Emerging Biopharmaceutical Companies: Ensuring a Favorable Environment for Continued Innovation

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Emerging Biopharmaceutical Companies: Ensuring a Favorable Environment for Continued Innovation

For at least two decades, the U.S. has been an engine of growth and innovation for the global biopharmaceutical sector.¹ The U.S. biopharmaceutical sector is also an important contributor to the U.S. economy and its future growth. In 2008, the sector provided 655,025 U.S. jobs directly and for every direct job, supported 3.7 jobs in other sectors. Also in 2008, the sector contributed $114.6 billion directly to the national gross domestic product (GDP), about three and a half times as much as any other sector.²

When one thinks of the biopharmaceutical sector, the image that most readily comes to mind is that of companies, with annual revenues between $100 million and $3 billion, representing roughly 30 percent of global pharmaceutical industry net sales annually and have historically exhibited growth significantly higher than that delivered by the rest of the biopharmaceutical industry.³ In 2009, this segment comprised 119 public companies worldwide, totaling nearly one-third of all publicly listed pharmaceutical companies. ⁴ Of these, 48 are headquartered in the U.S.

These emerging biopharmaceutical firms are often the start-up biotechs of yesterday that have become successful and now have one to three products on the market. In other cases, they may have started as specialized units within larger companies that have been spun off to enable them to prosper outside of a large corporate structure. Whatever their origin, their size and nimbleness allow them to operate in markets where larger firms usually do not venture. Most do not rely on success based on the expectation of developing a blockbuster drug. Rather, many of these firms seek to fulfill a specific niche, such as developing medicines to treat patients with a rare or uncommon disease for which few or no treatment alternatives are available.

For all their success, these firms, owing to their size and other features, are particularly vulnerable to changes in the business, regulatory, and policy environments, such as those resulting from the implementation of U.S. health care reform. Just as their focus on providing cutting-edge solutions to niche medical issues has made them successful, it also represents a key challenge. A single setback—for instance, an unexpected delay in review and approval of a patent application or new drug application, or a small regulatory challenge—can have a dramatic impact on the sustainability of these firms.

The increasingly unpredictable regulatory environment as well as the complexity of rules and regulations related to the review, approval, pricing, and reimbursement of medicines continue to test the future viability of this important market segment. As policymakers continue to seek to improve the health care system, it is imperative that appropriate consideration be given to how such policy changes may affect the

³. Data from EvaluatePharma (consulted 28 May 2010) and IMS Health Market Prognosis (March 2010) on midsize public pharma company 2009 revenue as a percentage of 2009 global market ($869 billion according to EvaluatePharma, $837 billion according to IMS); BCG analysis.
⁴. Based on publicly listed pharmaceutical companies with market capitalization values of less than $100 million to more than $30 billion; BCG analysis based on EvaluatePharma data.
Emerging Biopharmaceutical Companies

ability of this sector to secure the capital investment needed to develop tomorrow’s new treatments and cures.

With this in mind, this paper describes emerging biopharmaceutical companies, highlights their contributions, and discusses specific challenges they face.

This paper is based on various published sources as well as analyses previously conducted by The Boston Consulting Group (BCG) on the state and evolution of the biopharmaceutical industry and the environment in which it operates, in the context of advising senior executives on strategic decisions. In addition, analyses of key aspects of 119 emerging public biopharmaceutical companies worldwide were conducted specifically for this research. Finally, 37 executives from 9 U.S.-based emerging biopharmaceutical companies as well as several experts were interviewed. The work was sponsored in part by the Pharmaceutical Research and Manufacturers of America (PhRMA) but was conducted independently by a team from BCG.

Overview of the Biopharmaceutical Sector and Recent Trends

The success of the biopharmaceutical industry rests on its ability to discover, develop, and market drugs that meet patient needs. The industry depends on a robust business environment for its products in order to recoup the significant up-front investment required in drug discovery and development.

