PERSPECTIVE

Market Structure And Drug Innovation

Shifts in the ways markets and regulatory forces interact have brought changes to drug innovation in the United States and elsewhere.

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ABSTRACT: An explosion of knowledge and a growing array of tools and technologies have transformed modern drug R&D, while its cost has risen by a sizable amount. At the same time, the unchecked increase in health care and prescription drug spending has spawned cost containment policies that are restricting the demand for drugs in all major markets. This Perspective explores the interplay between technological advances and regulatory policies and their likely impact on the dynamics of the pharmaceutical industry.

ADVANCES IN THE LIFE SCIENCES have profoundly transformed the drug research and development (R&D) process. That transformation has come at a price, boosting the cost of developing a new molecular entity (NME) to $802 million by 2000.[1] More expensive R&D, combined with an aging population and better diagnostic techniques, has swelled drug spending in the United States, which reached $141 billion in 2001.[2] These increases have in turn induced a spate of cost containment measures that are affecting demand for pharmaceuticals in all major markets. This Perspective considers the impact of the interplay between technological advances and health care policy on the future dynamics of the pharmaceutical industry.

■ **Productivity and growth.** During the 1990s the U.S. pharmaceutical sector enjoyed remarkable productivity growth, measured by capital, labor, and total factor productivity (TFP).[3] Compared with Europe and Japan, the United States has attained the highest average growth in the value of pharmaceutical production. This can be chiefly attributed to two causes: First, there are strong differences in absolute sizes and rates of growth between the U.S. market and those of other countries. For instance, the U.S. pharmaceutical market has grown from being roughly equal to the European market at the beginning of the 1990s to being almost twice as large in more recent years.[4] Second, the U.S. industry has been able to respond to market dynamics through substantial growth in nonlabor inputs, such as research and capital.

How much of this increase is structural and how much is transient is an important question, at a time when growth seems to be abating. To a certain extent, productivity in pharmaceuticals will increase, as in other sectors, as a pure consequence of economic recovery, since firms have already reduced the share of personnel costs devoted to production value. Moreover, consolidation through mergers and acquisitions, together with a further diffusion of information and communication technology, can further fuel growth in productivity. In particular, substantial gains in efficiency can likely be achieved by redesigning and reorga-

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nizing distribution channels, to adapt them to the growing roles of buyers' groups and the Internet. However, in the long run, productivity and pharmaceutical innovation will be critically affected by the interplay between technological and demand dynamics.

■ **Application of new disciplines.** The past twenty-five years have witnessed a revolution in biological sciences, with basic advances in molecular and cell biology, biochemistry, protein and peptide chemistry, physiology, and pharmacology. The application of these new disciplines to the drug industry, together with the growing convergence between life sciences and information sciences, has had an enormous impact on R&D activities, on the organizational capabilities needed to discover and develop new drugs, and on the dynamics of industry evolution.[5] By most metrics used in pharmaceutical discovery and development, output per person-hour has risen impressively over the past fifteen years. Yet this has not yet had a measurable impact on the flow of new drugs. There can be several reasons for this paradox: On the one hand, as scientists gain an increasingly detailed understanding of pathological processes at the molecular level, they can formulate better hypotheses that avoid dead-end tracks. On the other hand, as more targets are discovered, the body of knowledge required to understand them, let alone use them for new therapies, increases dramatically, which delays the time when new or better therapies become available. In short, there can be sharply diminishing returns in drug R&D.

The balance between these two opposing trends will eventually tilt to the side of increased productivity, but this might be years away and, moreover, is critically dependent on regulation, demand, and the pricing of new products. In short, pharmaceutical R&D for complex pathologies might be facing sharply rising marginal costs, but the price/value of those drugs tends to be higher and higher (socially). It is not uncommon for a new target to require many years of painstaking discovery to sort through the divergent conjectures and research hypotheses, which reflect the uncertainty, irreversibility, and lock-in of pharmaceutical R&D.[6] Since geneticists have recently increased our supply of targets from several hundred to several thousand, the magnitude of the work required to turn this into drug innovation cannot be underestimated.

In fact, the task at hand is so momentous that a spontaneous division of labor in R&D has emerged that unites the traditional large pharmaceutical companies to thousands of "small pharmas" and public research institutes in complex, dynamic webs in which knowledge, assets, and technological know-how are traded.[7] This provides the flexibility necessary to accommodate an exploding body of knowledge and to match opportunities with capital and know-how. It is apparently already producing tangible gains in R&D productivity, since both the probability of success and the speed of development are higher for collaborative versus in-house R&D projects.

■ **Industry structure and evolution.** Competition dynamics in pharmaceuticals results from the market interaction of breakthrough products, imitative ("me-too") compounds that offer various degrees of incremental improvement, and generics.[8] Breakthrough molecules enjoy rapid growth until imitative products are introduced and slow the growth of the innovative drug. After a while, all drugs tend to grow at about the same rate, with highly asymmetric shares in favor of the early entrants.[9]

Interestingly, innovation is highly specific to indications, biological targets, and chemical families and is not easily transferred to other families or targets, even within the same therapeutic area or the same company. For instance, firms with solid franchises in selective serotonin reuptake inhibitors (SSRIs) or statins have been unable to parlay these strengths into leadership of newer modes of action, which would have helped refresh their franchises as they matured. More often than not, a company's franchise becomes extinguished with the expiration of the blockbuster patent that created it. There does not seem to be a durable, long-term first-mover advantage that can be exported to a different drug class. This has hindered the persistence of dominant posi-

tions and limited industry concentration.

In summary, growth and industry structure in pharmaceuticals are driven by two basic mechanisms: the creation of new markets through the introduction of new families of products and rare arrivals of major breakthroughs, and competition among products within each submarket, before and after patent expiry. Against this backdrop, it is easier to understand why some cost containment initiatives recently implemented or under study across the world could permanently and adversely affect competition in the industry. For example, convergence toward price-control schemes such as reference pricing for on-patent drugs within broad equivalency classes would reduce expected revenues from horizontal product differentiation and would reinforce first-mover advantages, which would in turn lead to higher concentration. In this scenario, fewer of the giant firms would survive. Survivors would be companies that succeed in retooling their innovation to produce a consistent flow of first-in-class breakthrough drugs (instead of "me-too" compounds). Other competitors would gradually lose their status as growth companies that can be relied upon to deliver consistent growth and profits. They would in effect become cyclical drug companies, whose fortunes would follow the cycles of their (rare) blockbusters. As cyclical companies go, their valuation would be severely penalized and would likely attract corporate raiders bent on unlocking their intrinsic value by taking over those firms and selling off the pieces. Industry concentration would increase. A few biotech companies might seize the opportunity to join the ranks of Amgen and Genentech, and some might pair off with like-minded larger drug firms to become specialist drug companies. But the financial vulnerability of both the large cyclical and the biotech firms would be a barrier to growth. Innovation in pharmaceuticals is influenced by market size and expected profitability, which are sensitive to regulation.[10]

All in all, international convergence toward price control and reference pricing for innovative drugs would have negative effects on industry structure and innovation. A new industry landscape would take shape, but one that might look quite different from what policymakers originally had in mind.

NOTES

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