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THE FORCES TRANSFORMING PHARMACEUTICAL INNOVATION MODELS

Introduction

The modern pharmaceutical industry has always been dominated by a few large pharmaceutical companies, or 'big pharma'. Until recent times, the pharmaceutical industry has enjoyed success through big pharma's integrated approach of exploiting growing scientific and technological know-hows and commercialising high value blockbuster drugs. However, a number of market forces are influencing the value of pharmaceutical innovation. In response, big pharma is transforming its innovation models to sustain growth. This chapter characterises the market forces that are affecting pharmaceutical innovation models within the current context of healthcare and pharmaceutical industry.

Historically, after the Second World War, a number of pharmaceutical companies in Europe and the US led the success of the modern pharmaceutical industry based on their integrated model of prescription drug commercialisation. These companies acquired capabilities in research and development (R&D) of new prescription drugs, as well as in large-scale clinical trials management, management of regulatory approvals, and marketing and distribution of pharmaceuticals around the globe. They became large integrated companies, and also became known as 'big pharma' with their oligopolistic dominance of the global pharmaceutical industry. By the 1970s, the discovery of DNA and genetic engineering created a new paradigm in pharmaceutical R&D, called 'biotechnology'. Hundreds of university research spin-off companies emerged to commercialise biotechnology R&D. Big pharma relied upon these biotechnology companies to exploit specialised biotechnology knowledge and applications in drug discovery and development. By exploiting biotechnology capabilities in discovery and development of small molecule and biological drugs, big pharma produced a number of billion dollar value 'blockbuster drugs' (such as GlaxoSmithKline's anti-ulcer drug Zantac, Pfizer's cholesterol lowering drug Lipitor, Roche's breast cancer drug Herceptin) that sustained the success of big pharma-dominated pharmaceutical industry (Chandler, 1990, Mckelvey, 1996, Henderson et al., 1999, Chandler, 2005, Pisano, 2006).

The forces behind shifting pharmaceutical innovation models

Currently, a range of market forces are making big pharma's growth through its integrated innovation model unsustainable. Market forces such as payers (health insurers), government policies (healthcare reforms and drug price controls), emerging market dynamics, and dominance of low-price generic drugs over patented ones are commanding the value of pharmaceutical innovation. These forces are creating intertwining opportunities and barriers to big pharma's growth. The following sections discuss the market forces that are affecting the value of pharmaceutical innovation. This is followed by a discussion of how big pharma is transforming its innovation models in response to these forces.

Healthcare reforms and drug price controls—benefits and hurdles

Crippled by the ballooning healthcare costs, policy makers (governments) around the world are implementing measures designed to contain public healthcare spending. Also, many countries are reforming their healthcare policies so that every citizen can access affordable healthcare services, as described in World Health Organisation's (WHO) 2010 World Health Report. Such reforms are extending affordable healthcare services to disadvantaged citizens by means of prepayment of healthcare services, or mandatory and subsidised health insurances (WHO, 2010).

In the US, the Health Reform Legislation (Affordable Care Act), passed in March 2010, will extend mandatory subsidised health insurance by 2014 to previously uninsured 32 million citizens (Tumulty et al., 2010). As millions more US citizens come under mandatory insurance cover by 2014, the pharmaceutical and biotechnology industry will gain from expanded market coverage.

In China, the government launched an ambitious healthcare reform in April 2009 to bring the entire Chinese urban and rural population under universal primary medical services. An estimated 1.2 billion people are now covered by a basic medical insurance system (Guo, 2011), including over 300 essential medicines (Wang and Li, 2011). This provides the international and local pharmaceutical manufacturers with the benefit of expanded pharmaceutical market, although government measures taken to control essential drug prices will partly diminish the benefit of such expanded market.

Similar to China and the US, a number of African, South American and other Asian countries have also undertaken healthcare reforms to expand healthcare coverage (WHO, 2010). Such reforms will expand the pharmaceutical market for international and local companies. However, as discussed below, government policies to contain healthcare costs are targeted towards controlling drug prices, which are harming big pharma's income.

Traditionally, the regulatory approval of a new drug based on its safety and efficacy has been the biggest barrier to its market entry. But now the biggest hurdle for a new drug's success is whether it would qualify for reimbursement from the payers (PricewaterhouseCoopers, 2013). The payers are increasingly becoming important in determining the value of new drugs. Rising healthcare costs are forcing governments and payers to drive drug prices down. To qualify for reimbursement, pharmaceutical companies are now required to demonstrate through clinical trial results that their new drugs offer significantly more clinical benefit than existing alternatives (comparative effectiveness), and also reduce the total cost of care (cost -effectiveness) (Ernst and Young, 2010; PricewaterhouseCoopers, 2012a; Burrill, 2013).