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to patients, with the effect of gating patients’ access to some of the most recent drug innovation and also of shifting a greater share of the cost to patients through increased premiums and co-pays.

In addition, the recently approved health care reform legislation includes a range of provisions that will give the government a central role in determining the value of new drugs and how they should be used. These measures should ultimately affect patient access to and payer coverage of new medicines. It will take many years before all the details of these measures are defined and all the consequences are understood. Emerging pharmaceutical companies—those that are neither small biotechs nor large multinationals—are particularly sensitive to the resulting increase in the uncertainty of the business environment.

Overview of the Environment for Emerging Biopharmaceutical Companies

Similar to the companies that populate the rest of the biopharmaceutical sector, emerging biopharmaceutical companies are concentrated in developed economies: the U.S., Europe, and Japan. Of the publicly listed pharmaceutical companies in this segment, defined as those with annual revenues between $100 million and $3 billion, 40 percent are headquartered in the U.S., where they are part of a rich ecosystem and serve as a “deep bench” for future growth and innovation for the industry as a whole (Figure 1). Unlike the typical emerging company in Asia or Europe, whose revenues hover near the $1 billion mark, emerging companies in the U.S. average roughly $600 million in annual revenues. This indicates that although emerging companies are continuing to act as an engine of innovation in the U.S., there may be an opportunity to support their growth more effectively.

Figure 1. Distribution of emerging companies ($100M-$3B in revenue) worldwide

40 percent of companies with annual revenues between $100M and $3B headquartered in the U.S.

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Similar to biotech start-ups, this market segment is characterized by wide variability in terms of profitability. As illustrated in Figure 2, many firms may not yet be profitable. For example, one emerging company, which specializes in ophthalmic and pulmonary diseases, reported $92 million in revenue in 2009 with a net operating loss close to $40 million; the company’s loss was largely driven by sustained research and commercial investment. When these companies become profitable, it is often after a decade or more in which they were unprofitable. This is consistent with the reality of biopharmaceutical R&D, in which the average cost to develop a new medicine is $1.3 billion and the time to develop a new drug exceeds 14 years.16

In the early 1980s, the biopharmaceutical industry was characterized by 30 to 40 large, vertically integrated companies that were self funding. In contrast, today’s biopharmaceutical sector is made up of a handful of large companies and hundreds of small and emerging firms, most of which are not profitable, do not yet have products on the market, and are heavily reliant on venture and other sources of private capital. Because many of these companies do not achieve profitability until 15 to 20 years or more after they were established, they are highly reliant on investors that are willing to assume the financial risk based on the potential for these companies to obtain approval for a new medicine and earn a return on investment.

The origins of these companies vary widely. Some are spin-offs from larger companies, focusing on products that were not a priority in the context of a larger pharmaceutical company. Others exist because of a scientific or technological discovery that was incubated in an academic setting and then commercialized. These companies have succeeded by building upon their knowledge of specific therapeutic areas and learning to leverage their size to compensate for limited financial resources, fostering flexibility, nimbleness, and speed within their organizations. They boast small teams and an entrepreneurial culture.

Emerging biopharmaceutical companies tend to focus on one or a few specific medical conditions within a limited range of therapeutic areas and are generally more likely to focus on specialty rather than primary care. Their revenue depends on very few products, making these companies particularly vulnerable to changes in the policy environment that may have a direct impact on a particular therapeutic class or product. An average of 90 percent of the pharmaceutical revenue of the emerging companies included in our sample is generated by their top three biopharmaceutical products (Figure 3).

**Figure 3. Product Portfolio concentration**
Emerging segment company revenues highly concentrated: Top 3 drugs represent ~90% total Rx/OTC sales

**Source:** EvaluatePharma, BCG analysis.

1 Twelve-company sample selected based on revenue, inclusion in Datamonitor’s PharmaVitae Universe.

2 Twelve-company sample selected based on revenue.

3 Twelve-company sample selected based on revenue, PhRMA smaller company members as of July 2010, inclusion in PharmaVitae Universe

**Incubators of Innovation, Platforms for Future Growth**

The specialized nature of emerging biopharmaceutical companies means that they can use their smaller size as a competitive advantage. Instead of focusing solely on blockbuster products in an attempt to sustain large revenues and a large market cap, they are able to target underserved markets with smaller patient populations and still recoup their R&D costs.

