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HARRIS-LUX CONSULTING 27 July 2014

MEMORANDUM THRU Michael Kelly, Acting Chief Financial Officer

FOR Robert A. Bradway, Chairman and Chief Executive Officer

SUBJECT: The Power of Substitutes in the Biopharmaceutical Market

1. Harris-Lux Consulting is pleased to deliver the second of five papers analyzing Amgen's current position within the biopharmaceutical industry. Using Michael Porter's five economic forces as a basis of analysis, we will discuss substitutes in the market (Porter, 1979). This paper addresses Amgen's market share, the effect of government regulations on the availability of substitute products, the unique biopharmaceutical market environment with regard to substitute products, and value-based pricing as a strategy for increasing Amgen's market share.

2. Amgen's Market Share. In 2013, Amgen's revenues increased 8 % to $18.7 billion (Amgen, 2013). This increase reflects the current biopharmaceutical market increase of 6% (Roth, 2013). The biopharmaceutical market is expected to grow between $190 and $200 billion by 2015. Biosimilars, a threat to Amgen's market share, will total between $2 and $2.5 billion in sales, impacting revenues (Amgen, 2014). Amgen ranked second in biopharmaceutical earnings in 2013. The four-firm concentration ratio is 0.79, with Amgen accounting for approximately 18% of the market in biopharmaceuticals (Roth, 2013). Figure 1 highlights the top 10 companies' revenues and research and development expenditures.

3. Government Regulations and Availability of Substitutes. The Biologics Price Competition and Innovation Act (BPCI Act), part of the Patient Protection and Affordability Act (Affordable Care Act) of 2010, reduces the period of time a pharmaceutical corporation has to recoup research and development costs. Competitors introduce biosimilar products using the FDA's fast track approval process, only allowing the reference product developer 12 years of exclusive rights. These regulations are an attempt to increase competition and help with cost containment.

   The European approval process involves application to the European Medicines Agency, review by the Committee for Medicinal Products for Human Use, and approval by the European Commission. Novel biopharmaceutical agents comprise 18% of the approvals. The other approvals are biosimilars or reformulated and related medications (Walsh, 2010).

   Many physicians may be wary about the safety and efficacy of these biosimilar medications for two reasons: 1) These biosimiliar medications are only "highly similar" to the reference drug, which means that there can be differences in clinically inactive components (Sherman,

2012) and 2) there may be differences in manufacturing processes which could trigger negative immune responses (Liao and Heyse, 2011). In contrast, small molecule generic medications need to be exactly the same as the reference medication. Reference medications from biopharmaceutical companies, with established manufacturing processes, may be better received by patients and providers. In addition, the cost advantage of biosimilars is less than with generics. Biosimilar payers can expect only a 15-30% reduction compared to the reference product price rather than the 60-80% reduction with generics (Liao & Heyes, 2010). The cost for development of biosimilars is approximately $100 million as opposed to $1.2 billion for the reference product and the process only takes 6 to 9 years, compared to 10 to 15 years (PhRMA, 2013). Extensive development time and costs of biosimilars may lessen the actual impact on Amgen.

Concern regarding the biosimilar substitution laws is warranted. Five states enacted legislation adding requirements for the pharmacist to inform the patient and notify the provider of potential substitutions (Mazer, 2014). However, most biologics are provided through hospitals, so this legislation may not have a large impact. Currently, Canada, Spain, and Germany do not allow automatic substitution of biosimilar products (Amgen, 2014).

4. Biopharmaceutical Market. Biopharmaceutical medications compete with each other and with other substitute products including generic medications, medical devices, surgeries, alternative therapies, and hospitalizations (Dou, Felsen, Jansen, Song, & Soetjipto, 2008) A listing of Amgen's products and competitors' products is given in Figure 2. For illustrative purposes we will highlight four of Amgen's products.

   Enbrel, used to treat rheumatoid arthritis, is a major source of revenue for Amgen with $8.8 billion. Enbrel competes with other medications with different mechanisms of action such as Remicade, Humira, Stelara (Marketline, 2014). Despite Amgen recently winning a new patent extending exclusivity rights in the U.S. until 2028, a biosimilar product is being sold in India, a country less concerned with patent protection, at 70% the cost of Enbrel (The 10 best selling drugs of 2013, 2014). Novartis' Sandoz presents an additional market threat as the company nears completion of the development of a biosimilar for Enbrel (Garde, 2014).

