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Biosimilar Makers Turn To IPRs Despite Mixed Results

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Despite mixed results, biosimilar makers continue to turn to inter partes review proceedings in order to challenge innovator patents protecting some of the most important biologics. IPRs have been attractive to biosimilar makers, not only because of the procedural and substantive advantages that IPRs currently provide, but because they allow litigation at a point when it is premature under the U.S. biosimilars statute, the Biologics Price Competition and Innovation Act of 2009, and when there is no case or controversy under the Declaratory Judgment Act and Article III of the Constitution. As the Federal Circuit explained in a case involving a proposed biosimilar version of Amgen Inc.'s Enbrel, it has never "found a case or controversy when the only activity that would create exposure to potential infringement liability was a future activity requiring an FDA approval that had not yet been sought."[1] IPRs, by contrast, allow biosimilar makers to challenge innovator patents prior to submission of their biosimilar application to the U.S. Food and Drug Administration.

Biosimilar makers have filed 13 IPR petitions in the last 16 months and hedge fund owner Kyle Bass also filed an IPR petition to challenge a patent protecting an innovator biologic. The Patent Trial and Appeal Board instituted three of the 14 IPRs at least as to some of the challenged claims and denied four in their entirety. A biosimilar maker voluntarily dismissed two of the 14 IPR petitions without prejudice, and five remain pending. This article reviews these recent challenges to patents that would normally be litigated in district court under the intricate patent litigation framework set forth in the biosimilars statute.

Challenges to Rituxan Patents

Boehringer Ingelheim, an innovator and biosimilar maker, filed petitions for IPR of patents protecting Biogen Idec's and Genentech's blockbuster antibody product, Rituxan. Rituxan is indicated for treating certain patients with rheumatoid arthritis that did not respond to other therapy and non-Hodgkin's lymphoma, among other indications. In December 2014, with its proposed biosimilar of Rituxan still in clinical trials, Boehringer filed IPR petitions challenging three patents covering methods of using Rituxan in the treatment of rheumatoid arthritis or low grade B-cell non-Hodgkin's lymphoma.

In July 2015, the PTAB instituted IPR (IPR2015-00417) on all claims of one of the patents. But it did not

institute IPR (IPR2015-00415) of half of the challenged claims of the second patent and it did not institute IPR (IPR2015-00418) of the third patent. Boehringer requested rehearing on one of its 10 grounds for instituting IPR of the third patent, arguing that the PTAB misapprehended the prior art. Boehringer then withdrew its request and also filed requests for adverse judgment against itself with respect to the two instituted IPRs. By early October 2015, the IPRs were terminated. In the same month, a report issued that Boehringer ended its Phase III clinical trials for its biosimilar version of Rituxan and stopped its development.

Celltrion Inc., another biosimilar maker, had tried to piggyback off the two Boehringer IPRs instituted by the PTAB. Celltrion filed its own petitions for IPRs (IPR2015-01733 and 1744) of the same claims of the same two patents on the grounds in the PTAB decisions and moved for joinder with the Boehringer IPRs. Celltrion's petitions are substantially identical to Boehringer's and rely on the same expert declaration as Boehringer. Celltrion represented that it would not offer separate argument, expert testimony, or briefing. But its strategy to leverage Boehringer's IPRs backfired. Boehringer sought an adverse judgment in the two IPRs prior to the deposition of its expert, and it did not permit Celltrion to retain its expert to continue the IPRs. Celltrion could not proceed without Boehringer's expert and sought a dismissal of its petitions contingent on the PTAB agreeing to a dismissal without prejudice, allowing Celltrion to refile its petitions with a new expert. The PTAB agreed and dismissed Celltrion's petitions without prejudice in October 2015. In November, Celltrion submitted a regulatory application in Europe for its proposed Rituxan biosimilar. Celltrion has not refiled its IPR petitions to date.

Challenges to Humira Patents

In June 2015, Amgen, an innovator and biosimilar maker, filed IPR petitions (IPR2015-01514 and 1517) against two patents held by AbbVie Inc. covering formulations of Humira, one of the world's most important biologics. Humira is a recombinant antibody approved for reducing signs and symptoms of various conditions including rheumatoid arthritis and Crohn's disease. In November 2015, Amgen announced that it had submitted its biosimilar application to FDA. In January 2016, Amgen announced that the FDA accepted its application for review. Earlier the same month, the PTAB denied both of Amgen's petitions for IPRs.

