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BioINSIGHTS

A Newsletter from the Life Sciences Practice Group

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We are pleased to share this latest issue of Wiggin and Dana's BioInsights Newsletter. We circulate this newsletter by e-mail periodically to bring to the attention of our colleagues in the biotechnology and life sciences industry reports on recent developments, cases and happenings at Wiggin and Dana. We welcome your comments and questions.

LMG Life Sciences

In LMG Life Science's 2019 rankings, Wiggin and Dana was recognized among a select group of fifteen elite law firms in the area of Licensing and Collaboration.

Humira: How far can drug makers go to protect their branded market?

Kristyn Hansen and Monica Kolinsky

Between 2005 and 2015, 78% of drugs associated with new patents were not new drugs.[1] The practice of obtaining patents covering these "new inventions," which include modifications of known drugs or new mixtures or delivery methods of known drugs, is commonly referred to as evergreening, and has become one of many tactics drug makers use to shield a product's market exclusivity long past the product's initial patent term and delay the entry of generic competition[2] into the market. Recent moves by legislators to increase generic competition, and thereby reduce drug prices, have inspired drug makers to explore other ways to use patents to protect their investment in blockbuster brand-name products. In the case of at least one particular drug therapy, this has meant evergreening to the extreme.

Patent Thicket

In 2019, drug maker AbbVie, manufacturer of the world's best-selling drug treatment Humira, was accused, in a series of consolidated class actions brought by indirect purchasers of Humira, of illegally shielding Humira from generic competition with a "thicket" of more than 100 patents.[3] Humira, a biologic treatment used primarily for arthritis and other autoimmune disorders, has generated more than $115 billion in global sales since 2010. Despite expiration of the primary Humira patent in December 2016, some of Humira's other patents stretch out to 2034 – more than three decades after the drug launched. Plaintiffs allege that this excessive patent portfolio creates unlawful exclusionary effects that stifle generic competition and render normal enforcement mechanisms, such as litigating invalid patents, financially impracticable.

CONTINUED

1 Robin Feldman, *May your drug price be evergreen,* 5 J. OF L. & THE BIOSCIENCES 590 (2018). https://academic.oup.com/jlb/article/5/3/590/5232981

2 Reforming Evergreening and Manipulation that Extends Drug Years Act (REMEDY Act), S.___, 116th Cong. (1st Sess. 2019).

3 *In re: Humira (Adalimumab) Antitrust Litig.*, No. 19-VC-1873 (N.D. Ill. consolidated Jun. 4, 2019); *see also* Jeff Overlay, *'Groundbreaking' AbbVie Suits Test Bold Anti-Generic Tactics,* LAW360 (Mar. 27, 2019, 8:43 PM), https://www.law360.com/articles/1055075/-groundbreaking-abbvie-suits-test-bold-anti-generic-tactics

The various plaintiffs allege that AbbVie and its would-be competitors engaged in **pay-for-delay** deals to delay the launch of competitive biosimilars.

Humira: How far can drug makers go to protect their branded market?
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Efforts by prospective competitors to slash through AbbVie's patent thicket through litigation have proven ineffective. Most recently, the last-remaining challenger, Boehringer Ingelheim, settled its claims and joined several other biosimilar manufacturers in the queue to await an agreed-upon release date in the U.S. Based on these patent settlement agreements, plaintiffs accuse AbbVie and its would-be generic rivals of entering unlawful pay-for-delay and market allocation agreements that permit AbbVie to maintain Humira's supra-competitive prices for years to come. According to the complaint, absent competition in the U.S., the cost of treatment with Humira can cost patients $50,000 per year. A cost which, in the absence of AbbVie's alleged agreements, should have decreased significantly with the entry of generics after expiration of the primary Humira patent. Despite the pending allegations, AbbVie started 2020 with a price increase in excess of 7% – making it among a handful of drugs with the highest jumps in the new year.[4]

Pay-for-Delay

The various plaintiffs allege that AbbVie and its would-be competitors engaged in pay-for-delay deals to delay the launch of competitive biosimilars. In particular, plaintiffs point to the agreement between AbbVie and competitor Amgen, which permits Amgen to enter the market earlier than any other generic. Plaintiffs contend this affords Amgen a substantial payout by being the first to reach a settlement with AbbVie. Namely, under its settlement, Amgen can launch its biosimilar in January 2023, while other competitors are excluded from the market until June that year at the earliest.

