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Rapid growth in biopharma: Challenges and opportunities

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Biopharmaceuticals could become the core of the pharmaceutical industry, but not without significant transformation in the laboratory and in strategy, technology, and operations.

Biopharmaceuticals are among the most sophisticated and elegant achievements of modern science. The huge, complex structures of these drugs don't just look extraordinary in the 3-D modeling systems used to design them; they also perform their jobs remarkably well, offering high efficacy and few side effects. And there is much more to come: existing treatment archetypes are evolving and becoming more sophisticated all the time, and continuing research is yielding entirely new types of products. Radically new concepts are making it to the market, such as the cell therapy Provenge, which is used to treat cancer, and, somewhat further out, gene therapies, which offer even more amazing promises of regenerative medicine or disease remission.

Yet there are operational and technological challenges. Reproducing large molecules reliably at an industrial scale requires manufacturing capabilities of a previously unknown sophistication. Consider this: a molecule of aspirin consists of 21 atoms. A biopharmaceutical molecule might contain anything from 2,000 to 25,000 atoms (Exhibit 1). The "machines" that produce recombinant therapeutics are genetically modified living cells that must be frozen for storage, thawed without damage, and made to thrive in the unusual environment of a reaction vessel. The molecules must then be separated from the cells that made them and the media in which they were produced, all without destroying their complex, fragile structures.

This sophistication comes at great cost. Large-scale biotech-manufacturing facilities require \$200 million to \$500 million or more to build, compared with similar-scale small-molecule facilities that may cost just \$30 million to \$100 million, and they can take four to five years to build. These facilities are costly to run, too, with long process durations, low yields, expensive raw materials, and, not least, the need for a team of highly skilled experts to operate them. There are myriad reasons the rapid growth and increasing importance of the industry is producing new challenges and opportunities. To keep pace, biopharma players must revisit and fundamentally reassess many of the strategies, technologies, and operational approaches they currently use.

Exhibit 1 Copying biopharmaceuticals is not a simple task.

Size of 3 well-known pharmaceuticals

Comparable objects¹

Relative cost of development and complexity

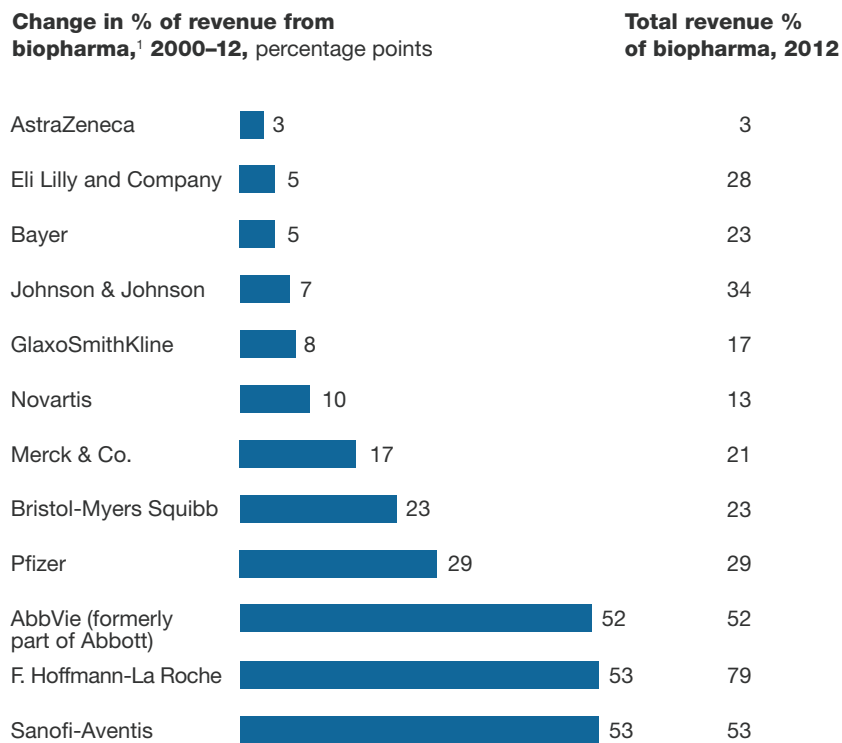
¹Objects are not to scale.

The opportunity: Biopharma goes mainstream

The opportunity in biopharmaceuticals is big and growing too rapidly to ignore. Today, biopharmaceuticals generate global revenues of \$163 billion, making up about 20 percent of the pharma market. It's by far the fastest-growing part of the industry: biopharma's current annual growth rate of more than 8 percent is double that of conventional pharma, and growth is expected to continue at that rate for the foreseeable future.