In some cases, the number of patients with a certain disease or condition is small enough that even the costs to develop and manufacture a drug to address those patients’ needs would be prohibitive without external incentives. Drugs developed to treat these small patient populations are referred to as “orphan drugs” by the U.S. Food and Drug Administration (FDA) when the affected population in the U.S. is fewer than 200,000 patients. The Orphan Drug Act (ODA) of 1983 has played an essential role by providing

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17. A blockbuster drug is a drug generating at least $1 billion in worldwide annual revenue and is most often used by a large patient population with a chronic condition. *Source:* Stan Kinkelstein and Peter Temin, *Reasonable Rx: Solving the Drug Price Crisis* (New Jersey: FT Press, 2008).
companies that develop orphan drugs with tax incentives, enhanced patent protection and marketing rights, clinical research financial subsidies, and advisory help during the drug approval process. Without the ODA, medicines for rare diseases – 6,000 of which are known today, affecting approximately 25 million people in the U.S. – would not be available for the patients who suffer from these diseases.

Contributions from emerging pharmaceutical companies go beyond the development of specialty and orphan drugs, however: an estimated 22 percent of the top 50 drugs on the market today originated in these companies, illustrating the importance of the emerging company sector to the overall pharmaceutical industry (Figure 4). Other studies highlight similar trends, showing that approximately 40 percent of new medicines unveiled by large biopharmaceutical companies worldwide between 2001 and 2006 originated in smaller companies, and that some 30 percent of new molecular entities (NMEs) and 50 percent of new biological entities (NBEs) submitted for approval in 2007 had been either licensed or acquired by large companies from smaller ones, including companies in the emerging sector we focus on here.

![Figure 4. Top 50 drugs in 2009 by originator size](image)

22 percent of current top 50 drugs originated in the $100M-$3B segment

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18. An orphan drug is one developed to treat a rare disease or condition. The Orphan Drug Act defines a “rare disease or condition” as “any disease or conditions which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.” Source: Orphan Drug Act, FDA.


20. National Institutes of Health. Fact Sheet from The Genetic and Rare Diseases Information Center.


These percentages illustrate the symbiotic relationship that has developed between emerging and large biopharmaceutical companies through either partnerships or acquisitions. The number of alliance deals that exceed $100 million in value between emerging and large biopharmaceutical companies has increased from approximately 10 in 2000 to more than 90 with a total announced value of nearly $45 billion in 2008. The median value of licensing deals has increased from about $25 million in 2000 to more than $200 million in 2009. Likewise, the median value of merger and acquisition (M&A) deals between large biopharmaceutical and biotechnology companies has grown from about $80 million in 2000 to about $400 million in 2008. The number of acquisitions of biotechnology firms by biopharmaceutical companies has surged from 52 in 2000 to more than 190 in 2009, for a total transaction value in 2009 exceeding $47 billion. Over this ten-year period, 1,171 mergers and acquisitions of biotechnology companies for a total transaction value of $295 billion were publicly announced.

Companies in this segment that are not acquired also provide significant value for investors that wager on their success over the long term. Emerging companies grew at an average annual rate of 14 percent between 2000 and 2008 in terms of net sales (Figure 5), and their market capitalization grew by 7 percent.

Figure 5. Global net sales growth for active companies in 2000
Companies in this segment have grown at 14 percent since 2000, compared with industry overall at 11%

Source: EvaluatePharma May 28, 2010; BCG analysis
Note: Includes all pharmaceutical companies that existed in 2000 and have not been acquired. Ranges describe companies’ net sales revenue in 2000. Excludes private companies.

