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HARRIS-LUX CONSULTING 29 August 2014

MEMORANDUM THRU Michael Kelly, Acting Chief Financial Officer

FOR Robert A. Bradway, Chairman and Chief Executive Officer

SUBJECT: Threat of Entry into the Biopharmaceutical Market

1. Harris-Lux Consulting is pleased to deliver the fourth of five papers analyzing Amgen's current position within the biopharmaceutical industry, using Michael Porter's five economic forces as a basis of analysis (Porter, 1979). In this memorandum, HL Consulting will analyze the barriers to entry for new and existing biopharmaceutical companies and the impact on Amgen.

2. Overview. The threat of entry by new competition is low to medium for the biopharmaceutical industry because multiple barriers exist. Traditional barriers identified by Porter including capital requirements, economies of scale, technological expertise, product differentiation, limited access to distribution channels, and government regulations restrict new market entrants (Porter, 1979).

3. Capital Requirements. The cost of entering the biopharmaceutical market as a new manufacturer of a novel biopharmaceutical agent is prohibitively high for small start-up biopharmaceutical firms. Established firms, having developed, manufactured, and marketed successful biologic medications, can more easily attract capital, or self-finance, to produce novel medications or biosimilars. Still, the typical $100 million cost of producing a biosimilar product, or the $800 million cost of producing a novel agent, is a formidable barrier for most companies (PhRMA, 2013). As illustrated in Figure 1, funding is difficult to acquire without an established market presence. Obtaining financing is a significant barrier for market entry (Ford & Nelson, 2014).

   The research and development process to develop a new agent often spans 10 years or more, requiring significant resources up front with the return on investment coming years later, if at all. Only one medication is likely to be produced from 10,000 compounds explored in the drug discovery stage (Castner, Hayes, & Shankle, 2007).). As highlighted in Figure 2 only approximately 10% of drugs beginning clinical trials will get Food and Drug Administration (FDA) approval (Hay, Thomas, Craighead, Economides, & Rosenthal, 2014).

4. Technological Expertise. Lack of technological expertise in manufacturing, research, and development presents a barrier to entry for start-ups as well as established companies. Established companies with this expertise face far fewer barriers to entry than bio-tech start-ups. However, generic companies such as Teva, Sandoz, and Hospira are trying to enter the

biosimilar development market, but lack the resident expertise in the biosimilars market resulting in significant barriers to entry (Humi, Chance, Baum, & Provost, 2013).

Lack of specialization in the sector is also a barrier to entry for any company looking to produce a biopharmaceutical medication. For example, Amgen, despite its expertise in erythropoietin stimulating agents, may initially struggle when trying to develop an oncology medication. The barrier to entry is high for companies wanting to enter a small sector of the biopharmaceutical industry due to a lack of intellectual capital specific to the disease.

5. Economies of scale. Large, established manufacturers benefit from economies of scale with respect to nearly all functions including manufacturing, distribution, marketing, sales, research, and development. When trying to enter the market for developing new or bio similar medications, established companies can capitalize on previously implemented systems, decreasing their barriers to entry (The industry handbook: Biotechnology, n.d.). For example, an established marketing department, may have some increases in semi-fixed costs associated with additional staff, but the marginal cost of using the established computer program for marketing new products is essentially zero. A new start-up is not able to achieve economies of scale because it must implement all departments, possibly for a single product.

6. Government and Legal Regulations. Companies lacking experience dealing with the FDA face a steep learning curve when entering the biopharmaceutical market. As described by Porter, the experience curve refers, in this case, to a well-honed ability of established manufacturers to navigate complex FDA regulations and procedures for drug approval (Porter, 1979). Since only 10% of medications successfully complete this costly process, government regulations present new entrants with both a logistical and financial challenge.

   Beyond the FDA, other government regulations related to financing a biopharmaceutical entry into the market are complex and changing. The National Institute for Health recently changed the rules regarding its Small Business Innovation Research Loans. In addition, the ability to obtain capital is affected by federal and state laws restricting who is allowed to invest in biopharmaceutical related industry. Some contradictory legal issues surrounding the Jumpstart Our Business Startups (JOBS) Act ironically make it difficult for company fundraising activities (Ford & Nelson, 2014).

   Patents can prevent companies from entering the market for a specific product or class of medications depending on the extent of the patent protection. As, discussed in previous memos, the FDA created a fast track procedure for the development of biosimilars, decreasing the cost of entry, but the biosimilar cannot enter the market until the 12th year the patented product has been on the market. By then, the reference company's product is well established in the marketplace.

7. Post-Manufacturing Challenges. Product differentiation and limited access to distribution channels present barriers for companies attempting to enter new markets. Amgen's contracts with dialysis providers presents a barrier for new entrants. New entrants face challenges since contracts in the market place and previously established informal relationships limit their abilities to distribute their products. Manufacturers of biosimilar medications, as

previously discussed in our memo on substitutes, also face a perception held by some medical providers that biosimilars may have inferior safety and decreased efficacy.