Coherus BioSciences Inc. and Boehringer have also filed IPR petitions challenging patents protecting Humira. In November and December 2015, Coherus filed IPR petitions (IPR2016-00172, 188 and 189) challenging three of AbbVie's patents. These three patents are different from those in Amgen's IPR petitions, and cover methods of using Humira to treat patients with rheumatoid arthritis. The PTAB's institution decisions are expected by June 2016. According to a press release, Coherus is planning to submit its biosimilar application for Humira in the second half of 2016. In late December, Boehringer filed two IPR petitions (IPR2016-00408 and 409) challenging the AbbVie patent at issue in one of the Coherus IPR petitions (IPR2016-00172) on other grounds. The PTAB's decisions are expected by July 2016. Boehringer's proposed biosimilar is in Phase III clinical trials.

Challenge to Orencia Patent

In July 2015, Momenta Pharmaceuticals Inc., another biosimilar maker, filed an IPR petition (IPR2015-01537) challenging a patent held by Bristol-Myers Squibb Co. (BMS) covering a subcutaneous formulation of Orencia. Orencia is a fusion protein approved for treating certain forms of rheumatoid arthritis. In January 2016, the PTAB instituted IPR of the BMS patent. BMS filed a request for rehearing the PTAB's institution decision although such requests are rarely granted. If the IPR continues, a final written decision is expected in January 2017, long before Momenta submits any regulatory application to the FDA.

Kyle's Bass' Challenge to an Enbrel Patent

A patent protecting Amgen's Enbrel is also the subject of an IPR challenge. Enbrel is a fusion protein marketed by Amgen for the treatment of rheumatoid arthritis and other conditions. Sandoz Inc. filed a biosimilar application for Enbrel. In October 2015, Sandoz announced that the FDA accepted its application for review. In June 2013, long prior to submitting its regulatory application, Sandoz sought a declaratory judgment that two of the patents protecting Enbrel were invalid. Sandoz's suit was dismissed for lack of case or controversy and also for failure to comply with the BPCIA.[2] The Federal Circuit affirmed the district court decision for lack of justiciability, without reaching the BPCIA ground.[3]

In August 2015 with the acceptance of Sandoz's biosimilar application on the horizon, Coalition for Affordable Drugs V LLC, an entity controlled by hedge fund owner Kyle Bass and his Hayman hedge fund groups, filed an IPR petition (IPR2015-01792) challenging the patentability of one of the patents previously challenged by Sandoz. On March 11, the PTAB denied the petition and did not institute IPR as to any of the challenged claims of the patent. Last month, the same patent, among others, was asserted against Sandoz's proposed biosimilar of Amgen's Enbrel in a lawsuit under the BPCIA.[4]

While it is clear that biosimilar makers continue to turn to IPRs to challenge innovator patents long before they can do so in district court, Boehringer's mixed results and Amgen's failed petitions show that IPRs are far from certain to provide biosimilar makers with patent certainty or permit them to bypass the BPCIA entirely. Moreover, although a biosimilar maker can put forward the same arguments in litigation in district court if its petition for IPR is denied, the fact of the denial in a proceeding where there is no presumption of validity and no clear and convincing burden of proof on top of other advantages to patent challengers undoubtedly strengthens the innovator patent and makes any subsequent challenge to its validity in district court all the more difficult. In cases where the best defenses were advanced in the IPR, the biosimilar maker may be left to litigate the infringement of a valid patent under the BPCIA.

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[1] Sandoz Inc. v. Amgen Inc., 773 F.3d 1274, 1279 (Fed. Cir. 2014).

[2] Sandoz Inc. v. Amgen Inc., 2013 U.S. Dist. LEXIS 161233, *3-5 (N.D. Cal. Nov. 12, 2013).

[3] Sandoz, 773 F.3d at 1278, 1282.

[4] Immunex Corp. et al. v. Sandoz Inc. et al., C.A. No. 16-1118 (D. N.J.).