25. This figure refers to the total value of upfront and future payments, which are typically contingent on the success of the drug during development, registration, and commercialization.
28. In 2008, the number of biotechnology M&A deals was 148, with a total transaction value of $93B.
annually over the same period. In 2009, the U.S. was host to 48 of the 119 publicly listed emerging companies worldwide, and these U.S.-based firms generated 30 percent of the biopharmaceutical segment’s global sales.

As these emerging firms continue to grow in number, they foster the creation of high-quality jobs. The larger among these companies employ several thousand people, many devoted to research and development activities. The number of jobs in emerging biopharmaceutical companies grew at an annual rate of 7 percent from 2000 to 2008, significantly more than the 1 percent growth rate of U.S. jobs in general over the same period. Some companies in this group have experienced even faster growth as they have introduced new medicines; in these cases, the increase in number of jobs has increased by as much as ten to twelve fold within the period. These jobs tend to be well paid: the average base salary among all employees of biopharmaceutical firms, including emerging companies, was about $114,000 in 2009, more than twice the average of mean annual wages in California, Massachusetts, New Jersey, and Pennsylvania, where many of these firms are based (Figure 6).

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**Figure 6. Distribution of emerging pharma companies across U.S.**

Companies in the $100M-$3B segment have impact in communities across the U.S.

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30. Revenue and market capitalization CAGRs based on all emerging pharmaceutical companies existing in 2000. Does not include companies that were acquired by larger firms during the 2000-2008 period (e.g., Pharmacia); BCG analysis based on EvaluatePharma data.

31. Jobs CAGR based on all emerging pharmaceutical companies existing in 2000 that are headquartered in the U.S. and were reporting total number of employees in 2000. If companies headquartered outside the U.S. are included, annual jobs growth rate is also 7 percent. Does not include companies that were acquired by larger firms during the 2000-2008 period (e.g., Pharmacia); BCG analysis based on EvaluatePharma data.


33. Based on a review of employment figures in Endo Pharmaceuticals and Biogen Idec annual reports.


The Challenges Ahead

The entire pharmaceutical industry is experiencing increasing difficulty in bringing innovative science through the long and uncertain process that leads to regulatory approval and then generating enough revenue to provide a return for the many years of investment. Timelines are stretching, the proportion of drugs that succeed is decreasing, and returns on investment in R&D are dropping for all companies, large and small.

Emerging companies, however, are particularly vulnerable to this deteriorating business environment. It is certainly increasingly difficult to persuade investors to continue, over the span of one or two decades, to plough money into a loss-making venture when the outcome is so uncertain. Even emerging companies that operate profitably are affected because they are often built on a technological or scientific specialty and rely on few products. The very factors that have led to the success of those companies – specialization and a focus – make them potentially more vulnerable to the decline in the business condition than larger players.

We have had in-depth interviews with senior leaders of emerging companies, all of whom conveyed a real sense of concern for the future of their industry segment. These conversations helped us identify three specific areas that impact emerging companies’ ability to continue to innovate.

- FDA review and approval, along with related regulatory issue
- Challenges related to pricing and reimbursement and increasing burdens resulting from new federal and state requirements
- Changes to the business environment: tax, economic policies, and intellectual property

As policymakers consider health care, tax, regulatory, and other policy changes, it is important that they realize that even small policy changes can have disproportionately large consequences for a vital segment of the biopharmaceutical sector – the emerging segment -- and for the patients who rely on the products that those companies produce.

