biotechnology has opened new pathways to treat disease. In comparison to traditional chemical drugs, biologic drugs are often able to more precisely and effectively target disease and cause fewer unintended side effects. Further advancements in biotechnology research continue to hold promise for future drug discoveries. While biologic drugs are expensive to make, developers find them attractive because once their patents expire, there is currently less competition from generic drug companies compared with traditional drugs, given the high cost of development and regulatory hurdles.

Understand the Investment Risks

We believe investors should understand the risks when investing in the biotechnology sector. Drug development entails significant risks, in our view, and many companies in the industry may not be appropriate for certain investors. Two important factors to consider when investing in the industry are profitability and diversification. Roughly one-quarter of the value of the NASDAQ biotechnology sector is derived from companies that are not profitable. We recommend investors avoid companies that are not profitable, have high product concentration, or have an unproven track record.

• High development expenses – The research and development of new drugs is expensive, time consuming, and carries a low success rate. Often, it takes thousands of compounds entering the discovery process to gain approval for just one new drug, which can take over a decade to go from discovery to approval. Additionally, it is estimated that, on average, companies spend over $1 billion on research and development per new drug approved. As a result, it may take time for a biotech company to become profitable, if at all.

• Product concentration – Many companies classified as biotech are often heavily reliant on a small number of drugs, either on the market or in development, for success. This can lead to large swings in stock prices. In our view, diversified portfolios of marketed and pipeline products help minimize risk from any one product.

How to Invest in Biotechnology

When investing in biotechnology, we recommend investors look to mature companies with strong fundamentals that are profitable, have a diversified product portfolio, a proven track record, and an experienced management team.

Pharma and biotech are converging – Over time, the traditional pharmaceutical industry and the biotechnology industry have been converging. Today, most drug-development companies, regardless of how they’re classified, use a variety of techniques to develop new drugs. This includes both biotechnology and traditional chemical drug development. Additionally, traditional pharmaceutical companies are increasingly pursuing their own biotech research in addition to collaborating with and acquiring biotech companies. In fact, some of the traditional pharmaceutical companies have the largest exposure to biologic drugs. We classify the entire industry as biopharmaceuticals. More than half of the 15 top-selling drugs are biologic and are sold by a wide mix of large biopharmaceutical companies.

Figure 1

<table>
<thead>
<tr>
<th>Top 15 Drugs by Sales</th>
<th>Biologic Company</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Humira (autoimmune disease)</td>
<td>Yes AbbVie</td>
<td>$16.0 B</td>
</tr>
<tr>
<td>2. Harnoni (hep C)</td>
<td>No Gilead</td>
<td>$9.1 B</td>
</tr>
<tr>
<td>3. Enbrel (autoimmune disease)</td>
<td>Yes Amgen/Pfizer</td>
<td>$8.9 B</td>
</tr>
<tr>
<td>4. Remicade (autoimmune disease)</td>
<td>Yes JNJ/Merck</td>
<td>$7.3 B</td>
</tr>
<tr>
<td>5. Rituxan (cancer)</td>
<td>Yes Roche/Biogen</td>
<td>$7.0 B</td>
</tr>
<tr>
<td>6. Revlimid (cancer)</td>
<td>No Celgene</td>
<td>$7.0 B</td>
</tr>
<tr>
<td>7. Avastin (cancer)</td>
<td>Yes Roche</td>
<td>$6.8 B</td>
</tr>
<tr>
<td>8. Herceptin (cancer)</td>
<td>Yes Roche</td>
<td>$6.8 B</td>
</tr>
<tr>
<td>9. Lantus (diabetes)</td>
<td>Yes Sanofi</td>
<td>$6.0 B</td>
</tr>
<tr>
<td>10. Prevnar (pneumonia vaccine)</td>
<td>Yes Pfizer</td>
<td>$5.7 B</td>
</tr>
<tr>
<td>11. Xarelto (blood clots)</td>
<td>No JNJ/Bayer</td>
<td>$5.4 B</td>
</tr>
<tr>
<td>12. Lyrica (pain)</td>
<td>No Pfizer</td>
<td>$5.0 B</td>
</tr>
<tr>
<td>13. Neulasta (neutropenia)</td>
<td>Yes Amgen</td>
<td>$4.6 B</td>
</tr>
<tr>
<td>14. Cogadaxone (multiple sclerosis)</td>
<td>No Teva</td>
<td>$4.2 B</td>
</tr>
<tr>
<td>15. Suvanto (hep C)</td>
<td>No Gilead</td>
<td>$4.0 B</td>
</tr>
</tbody>
</table>

Source: Company reports, Bloomberg

Investment recommendations – In our view, our Buy-rated biopharmaceutical companies are well-positioned to take advantage of new innovations in
drug development. Additionally, we believe these
companies trade at attractive valuations and possess
strong fundamentals, such as
• Diversified product portfolios and pipelines;
• Successful track records of drug development; and
• Solid financial positions with investment-grade
credit ratings.

Our Buy-rated ideas within the biopharmaceuticals
subsector include Allergan (AGN), Bristol-Myers
Squibb (BMY), Johnson & Johnson (JNJ), Merck
(MRK), Novartis (NVS), and Pfizer (PFE). Below,
we list Buy-rated biopharmaceutical companies and
the new approvals that are expected to contribute to
long-term growth for the companies.

Figure 2: Exposure to Innovation - New approvals
expected to contribute to long-term growth

![Figure 2: Exposure to Innovation - New approvals expected to contribute to long-term growth](image-url)

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<table>
<thead>
<tr>
<th>Buy-rated Company</th>
<th>Drug</th>
<th>Description</th>
<th>Consensus Est. 2021 Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergan</td>
<td>Botox</td>
<td>Paralytic agent that’s expected to grow sales through approvals in new therapeutic areas</td>
<td>$4.4 B</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>Opdivo</td>
<td>Breakthrough cancer treatment that uses the body’s own immune system to target various forms of cancer</td>
<td>$8.5 B</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Darzalex</td>
<td>Recently approved cancer drug for treatment-resistant multiple myeloma</td>
<td>$3.9 B</td>
</tr>
<tr>
<td>Merck</td>
<td>Keytruda</td>
<td>Breakthrough cancer treatment that uses the body’s own immune system to target various forms of cancer</td>
<td>$8.9 B</td>
</tr>
<tr>
<td>Novartis</td>
<td>Entresto</td>
<td>New treatment for heart failure, reduces risk of cardiovascular death and hospitalization</td>
<td>$32 B</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Ibrance</td>
<td>New treatment approved for certain types of breast cancer, but could expand to other tumor types</td>
<td>$5.9 B</td>
</tr>
</tbody>
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Source: Bloomberg as of 8/2/17

Valuation

In valuing health care companies, we use various
methods, including price-to-earnings ratios, dividend
yields, discounted cash flow estimates, and return-on-investment calculations.

Additional Risks

General risks to consider when investing in
biopharmaceutical companies include pricing
pressure, product failures and liabilities, and political
and regulatory risk.

Please see the full opinions of the individual
companies mentioned in this report for additional
information, including valuation and risks.

Required Research Disclosures

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1 Bloomberg as of August 2017
2 Tufts University