   Neupogen, an adjunct chemotherapy medication, competes with Teva's Granix and Lonquex (Marketline, 2014). Recently, the FDA approved an application for Novartis to produce Zarzio, a biosimilar. Zarzio is currently marketed in over 40 countries (Garde, 2014). In addition, Therapeutic Proteins International, LLC is in the process of producing a biosimilar that will be marketed in developing countries (Schorsch, 2014).

   Epogen treats anemia caused by chronic kidney disease for 1.4 million Medicare patients. This biopharmaceutical, an injectable administered three times per week at a yearly cost of $6000 per patient, has been used with dialysis patients. Amgen negotiated contracts with DaVita and Fresenius, two dialysis companies who treat two-thirds of US dialysis patients. DaVita agreed to use Epogen for 90% of its needs through 2018 and Fresenius agreed to a non-exclusive deal for three years (Pollack, 2012). Omontys, marketed by Amgen's competitor Affymax, an Epogen biosimilar requires only one administration per month,

reducing nursing costs and decreasing overall costs. In addition, five biosimilar products are available in Europe (Walsh, 2010).

Amgen's Sensipar, an oral agent used to treat hyperparathyroidism, will not be included as part of Medicare's bundled reimbursement for dialysis until 2016 (Goozner, 2013). When bundled, cheaper, less efficacious Vitamin D substitutes will likely be selected to help contain costs. One pharmaceutical company, Teva, produced a Sensipar generic, but it will not be allowed to sell the generic until 2016 at the earliest (Decker, 2011).

5. Value-Based Pricing. Medicare and other international government payers are seeking value-based pricing information, an evaluation of a product based on its economic value (Woolmore, Standing, & Wells, 2013). Treatment distinctions which improve patient outcome, reduce required dosages, slow disease progress, or reduce delivery costs contribute to improved value pricing. In essence, a more expensive but more effective treatment can be more cost effective than a cheaper, less effective option due to the improved outcomes and reduced treatment frequency or duration. Amgen would be wise to consider value-added components when developing new medications. Figure 3 illustrates value-based pricing.

   For example, Epogen was developed as an infusion medication without a buffering agent rather than a patient administered subcutaneous injection with a buffering agent (to reduce stinging) in order to maximize reimbursement from Medicare. European health care systems use Epogen as a lower dose subcutaneous injection to keep costs down; their patients simply endure the stinging. By doing this, the European health care systems decreases costs, purchasing significantly less Epogen. The drug delivery system in the U.S was designed so more Epogen was used per patient, because it was processed through the liver, than would be used in a subcutaneous injection (Ziskind, 2014). Creating a buffered, subcutaneous version, reducing product and delivery costs, will create a value-added product.

   Similarly, as Amgen begins manufacturing biosimilars, the company can assign a value to its 30 year manufacturing expertise increasing the added value of the biosimilar (Woolmore, Standing, & Wells, 2013). With increasing competition from biosimilars, Amgen is wise to stress the added value of its currently available biopharmaceuticals, proven products marketed for an extended time and manufactured through established safe processes.

6. Conclusion. Amgen's competition from substitutes should be a growing concern for the company. As patents expire and biosimilars come on the market, Amgen may be looking at decreased profits in the near future. To combat this HL Consulting recommends that Amgen continue to invest in research and development of new biopharmaceuticals, engage in value-based pricing models, and develop biosimilars. These recommendations will increase Amgen's competitive position in the rapidly changing biopharmaceutical market.

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Figure 1: Top 10 Biopharmaceutical Companies Based on 2012 Revenues

1	Roche/Genentech	$37,582
2	Amgen	$17,265
3	Novo Nordisk	$13,475
4	Merck Serono	$8,234
5	Baxter	$6,237
6	Biogen Idec	$5,304
7	CSL	$4,550
8	Allergan	$1,766
9	Alexion	$1,134
10	Regeneron	$858

2012 R&D Expenditures

1	Roche	$8,031
2	Amgen	$3,380
3	Novo Nordisk	$1,882
4	Merck Serono	$1,526
5	Biogen Idec	$1,335
6	Baxter	$1,156
7	Allergan	$986
8	Dendreon	$626
9	CSL	$364
19	Alexion	$223

Note: In all top company profiles, dollar amounts are in millions. (Roth, 2013)

Figure 2:

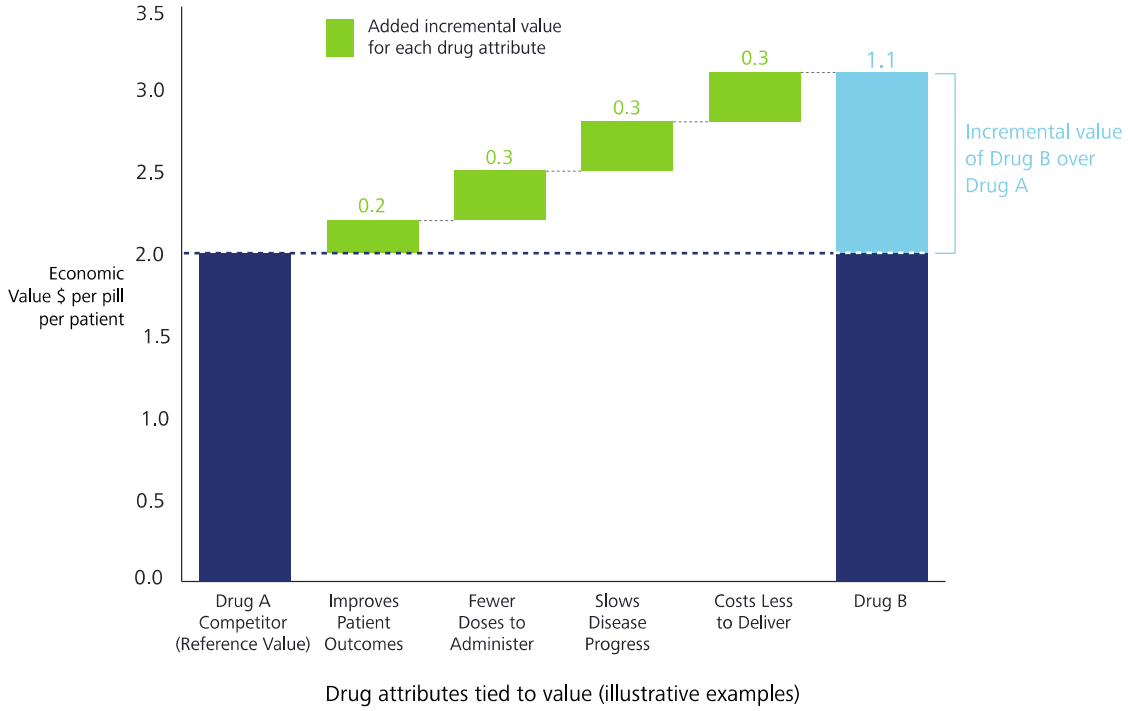
This table depicts some of the current Amgen medications on the market and their substitutes (Amgen, 2013).

Amgen Product	Territory	Competitor Marketed Product	Competition
Nuelasta/ Neupogen	US Europe Europe	Granix Lonquex Filgrastim biosimilars	Teva Pharmaceutical Industries Teva Various
Enbrel	U.S. & Canada U.S. & Canada U.S. & Canada	Remicade Humira Stelara	Janssen/Merek & Company AbbVie, Inc. Janssen
Aranesp	U.S. Europe Europe Europe	Procrit Eprex/Erypo Epoetin alfa biosimilars Mircara	Janssen Janssen-Cilag Various F. Hoffman-La Roche (Roche)
Xgeva	U.S. & Europe U.S. & Europe	Zometa Zoledronate generics	Novartis AG (Novartis) Various
Prolia	U.S. & Europe U.S. & Europe U.S. & Europe	Alendronate generics Evista Zoledronate generics	Various Eli Lilly and Company (Eli Lilly) Various
Sensipar/ Mimpara	U.S. & Europe	Active Vitamin D analogs	Various
Vectibix	U.S. & Europe U.S. & Europe	Erbitux Avastin	Eli Lilly/Bristol-Meyers Squib Genentech, Inc.
Nplate	U.S. & Europe	Promacta/Revolade	GlaxoSmithKline plc
Kyprolis	U.S. U.S. U.S.	Velcade Revlimid Pomalyst	Millennium Pharmaceuticals Celgene Corporation Celgene Corporation

Figure 3: Clinical and Economic Value

The graph below illustrates value-based pricing that could be utilized by Amgen. This particular graph was taken directly from Woolmore at Deloitte (Woolmore, Standing, & Wells, 2013).

Figure 2: Comparative Economic Value for Two Therapeutic Alternatives (illustrative example)



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