While the Supreme Court's landmark *Actavis*[5] decision left open the possibility that pay-for-delay agreements could be anticompetitive, plaintiffs will face multiple challenges in demonstrating AbbVie's particular arrangements constitute pay-for-delay. While some courts have suggested that payments could be non-monetary, courts have struggled to adopt definitive standards of what constitutes a "payment."[6] Here, plaintiffs must demonstrate that the earlier biosimilar access to the EU market constitutes a large and unjustifiable payment. Moreover, under the *Actavis* decision, the arrangements could be scrutinized under the flexible and defendant-friendly rule of reason standard, which allows defendants to propose procompetitive justifications to overcome allegations of anticompetitive conduct. Defendants could then argue that the settlement agreement is procompetitive because it allows Amgen's biosimilar product to come to the U.S. market years before the expiration of all of AbbVie's asserted patents.

Market Allocation

Of the $20 billion in earnings from sales of Humira in 2018, $14 billion was reportedly generated from sales in the U.S. Following the launch of the first biosimilar in Europe, European

4 Christopher Rowland, *Why price of Humira keeps rising despite FDA approval of generic competition*, The Washington Post (Jan. 8, 2020, 7:00 AM), https://www.washingtonpost.com/business/economy/why-humiras-price-keeps-rising-despite-fda-approval-of-generic-competition/2020/01/07/549ed0ce-2e3a-11ea-bcb3-ac6482c4a92f_story.html.

5 *Fed. Trade Comm'n v. Actavis, Inc., et al.*, 133 S. Ct. 2223 (2013).

6 *See, e.g., In re Loestrin 24 Fe Antitrust Litig.*, 45 F.3d 538, 549 (1st Cir. 2016) (overturning a district court decision only Actavis applies "only to cash settlements or to their very close analogues" and expanding Actavis' holding to noncash forms of settlement payments).

Humira: CONTINUED

prices for a course of treatment with Humira dropped between 10-80%.[7] Anticipating a similar drop in prices in the U.S. following entry of the first biosimilar, plaintiffs allege that AbbVie conspired with its competitors to unlawfully divide the U.S. and European markets.

According to a complaint filed by New York's largest grocery workers union, AbbVie's agreements permit a deliberate sacrifice of profits in an already less lucrative European market to sustain astronomical prices in the U.S. This division of European and U.S. markets is *per se* unlawful under Section 1 of the Sherman Act as unlawful market allocation. Plaintiffs contend that the agreements between competitors to cease competing is "anticompetitive regardless of whether the parties split a market within which both do business or whether they reserve one market for one and another for the other."[8]

Since the union launched these claims in March 2019, several other third parties have also filed suit, including Miami police officers, the mayor and city council in Baltimore, as well as other unions representing Minnesota and New York workers.[9] While the *per se* nature of the claim puts plaintiffs in a somewhat easier position, some commentators remain skeptical that courts will adopt plaintiffs' arguments. For instance, there remains a question of whether a generic defendant's actions could be considered "ceasing to compete" in a market if its product had not yet launched and competition had not yet begun.

AbbVie's Response

In October 2019, in a memorandum in support of its motion to dismiss the case[10], AbbVie argued that the antitrust accusations around its accumulation of patents around Humira should be dismissed because there is no law limiting the number of patents a company can hold. AbbVie further argued that its settlement agreements are early-entry-only settlements, which are not subject to antitrust scrutiny, in contrast to settlements that provide for a reverse-payment flowing from the patent holder to the licensee.

Conclusion

In the past year, bipartisan measures proposed in the U.S. Senate aim to "[curb] patent manipulation by brand name drug makers"[11] and private parties similarly seek to erode barriers to generic market entry through class action lawsuits. While allegations against AbbVie are not atypical to antitrust actions in the pharmaceutical space, AbbVie's conduct with respect to protecting Humira raises new issues surrounding drug makers' unilateral ability to shield blockbuster therapies from generic competition. Perhaps on a scale not seen before, the Humira litigation forces courts and policymakers to confront the market consequences that coincide with the grant of patent monopolies, including the harms to competition and threats to consumer access to needed therapies.

AbbVie argued that the **antitrust accusations** around its accumulation of patents around Humira should be dismissed because there is no law limiting the number of patents a company can hold.

7 Sarah Jane Tribble, *Why the U.S. Remains the Most Expensive Market for 'Biologic' Drugs in the World*, NPR (Dec. 19, 2018, 1:02 PM), https://www.npr.org/sections/health-shots/2018/12/19/676401634/why-the-u-s-remains-the-most-expensive-market-for-biologic-drugs-in-the-world.

8 Complaint at 36-37, *UFCW Local 1500 Welfare Fund v. AbbVie Inc., et al.*, No. 19-CV-01873 (N.D. Ill. filed Mar. 18, 2019) (citing *Palmer v. BRG of Ga., Inc.*, 498 U.S. 46, 49-50 (1990)).