Pharmaceutical companies are increasingly losing their control over drug pricing as governments around the world are taking radical measures to gain control over drug prices and determine reimbursement. Following are some country-specific examples.

In the UK, National Institute for Health and Care Excellence (NICE) of National Health Service (NHS) uses clinical data on new drugs to assess their cost and clinical effectiveness (value) and whether they could be reimbursed (PricewaterhouseCoopers, 2012a). Also, effective from January 2014, the UK government will switch to a 'value-based pricing' scheme, whereby medicines will be priced according to the benefits they deliver to patients. The scheme will reward only 'breakthrough' medicines rather than 'incremental' developments (Cooper, 2012).

In Germany, according to the 'reimbursement modernisation act' passed in 2011, the launch price of new drugs fixed by drug developers stays effective for one year, and after that new drugs will be assessed for their extra clinical benefits over reference drugs in the market. If no superior clinical benefit is found, the pricing will be matched with that of reference drugs (PricewaterhouseCoopers, 2012a).

In the US, the Affordable Care Act sets out provisions (e.g. discounts) to reduce out-of-pocket pharmaceutical costs, which means branded drugs could see $97 billion in lost revenues over the next decade despite the gains from expanded health insurance coverage (PricewaterhouseCoopers, 2012b).

China is no exception to such price control measures. In August 2012, China announced to double its number of price-controlled 'essential drugs' to 700 in pursuit of affordable and universal healthcare for its population of 1.3 billion (Sweeney, 2012).

Emerging markets—opportunities and challenges

Emerging markets like China, India, Latin America and Africa hold big promises

for the global pharmaceutical industry. Rising burden of chronic diseases like diabetes and expanding middle-class affluence in these markets are creating big opportunities for pharmaceutical companies (PricewaterhouseCoopers, 2012b). According to IMS Institute for Healthcare Informatics (IMS Institute for Healthcare Informatics, 2012), drug spending in emerging markets is estimated to increase from 20% of global spending in 2011 to 30% in 2016, whereas US and Europe's combined share will shrink from 58% to 49%. The current African market size will double to $45 billion by 2020, and chronic non-communicable diseases such as heart disease, lung disorders, cancer and diabetes, are estimated to account for almost half of all deaths in sub-Saharan Africa by 2030 (Berton, 2013).

But many challenges remain in emerging markets. Weak regulatory regimes and Intellectual Proprietary (IP) protection system, and underdeveloped infrastructure are some. Also, lack of health insurance for the majority of population in emerging markets means the patients themselves fund a larger share of drug costs than that in developed markets, and thus cannot support specialised drugs, e.g. biologic cancer drugs, that cost several thousands of dollars each (PricewaterhouseCoopers, 2012b, Burrill, 2013).

Though the middle-class affluence is growing, significant differences in per capita drug spending between developed and emerging markets will remain. According to IMS Institute for Healthcare Informatics (IMS Institute for Healthcare Informatics, 2012), per capita drug spending in 2016 will be $609 and $91 for developed and emerging markets respectively. Such difference in drug spending capacity mean that big pharma cannot expect to reap much of the value of their high-priced patented drugs in emerging markets, and have to rely on large volume generic drug sales.

Healthcare reforms across many parts of the world and growing emerging markets are expanding global pharmaceutical markets and, hence, the value opportunities for pharmaceutical companies. However, the value of new drugs is now determined and perceived by value users, in particular payers and policy makers, based on the performance and benefits the new drugs deliver, and also based on market-specific needs. Therefore, the value of pharmaceutical innovation is no longer embodied in new drugs and new markets alone, or commanded by pharmaceutical companies; rather the benefits of new drugs delivered to and perceived by users in existing and new markets embody the value of pharmaceutical innovation. This can be called the 'perceived value'.

Patent cliff—the end of 'blockbuster era'

The patent expiry of many blockbuster drugs, also regarded as the 'patent cliff', is displacing the 'blockbuster era' of big pharma. As many of the blockbuster drugs are crossing the period of patent expiry and generic competition, the pharmaceuti-

cal industry is looking at $290 billion of global prescription drug sales at risk (the value corresponds to sales in years prior to patent expiry), and $148 billion in potential loss due to patent expiry of branded drugs between 2012-18 (EvaluatePharma, 2012). Top ten drugs (according to their annual US sales in 2012) facing patent expiry in 2013, generated combined sales of nearly $15 billion in 2012, and are predicted to lose nearly $8 billion of that value by 2016 (EP Vantage, 2013).

