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Humira® Update: Big Guns Take Aim at Top-Selling Biologic

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AbbVie Inc.'s Humira® (adalimumab) was the top selling drug in 2015. Unsurprisingly, it is the focus of biosimilar applicants and patent challengers aiming to get into the market. We provide this update on three events regarding Humira® that took place over the past two months: (1) Amgen Inc., which is pursuing a biosimilar version of Humira®, received a recommendation toward approval from the U.S. Food and Drug Administration ("FDA"); (2) AbbVie sued Amgen for patent infringement in the U.S. District Court for the District of Delaware, alleging that Amgen infringed several of its patents by seeking FDA approval of its biosimilar version of Humira®; and (3) the U.S. Patent and Trademark Office instituted *inter partes* review ("IPR") of a Humira® patent at the request of Boehringer Ingelheim.

Background

We previously reported that, in November 2015, Amgen submitted a biologics license application ("BLA") seeking approval to market a biosimilar version of Humira®.[1] Amgen filed its BLA under the Section 351(k) biosimilar approval pathway[2] — an abbreviated pathway for products shown to be "biosimilar" to an FDA-licensed biological product (the "reference product").[3] This pathway allows biosimilar applications to rely on certain existing scientific knowledge about the safety and effectiveness of the reference product and to be licensed without providing a full complement of nonclinical and clinical data.[4]

However, FDA approval of a company's biosimilar does not necessarily mean that company can start selling the drug. A biosimilar maker typically faces several legal hurdles related to patents covering the reference product, notwithstanding any FDA approval, including patent infringement lawsuits pursuant to 35 U.S.C. § 271(e)(2)(C).

FDA Committee's Decision

On July 12, 2016, the FDA's Arthritis Advisory Committee determined by a vote of 26–0 that based on the "totality of the evidence" Amgen demonstrated its proposed biosimilar to Humira®, called "ABP 501," was "highly similar" to the U.S.-licensed version of Humira®.[5] Specifically, the FDA Committee found Amgen's data "support a demonstration that there are no clinically meaningful differences between ABP 501 and U.S.-licensed Humira in terms of the safety, purity, and potency" and show that "ABP 501 is biosimilar to the U.S.-licensed Humira in the studied indications."[6]

Amgen sought approval of ABP 501 for seven indications of use, but only submitted clinical studies concerning two of those indications — rheumatoid arthritis and plaque psoriasis.[7] The FDA Committee found, however, that Amgen provided an "extensive data package" "to support biosimilarity to other conditions of use and potential licensure of ABP 501 for each of the [seven] indications for which U.S.-licensed Humira is currently licensed and for which Amgen is seeking licensure."[8] The data package included comparisons between ABP 501

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and the European version of Humira® — a concept known as "bridging," which has previously been successful in Section 351(k) biosimilar approvals.[9]

PTAB Review of Humira® Patent

On July 7, 2016, the Patent Trial and Appeal Board ("PTAB") instituted an IPR of all five claims of a patent related to Humira® — AbbVie's U.S. Patent No. 8,889,135 (the "'135 patent").[10] Specifically, the PTAB determined that Boehringer Ingelheim[11] presented sufficient evidence to show a "reasonable likelihood" of unpatentability with respect to at least one of claims 1–5 of the '135 patent. The '135 patent covers methods of treating rheumatoid arthritis with a "human anti-tumor necrosis factor α (TNFα) antibody."

Two months earlier, the PTAB similarly instituted an IPR of the same five claims of the '135 patent in a petition filed by biosimilar maker Coherus BioSciences Inc.[12]

District of Delaware Litigation

In AbbVie's August 4, 2016 complaint, AbbVie asserts that Amgen has infringed ten of its patents concerning Humira®, based primarily on Amgen's attempt to receive FDA approval for ABP 501.[13] AbbVie is seeking an injunction.

While the lawsuit itself is limited to only ten patents, AbbVie alleges that Amgen has infringed claims in sixty-one patents. AbbVie brought suit on only ten because, under the Biologics Price Competition and Innovation Act ("BPCIA"), the parties may agree on the number of patents to be litigated.[14] Despite this limitation, AbbVie's complaint assures Amgen and the court that "as circumstances otherwise warrant, AbbVie will assert the remainder of the patents," including "if and when Amgen provides its 180-day Notice of Commercial Marketing."[15]

Looking Forward

The FDA is expected to render a final decision with respect to Amgen's ABP 501 by September 25, 2016. If successful, Amgen will be just the third company[16] to gain FDA approval under the Section 351(k) biosimilar approval pathway since enactment of the BPCIA in 2010, but it may be some time until there is more clarity with respect to when biosimilar alternatives to Humira® will be available in the marketplace. As noted in AbbVie's complaint, a second round of litigation between these parties is likely, and decisions in the IPRs may not come for at least twelve months. K&L Gates will continue to monitor and send updates regarding developments, including the FDA's impending final decision and outcomes of the above litigation and pending IPRs.

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[1] *See* BPCIA: Amgen Begins the Patent Dance With AbbVie.
[2] ARTHRITIS ADVISORY COMM., U.S. FOOD AND DRUG ADMIN., FDA BRIEFING DOCUMENT: BLA 761024: ABP 501, A PROPOSED BIOSIMILAR TO HUMIRA (ADALIMUMAB) 8 (July 12, 2016), *available at* http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM510293.pdf.
[3] *Id*.
[4] *Id*.
[5] *Id*. at 11.
[6] *Id*.
[7] *Id*.at 10.
[8] This included, in addition to rheumatoid arthritis and plaque psoriasis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, and ulcerative colitis. *Id*. at 7.
[9] *See id*. at 10.
[10] Boehringer filed two similar IPR petitions regarding the same claims 1–5 of the '135 patent, but based on different prior art. See Boehringer Ingelheim Int'l GmbH et al. v. AbbVie Biotechnology Ltd., IPR2016-00408 (P.T.A.B. July 7, 2016); Boehringer Ingelheim Int'l GmbH et al. v. AbbVie Biotechnology Ltd., IPR2016-00409 (P.T.A.B. July 7, 2016).
[11] For purposes of this discussion, "Boehringer Ingelheim" refers to the parties "Boehringer Ingelheim International GmbH" and "Boehringer Ingelheim Pharmaceuticals, Inc." Each party is a petitioner in each of the two IPR petitions.

[12] *See* Coherus Biosciences Inc. v. AbbVie Biotechnology Ltd., IPR2016-00172 (P.T.A.B. May 17. 2016).
[13] Complaint at 1, AbbVie Inc. et al. v. Amgen Inc. et al., No. 1:16-cv-00666-SLR (D. Del. Aug. 4, 2016).
[14] *Id*. at 3–4. As allowed by the BPCIA, Amgen allegedly limited the choice to six patents each, and two of the patents each party identified overlapped, resulting in a final number of ten.
[15] For more information on the 180-day Notice of Commercial Marketing, see Federal Circuit Confirms Post-Licensure Notice of Commercial Marketing Is Mandatory in Biosimilar Litigation.
[16] Coincidentally, Amgen found itself on the other side of the equation when, on July 13, 2016, the FDA Arthritis Advisory Committee paved the way for approval of Sandoz's biosimilar version of Amgen's Enbrel® (etanercept) also used to treat, among other things, rheumatoid arthritis and plaque psoriasis. Approval of Sandoz's biosimilar would mark the fourth instance of biosimilar approval under the BPCIA.