FDA Review and Approval and Related Regulatory Issues

The key areas of concern that emerging companies identified as creating hurdles to innovation are as follows:

- Increased complexity and costs related to clinical trials
- Increasingly uncertain FDA review and approval process
- Challenges related to FDA Advisory Committee (AC) formation
- Increasing frequency, scope, and complexity of extensive post-approval requirements, especially Risk Evaluation and Mitigation Strategy (REMS)
- Concern that comparative effectiveness requirements could become a significant cost burden

The process of bringing a drug to market and surmounting the hurdles along the way is the single greatest concern for the emerging companies in our sample. Because most of them develop therapies for small and underserved patient populations, they experience a unique set of challenges during development. At the clinical trial stage, they report two main challenges. First, in contrast with clinical trials to address widespread conditions like high cholesterol or diabetes – trials that involve scores of patients over many years -- recruiting participants from small or deeply affected patient populations can be difficult and time-consuming. One company reported a period of two years before a trial enrolling only 250 patients could begin. Second, clinical trials for most conditions are usually designed based on previous trials, but for many of the specialized or orphan products that emerging companies are developing, reference points are few or nonexistent. This lack of precedent can slow the process of designing and executing a clinical trial and add time to the already-lengthy development process.
Once they reach the point of submitting a drug to the FDA for approval, emerging companies report a substantial uncertainty both during the process and at the final outcome. The stakes could not be higher. After a long and costly development process, the future of these companies depends on a successful outcome: the FDA approval and commercial release for which investors and patients have waited. However, over time, both the process and outcomes have become more uncertain. Even short delays in the review and approval of a new drug can have a dramatic impact on a company's economics if it has very few drugs in its product portfolio.

One part of the process that particularly affects this group of companies is the assembly of an FDA AC. The FDA has the option of consulting an AC as part of the drug approval process, and FDA data show that the use of ACs to review specific products has grown in recent years, from 12 in 2004 to 26 in 2008. However, finding experts to serve on these committees can be difficult given the stringent guidelines in place to prevent conflicts of interest. It is even more difficult for the specialized drugs developed by emerging companies because experts on specialized drugs that address smaller-population diseases are usually limited in number and often have already been consulted to some degree during the drug development process. In recent years, many potential experts have been eliminated from service on an AC, from 10 percent of applicants in 2006 to 25 percent in 2009. Only 2 percent of applicants were granted waivers in 2009 to serve in spite of conflicts of interest. The more frequent use of ACs and the fewer exceptions granted create a dilemma for companies focusing on smaller diseases for which only a very small scientific community exists. They want to partner with the best scientific experts to conduct their R&D, but by doing so they could jeopardize the FDA's ability to invite the best experts in the field to sit on the AC that will review the drug application.

Post-approval requirements have increased substantially in recent years and range from establishment of patient registries to additional post-marketing surveillance studies. Drug approval, which was traditionally the endgame for pharmaceutical companies, is now often followed by a Risk Evaluation and Mitigation Strategy (REMS) program required by the FDA. REMS is a post-approval requirement that attaches conditions and protocols to the rollout of a drug to continue measuring benefits and risks to patients. REMS might include a detailed medication guide for patients, required patient monitoring, or a number of other procedures. Approvals with subsequent requirements increased from 75 percent of all new molecular entity (NME) approvals in 2001 to 91 percent of NME approvals in 2008. The emerging companies in our sample cite REMS as a significant burden and expense, particularly when the FDA request for a REMS program is defined late in the process.

Another potential burden for biopharmaceutical companies, including those in our sample, arises from the growing concern of private and public payers regarding the economics of any new treatment, particularly treatments for conditions for which there are already several effective therapies on the market. These payers, through their reimbursement policies, are requiring studies above and beyond regulatory requirements, including comparative efficacy trials. Whether the requirement for post-approval comparative effectiveness data is driven by regulatory bodies or by payers, it may become the norm.

Some executives see comparative effectiveness as a societal benefit if deployed correctly, especially if it could lead to better appreciation for the highly innovative products that emerging companies develop. However, they worry about the additional cost burden, which, if applied to the economics of products destined for small patient populations, might contribute to deterring the development of therapeutic options for underserved patient groups.