Patent cliff is changing the drug spending landscape in developed markets. According to forecasts by IMS Institute for Healthcare Informatics (2012), patent expiry of many blockbuster drugs will bring total drug spending in developed markets down by $127 billion from 2011 to 2016. Also, global brand drug spending is forecast to grow by only 8% from 2011 to 2016, compared to nearly 80% growth in global generic drug spending. According to the US prescription data from Express Scripts, a pharmacy benefits management organisation in the US, for the first time in more than 20 years, traditional prescription drug spending for common diseases (cholesterol or heart problems, ulcer, pain, depression, neurological disorders, and infections) fell in 2012 due to increased use of low-cost generics. There was significant increase in the use of these drugs by Medicare and Medicaid patients in many therapeutic areas (e.g. diabetes); however, low-cost generics replacing patented blockbuster drugs brought traditional prescription drug spending down. This trend will continue in the short term, and by 2015, spending on traditional prescription drugs for different diseases in the US is expected to drop between 10-25% (Frazee, 2013, Stettin, 2013).

In contrast, spending on specialty drugs for chronic, rare and complex diseases is increasing. It represented one-fourth of total 2012 drug spending within pharmacy benefit in the US, and is predicted by Express Scripts to grow 67% over the next three years. Specialty drugs treat diseases like cancer, HIV, hepatitis C, multiple sclerosis, and rheumatoid arthritis (Frazee, 2013, Stettin, 2013).They are mostly high-priced drugs prescribed by specialists, and involve ongoing patient follow-up and clinical monitoring (IMS Institute for Healthcare Informatics, 2012). Many specialty drugs are biological drugs (or, biologics) that include vaccines, recombinant proteins, and cell, tissue or gene-based therapeutics produced from microorganism, animal or human sources (FDA, 2010).

Transformation of big pharma's innovation models

The big pharma-dominated pharmaceutical industry has long enjoyed the success of innovation through its integrated model of commercialising blockbuster drugs. The success was achieved through big pharma's ability to create and command the value that was embodied in its blockbuster drugs. Healthcare reforms, drug pricing pressures, growing emerging market needs and increasing dominance of generic drugs

over patented blockbuster drugs are forcing big pharma to shift away from its successful integrated model. As the analyses of market forces in this chapter point out, while the value of pharmaceutical innovation is embodied in new drugs, the value of new drugs is now determined by market-specific users based on the benefits of these drugs they can access. The success of new drugs now depends on how users in differentiated markets access and perceive their value. Consequently, big pharma is complementing its model of creating value through new drugs and new markets with one that is focused on making the benefits (perceived value) accessible to users.

As payers are taking charge of determining the value of new drugs, big pharma is collaborating with payers, including healthcare insurance companies and pharmacy benefits management organisations, to develop models of identifying and pinpointing value users (treatment responsive patients), evaluating comparative effectiveness of new drugs, and delivering perceived value to users through improved healthcare practice, treatment adherence and patient outcomes (Burrill, 2013). Also, big pharma is pursuing risk-sharing agreements with payers whereby rebates, discounts or refunds on new drugs are offered by them to cover the cost of drugs having treatment response failure or response rates below expectations compared with existing alternatives (Ernst and Young, 2013). To better demonstrate the effectiveness and value of new drugs to regulators and payers, big pharma is focusing on the development of personalised medicines that work on a specific patient subgroup who express a particular disease trait. The disease trait is identifiable by a companion diagnostic test. So, by using the diagnostic test the patient subgroup can be selected for treatment with personalised medicines (Burrill, 2013). Big pharma is also building innovative healthcare delivery models in many emerging markets through engaging doctors, patients and policy maker stakeholders in various healthcare initiatives. These include training and mentoring of rural doctors, and raising awareness among patients through patient education programs.

Big pharma is expanding its R&D, manufacturing and marketing activities in many emerging markets like China and India not only to grab the share of these rapidly growing markets, but also to take control of global commercialisation of low-price generic drugs through exploitation of local generic manufacturers in emerging countries. Finally, big pharma is offering huge discounts on its high-price specialty drugs and patented drugs for low-income patients in emerging markets.

Conclusion

This chapter examines the market forces that are shifting traditional pharmaceutical innovation models. Although expanding pharmaceutical markets in both developed and emerging markets are boosting growth opportunities, drug pricing and reim-

bursement pressures from governments and payers, and patent expiry of many blockbuster drugs are impeding big pharma's growth. Big pharma is responding to these opportunities and challenges by adapting its innovation models. As healthcare demands of emerging markets are steadily increasing, the long prevailing developed market-centric pharmaceutical industry is becoming increasingly focused on emerging markets. Since the value of traditional blockbuster drugs are diminishing rapidly, big pharma is seeking ways to capture value from new markets, such as specialty drugs for unmet, rare diseases, and drugs for disadvantaged and uninsured consumers in vastly untapped global markets. In the new landscape of the global pharmaceutical industry, the value of pharmaceutical innovation lies in the path towards new opportunities. The path forward for the big pharma-dominated pharmaceutical industry is one that makes a shift from product-centric innovation towards market-centric innovation.

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