The efficacy and safety of biopharmaceutical products, combined with their ability to address previously untreatable conditions, allows pharma companies to command high prices for innovative drugs. Strong demand has driven significant profits, despite the high cost of goods sold. Biopharmaceuticals have set new standards for blockbuster drugs as well. Blockbusters are traditionally defined as drugs that have \$1 billion or more in annual sales; the top 15 biopharma products each enjoy annual revenue of more than \$2 billion, with some, such as the antiinflammatory drug Humira, generating sales of more than \$10 billion a year. For many players, the biggest challenge has been simply making enough product to sell. It's no surprise that major pharmaceutical companies around the world are increasingly shifting their R&D and sourcing focus to large-molecule products (Exhibit 2).

Exhibit 2 Many large pharmaceutical companies are shifting their presence to biopharma.



¹Revenue shares are divided between biopharma and small molecules.

Source: EvaluatePharma

Investing in biotech R&D has yielded better returns than the pharma-industry average. The current biologics-development pipeline supports an outlook of continued healthy growth. The number of biotech patents applied for every year has been growing at 25 percent annually since 1995. There are currently more than 1,500 biomolecules undergoing clinical trials, and the success rate for biologics has so far been over twice that of small-molecule products, with 13 percent of biopharma products that enter the Phase I trial stage going on to launch.

The success of the clinical pipeline will lead to an unprecedented number of new molecule launches, rising from a handful a few years ago to 10 to 15 annually, as biopharma products make up an increasing share of new approvals from the US Food and Drug Administration in the future. A further steep increase is to be expected as multiple players begin to receive approval for the production of biosimilars after 2015.

If anything, the emerging long-term picture is even more exciting, with disruptive innovations such as immunotherapies, antibody drug conjugates, and gene and cell therapies all making progress toward commercial launch in the next few years. Biopharma looks poised to transform the industry once more, as increasing understanding of the interaction between drugs and the genetic makeup of patients helps to improve the targeting of therapies. Combined with robust, low-cost genetic profiling, this knowledge will improve treatment outcomes and serve to accelerate and improve the outcomes of clinical trials, helping to reduce the cost of drug development.

The challenge: Cost, complexity, and regulatory scrutiny

As biopharma moves from the scientific frontier to the business mainstream, the industry will increasingly be forced to confront the same challenges faced by other businesses: maintaining competitiveness by ensuring affordability, quality, and delivery performance.

Demand for affordability and improved access

Downward cost pressure will intensify as healthcare systems struggle to balance rising demand with flat or declining budgets. In this environment, payors may find it difficult to justify the annual treatment costs of \$50,000 to \$100,000 that some biopharma products currently demand. It is hard to imagine that these price premiums will be sustainable for any but the most innovative drugs. Furthermore, governments in emerging markets understand the critical role that biopharma will play in boosting healthcare outcomes, and they are aggressively supporting alternative ways to fulfill demand for these products.

The result of these pressures will be the inevitable development of the biosimilars industry. The availability of biosimilar versions of human-growth hormones and interferons has already opened access to these products to a far larger number of patients. As patent protection on more complex biopharmaceuticals expires, biosimilars will surely follow the same path.

Early regulatory and customer concern is already being overcome. In June 2013, for example, the European Union approved Remsima, Celltrion's biosimilar version of the monoclonal antibody Remicade. In emerging markets, where consumers are able to access products only if they are available at considerably lower prices, enthusiasm for biosimilars is likely to be even stronger. The biosimilars industry has the potential to change the commercial landscape as profoundly as generics players have done in conventional pharma. Pressure from biosimilars will force the innovators to accelerate the search for better products and will increase pressure on the industry as a whole to reduce its cost of goods sold.

Complexity of biopharma supply chain and operations

As the number of products rises and new process technologies such as continuous manufacturing are introduced, the complexity of biopharma operations and the biopharma

supply chain will increase. Evidence indicates that current production programs are already stretching the industry, with several players failing to deliver to the market. This challenge will only increase as sites move from the current “one line, one product” setup toward nimble and flexible multiple-product operations and are required to manage both current and future technologies under one roof.

The high premium on biopharmaceutical products and the relatively smaller share of revenues they have historically accounted for in big pharmaceutical companies have led to industry-wide challenges in the supply chain. Complexity, cost, and service levels are far from small-molecule best practices, even considering the additional complexity of cold-chain requirements.

New manufacturing technology platforms

The new classes of molecules discussed above, from drug conjugates to the cell and gene therapies arriving in the next five years, will each require its own novel manufacturing, supply, and quality-assurance approaches. Today, many companies that are insourcing these products in the late clinical or early commercialization phase are struggling to set up the novel technologies and processes required to produce them. Making the right decision about how to set up operations for an autologous cell therapy is not an obvious exercise, and there will naturally be many suboptimal solutions before sufficient experience is built.