8. Conclusion. New entrants trying to produce medications that are biosimilar to Amgen's non-patent protected products will likely face significant barriers to successful development and marketing of their products. Amgen should conduct financial studies evaluating the elasticity of the branded product compared with the elasticity of the biosimilar to determine appropriate price points for profit maximization. Secondly, Amgen is already partnering with Watson to develop biosimilars for some leading cancer therapies (Humi, Chance, Baum, & Provost, 2013). Amgen should expand partnerships and capitalize on its experience curve managing research and development; navigating both national and international governmental regulations; using established safe manufacturing processes; and marketing globally.

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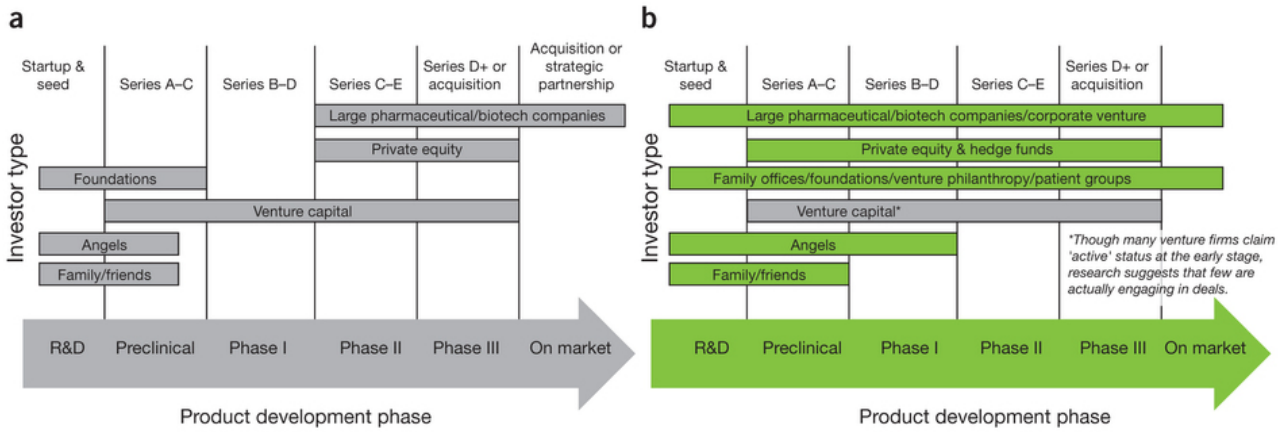

(a) The traditional landscape. (**b**) What the new landscape looks like.

Figure 1. Funding sources for new product development in the biopharmaceutical industry have changed for the different stages of development. Figure adapted from Ford and Nelsen (2014).

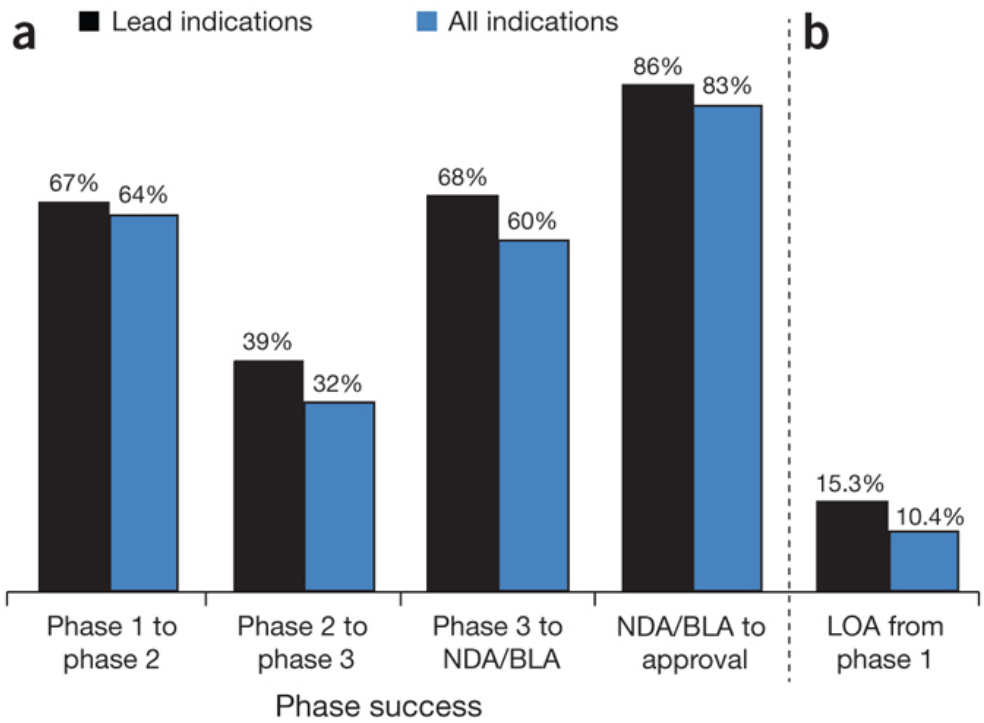

Figure 2. (**a**) Phase success rates for lead and all indications. The rates represent the probability that a drug will successfully advance to the next phase.
(**b**) LOA from phase 1 for lead and all indications. Rates denote the probability of FDA approval for drugs in phase 1 development. NDA refers to new drug application. LOA refers to likely hood of approval. BLA refers to biologic license applications. This figure was adapted from Hay, et. al (2014).