**Challenges Related to Pricing and Reimbursement and Increasing Burdens Resulting from New Federal and State Requirements**

Emerging pharmaceutical companies benefit from a lean structure and an entrepreneurial culture that eschews bureaucracy and contributes to fast decision-making, a spirit that is directly in contrast with the

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Increasingly bureaucratic business environment. Broad measures like the 2002 Sarbanes-Oxley Act, which regulated corporate accounting and financial disclosure in the wake of Enron's collapse, have been applied to all business activities, but more specific rules and regulations have also been created for the biopharmaceutical industry. Industry executives are particularly worried by the increasing bureaucratic burden imposed by states developing their own sets of specific rules. The cost of building and maintaining the infrastructure to track compliance with various existing rules and regulations is similar regardless of company size or number of marketed products and hence can disproportionately affect emerging companies.

While state-by-state regulations for physician marketing disclosure are already a reality, emerging companies also cite the looming implementation of U.S. health care reform. Not only is the industry working to interpret the implications of the legislation at the national level, but there is real concern that individual states may enact legislation to increase the specificity of implementation at the state level. Such new legislation would further add to the administrative burden and complexity of a business that is already inherently complex because of its scientific nature.

Because emerging companies have few products in their portfolio, often clustered in a therapeutic area, they are especially vulnerable to swings in reimbursement or pricing that affect their category of drugs. For example, the 340B Drug Pricing Program established in 1992 limits the price of some outpatient drugs for selected qualified dispensers, including some health centers that serve disadvantaged populations. If 340B drug pricing were fully extended to inpatient facilities, a number of emerging companies in our sample report that the economics of their business would be severely impacted.

More broadly, any unexpected pricing or reimbursement shift that would be absorbed by the industry on a macro level could still have painful consequences at a micro level for specialized companies and the patients they serve.

**Changes to the Business Environment: Tax, Economic Policies, and Intellectual Property**

The transition from start-up to emerging company is often lengthy and reflects an extended period of unprofitability and uncertainty; ultimately a small number survive and emerge with a successful product and, finally, some profit. At this stage, the challenge for them is to re-invest in R&D with the aim of building a sustainable future beyond the initial success. Company leaders have to face the fact that angel investors and innovation tax credits fall away, and that they are left with fewer fiscal tools. They also have to worry about the strength of their intellectual property and, in particular, how long they have before the product they have spent years creating will be attacked by a generic competitor.

Due to increasingly challenging industry economics, growing global competition, and ever-increasing R&D complexity, emerging companies believe there is a need to examine R&D incentives and related public policies that impact their ability to innovate and compete globally. In their view, the R&D incentives and related public policies should be revised to ensure they provide a level playing field for emerging companies. This would include, for example, exploring the adequacy of R&D incentives ranging from R&D tax credit enhancements to IP incentives.

Decisions about where to locate a business can have major financial implications not just for the company but for the local and regional economy in which it is based over time. From a fiscal point of view US-based companies feel at a disadvantage over their international counterparts. U.S.-based emerging pharmaceutical companies pay taxes at a higher rate – more than 29 percent – than emerging companies based in other nations; companies based outside of the U.S. pay closer to 25 percent tax on average. This difference is largely driven by emerging companies headquartered in Europe, where the average tax rate in 2009 was just over 20 percent.

A pharmaceutical company’s major assets are the patents it holds to protect its IP from infringement. Patents provide a degree of assurance for investors to risk their capital in the long development process and to fund new R&D initiatives. Legislative changes that diminish the value of patents could have an immediate, detrimental impact on decision makers investing in R&D-based ventures and will negatively affect needed long-term innovation.

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Emerging Biopharmaceutical Companies

Under the Hatch-Waxman Act of 1984, generic drug companies are encouraged to challenge the patents of brand drug companies prior to patent expiration. Generally, a brand drug will be subject to a patent challenge by a generic company (a process called a Paragraph IV certification), in which the generic company states that its product does not infringe on the patent at issue or that the patent is invalid. If the generic company files a challenge with the FDA seeking to market a generic of a brand drug prior to expiration of that brand drug’s patent, then the brand company is notified. After the notice, the brand company can file a patent infringement action against the generic company. If a suit has been filed within 45 days of receipt of the notice, the FDA cannot approve the generic’s application to market its drug until the generic company successfully defends the suit or until 30 months, whichever comes first. Under Hatch-Waxman, the generic company is not subject to damages for developing its product and submitting its application to FDA, even though it may have infringed the patent when it submitted its application to FDA.