Quality compliance and regulatory scrutiny

Quality functions are struggling to keep up with the rising demands of regulators, primarily the US Food and Drug Administration. The industry has received an unprecedented number of warning letters and remediation programs in the last five years, and scrutiny is unlikely to decrease. Furthermore, the increasing relevance of global markets (beyond the United States, European Union, and Japan) is adding the complexity of multiple quality standards and regulatory regimes. Compliance, robustness of processes, and efficiency will need to be squared in one equation.

What's next: Evolving in a booming industry

These trends will fundamentally reshape the industry. The changes will not be the same for everyone; a variety of business archetypes will coexist in the industry, and their strategies and success factors will differ in important ways.

Global innovators will have to drive product innovation in order to continue to command premium prices, shifting the frontier of technology and exploring new operational setups (such as the design and deployment of their future network). Biosimilars players will have to focus on cost, quality, and scale. For them, speed, process innovation, and operational

excellence are must-win battles. Players based in emerging-market nations will have to find their own niches with the right operational and quality performance to make the best use of privileged access to, and knowledge of, their local markets. Contract-manufacturing organizations will have to be at the leading edge of process innovation and operational efficiency while retaining or building a spotless reputation for service and performance. Beyond these generic player archetypes, each company will need a detailed view of its own strategic position, asking itself what it stands for in the market and what it needs to do in order to win.

Whatever their competitive niche, companies must continually evolve both their manufacturing technologies and their operational capabilities. Technologies are not yet sufficiently mature to rely only on operational improvement to drive quality and productivity up and cost down. Nor will technological improvements alone be sufficient to do those things.

We believe that the biopharmaceutical companies best positioned to succeed in tomorrow's market will be those that master a broad set of technical and operational capabilities. Decisions that companies are making today will have a critical influence on that success for two important reasons. First, operational excellence is a hard-won skill. Capabilities such as lean, agile, and efficient manufacturing require sustained effort and commitment to develop and hardwire into the organization. Second, decisions made today will affect companies' competitive positions years or even decades into the future. This is particularly true in areas such as footprint design and the choice of core manufacturing technologies.

A full discussion of all the technical and operational decisions facing biopharma companies today and in the coming years is beyond the scope of this article, but some of the most important considerations include the following:

- reducing operating costs across manufacturing and quality divisions by methodically adopting lean practices (for example, eliminating waste and improving labor and asset efficiency) and improving process technology (including possible change controls and regulatory approvals), as well as finding new ways to improve the performance of the production process, from increases in expression systems to purification improvement and process stabilization
- improving operational agility and equipment utilization to increase manufacturing-site capacity for individual molecules by removing bottlenecks from existing assets, introducing the ability to run multiple products in fewer lines, and improving the industry's readiness to respond quickly to the needs of a volatile market—all without compromising quality

- expanding capacity, which may encompass decisions on risk taking for postponement of asset deployment, capital-expenditure efficiency, and adoption of new technologies (such as the design of flexible facilities based on stainless steel, disposables, or hybrid systems to suit specific product and market conditions)
- undertaking the right make-or-buy decisions as biopharma contract-manufacturing organizations become increasingly capable and available, forcing companies to reevaluate where their core operational skills should lie and how they will ensure the cost, quality, and availability of those they choose to outsource
- defining the manufacturing footprint—that is, building or acquiring a strong, competitive network with the right suppliers, manufacturing plants, and distribution capabilities to balance cost, service, and customer acceptance—and, in particular, considering a presence in emerging markets and the associated cost, regulatory, and market-access implications with great care
- improving efficiency in the supply chain to manage inventory, distribution logic, and the complexities of the cold chain
- streamlining the introduction of new products and new technology platforms to support the ambition of pushing a far greater number of molecules through technical development and manufacturing launch
- becoming a high-performing organization with access to talent capable of handling these challenges and the new ones that will inevitably emerge in such a rapidly evolving environment



The prize for organizations that master these operational challenges is far more significant than just short-term competitive advantage. Many of the next major opportunities for biotech will require companies to develop new and different technologies and operating models. Today's actions will shape companies' readiness to grasp these opportunities as they come to fruition.

At one end of the scale, for example, the industry must develop the capabilities to quickly and reliably produce the small batches of fully personalized medicines required to deliver cell therapies. At the other, it needs the high-volume, low-cost manufacturing capabilities necessary to deliver inexpensive insulin and vaccines against diseases such as malaria that take so many lives today in low- and middle-income countries. Between these two extremes, companies will need to accelerate the development and commercialization of new molecules to allow a broader range of illnesses to be addressed, and they must reduce manufacturing costs, improve quality, and build capacity to broaden access to the industry's life-changing products.

Only through a combination of strong science and deep operational excellence will the biopharma industry be able to fulfill its potential to transform the health expectations of millions of people across the globe, successfully navigating both the promising and challenging elements of the sector. □

This article is excerpted from the book *From Science to Operations: Questions, Choices and Strategies for Success in Biopharma*. For more information, visit McKinsey's Pharmaceuticals & Medical Products site, on mckinsey.com.

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