9 Eric Sagonowsky, *AbbVie's Humira antitrust woes snowball as class-action plaintiffs pile in*, FIERCEPHARMA (Apr. 3, 2019, 12:16 PM), https://www.fiercepharma.com/pharma/police-miami-city-officials-baltimore-and-trade-workers-minnesota-join-class-action-over.

10 Memorandum in Support of Defendants' Motion to Dismiss, *In re:* Humira (Adalimumab) Antitrust Litigation, No. 19-CV-1873 (N.D.Ill. filed October 10, 2019).

11 Press Release, Bill Cassidy, M.D., Cassidy Introduces Package of Legislation to Lower Drug Prices (Apr. 11, 2019), https://www.cassidy.senate.gov/newsroom/press-releases/cassidy-introduces-package-of-legislation-to-lower-drug-prices.

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ABOUT WIGGIN AND DANA LLP

Wiggin and Dana is a full service firm serving clients domestically and abroad from offices in Connecticut, New York, Philadelphia, Washington, DC and Palm Beach. For more information on the firm, visit our website at www.wiggin.com.

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Affibody AB's collaboration and license agreement with **Alexion Pharmaceuticals, Inc.** to co-develop ABY-039 for rare Immunoglobulin G (IgG)-mediated auto-immune diseases. Currently in Phase 1 development, ABY-039 is a bivalent antibody-mimetic that targets the neonatal Fc receptor (FcRn). Affibody retained the rights to lead clinical development of ABY-039 in an undisclosed indication and has the option to co-promote ABY-039 in the United States. Also, **Affibody AB**'s strategic collaboration with **GE Health-care** to develop and commercialize Affibody®-based PET imaging tracers, with initial focus on the targets HER2 and PD-L1. ABY-025, a HER2-detecting tracer, is currently in clinical development and provides a novel non-invasive and cost-effective approach to diagnose global HER2 expression in metastatic breast cancer patients using PET imaging. The PD-L1-binding Affibody® molecule is being developed as a diagnostic tool to improve selection and monitoring of patients with immuno-oncology treatments.

Alligator Bioscience AB's license agree-ment with **Biotheus Inc.**, granting rights to Biotheus in Greater China to an antibody from ALLIGATOR-GOLD® for the creation of up to three bispecific molecules, with an option to expand the license to global rights.

Expanded agreement between **Swedish Orphan Biovitrum AB (publ) (Sobi)** and **Sanofi** to exercise early opt-out for the development and commercialization of BIVV001, an investigational extended half-life factor VIII therapy with the potential to provide once-weekly dosing for people with hemophilia A.

Rallybio, LLC's (i) collaboration with **Exscientia** to form a joint venture – called RE Ventures – that will use artificial intelligence to accelerate discovery of small molecule drug candidates for undisclosed rare disease indications; and (ii) acquisition of two orphan drug programs, NAITgam and a follow-on therapy, from **Prophylix AS**, for the treatment of fetal and neonatal alloimmune thrombocytopenia (FNAIT), a potentially disabling or life-threatening disorder in fetuses and newborns.

Olink Proteomics Holding AB's sale of **Olink Proteomics** to **Summa Equity**, a Swedish-based private equity firm. Olink Proteomics is a life science company that has developed a unique technology for human biomarker discovery.

Swedish Orphan Biovitrum AB's exclusive license and acquisition of global rights for emapalumab from **Novimmune SA**. Emapalumab is a late stage orphan drug candidate that addresses a high unmet medical need in primary haemophagocytic lymphohistiocytosis, a rare and life-threatening syndrome of extreme immune activation.

PledPharma AB's expansion of its license agreement with **Solasia Pharma K.K.** for exclusive development and commercial-ization in several major Asian markets of PledPharma's product PledOx® for prevention of chemotherapy-induced peripheral neuropathy in expanded indications, in addition to the initial indication, colorectal cancer. PledPharma and Solasia Pharma will jointly develop the expanded indications.

The option exercise under **Diaprost AB**'s research and option agreement with a top 10 pharmaceutical company strategic partner to acquire h11B6, the lead candidate in Diaprost's kallikrein-related peptidase 2 (hK2) antibody program, which has advanced to clinical develop-ment for prostate cancer.

Photocure ASA's agreement with **Asieris Meditech Co., Ltd** for world-wide license rights to develop and commercialize Photocure's Cevira®, a fully integrated drug delivery and light device, for the treatment of HPV-induced cervical precancerous lesions. Asieris plans to launch a global clinical development program with an initial focus on the China market based on Photocure's Phase 2b data and the Phase 3 study design elements agreed with the US FDA. Under the agreement, Photo-cure will receive signing fees totaling $5 million, clinical and regulatory achieve-ment milestones of up to $18 million in China and up to $36 million in US/EU, in addition to sales royalties.