Generics have an incentive to challenge brand patents because the first generic to file an application with a patent challenge can obtain 180 days of marketing exclusivity, during which time it would be the only generic on the market. The incentives are so great that, from 2001 to 2008, brand companies filed 749 lawsuits responding to Paragraph IV challenges on 243 unique brand name products.40

History has shown that generic drug companies are successful less than 50 percent of the time when they pursue patent challenges in court.41 Because no one can predict the outcome of litigation, the best alternative in many cases is for the generic company to negotiate an agreement with the brand manufacturer that allows the generic drug to come to market before the patents on the brand drug expire.

Conversely, particularly for smaller pharmaceutical companies whose entire market value rests on protecting the patent rights that support a handful of products, the uncertainty of litigation can be untenable – even when the company has no doubt about the validity, scope, and term of its patents. Settlements in this case are crucial to finding a solution to generic threats that could be devastating to the company, its shareholders, and its employees.

Another challenge that companies identify are delays in the granting of patents. Companies report waiting up to two years for a patent to be granted and complain that investors and partners can be reluctant to invest all the capital necessary to pursue an innovative compound until its legal status is clear.

The Promise of Emerging Biopharmaceutical Companies

Though successful to date, emerging companies are like the canary in the coal mine for the pharmaceutical industry – simultaneously helping to drive the industry forward and warning of harder times ahead. Focus, which once seemed a recipe for success, now puts these emerging companies at risk and magnifies the overall uncertainty of the business environment. From the midsize pharmaceutical “class of 2000,” with 82 public companies worldwide reporting revenues between $100 million and $3 billion, 28 were acquired. Those remaining have achieved a 14 percent average annual growth rate, but the rate of growth has varied widely among companies in this group. While nearly one-third of them have surpassed $3 billion in revenue since 2000 and a couple have dropped below the $100 million mark, the rest are still considered midsize. In the intervening years, they have been joined by 83 other companies that have grown big enough to enter the midsize cohort or have spun off from a larger company and are midsize in their new incarnation.42 All these companies have the same goal: to graduate from this cohort and become the next $10 billion company.

What really challenges these companies is the fact that they are trying to thrive in an environment where the rules of the game seem to change continuously. They are confronted with an increasingly complex and
uncertain regulatory regime at the FDA, continued challenges related to achieving adequate pricing and reimbursement, lack of recognition and understanding of the value of innovation due to a narrow focus on cost containment, increasing challenges to IP (which is critical to incentivizing the substantial and ongoing R&D commitment needed) and a treacherous IP regime, and additional complexity throughout the system, particularly the uncertainty and potential scope of impact related to implementation of health care reform at the state and federal levels. In an industry in which it takes more than a decade to develop and bring a product to market, such uncertainty about the future can negatively impact current and future investment in this sector. Other possible outcomes of the uncertainty are the potential that R&D focusing on critical but risky disease areas could be eliminated given the increased need for certainty and that the ability of this segment to sustain and grow jobs vital to the U.S. economy could be compromised.

Given these significant challenges, senior leaders in emerging companies are often challenged by the great promise and opportunity that science provides on the one hand and the increasing pressures in the external environment on the other. These pressures include public policies that can have a dramatic, unanticipated impact on this vital segment of this sector.

In terms of policy implications, policymakers can help ensure stability and predictability in the regulatory environment through more clear and transparent guidance development at the FDA. Emerging companies rarely have the infrastructure to comfortably deal with the complexity of the environment – in terms of both the sheer volume of information and the opacity of requirements. Increasing transparency and considering potential unintended consequences on smaller firms as a criteria or key element in assessing potential policy changes would help ensure that these firms remain economically viable.
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