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Phone: +1 646 783 7100 | Fax: +1 646 783 7161 | customerservice@law360.com

Apotex Challenges Amgen Cancer Biologic Patent As Obvious

By **Chuck Stanley**

Law360, Washington (December 13, 2017, 7:11 PM EST) -- The maker of a competitor to the chemotherapy companion drugs Neulasta and Neupogen took aim at Amgen Inc.'s underlying patent on the biologics Wednesday at the Patent Trial and Appeal Board, saying processes described in the patent were obvious given prior art.

Apotex Inc. told a PTAB panel the process for breaking up and refolding proteins used to make the white blood cell treatments for chemotherapy patients is an obvious combination of two previously existing processes for unfolding and refolding proteins with disulfide bonds.

Patents referred to as Schlegl and Hevehan made obvious the process for refolding proteins with disulfide bonds at high concentrations using a reductant and oxidant combination referred to as a redox component, as described in U.S. Patent No. 8,952,138 held by Amgen, Crowell & Moring LLP's Deborah Yellin, arguing for Apotex, told a PTAB panel.

But Hogan Lovells' Arlene Chow, arguing for Amgen, told the panel that the Schlegl and Hevehan patents do not deal with the sort of complex proteins covered by the '138 patent, nor do they specify the volumes of redox components in the process that allows Amgen to reliably refold the proteins at high concentrations and volumes when producing Neulasta and Neupogen.

Hevehan, Chow said, describes a "trial and error" system for using a redox system to refold proteins that is not sufficiently reliable for use in large-scale production of a white blood cell treatment.

The '138 patent by contrast is a "rational system" that carefully balances oxidant and reductant formulas referred to as TPR and RBS, in order to deliver reliable outcomes.

"The '138 patent is all about control," Chow said. "It describes a balance of TPR and RBS: how much and where the redox components are found."

The process used for Neulasta and Neupogen was not obvious given the Schlegl and Hevehan patents, Chow said, adding that a reasonable person of skill in the art would not have combined the processes, because they deal with different concentrations of proteins.

But Yellin said the type of protein described in the patents was immaterial, because complex proteins had been unfolded through a variety of existing processes, meaning a person of normal skill in the art

would have known that the processes described in Schlegl and Hevehan could have been applied to many different kinds of proteins, including those used in Neulasta and Neupogen.

Apotex sought approval of biosimilars of Neulasta and Neupogen from the U.S. Food and Drug Administration in 2015.

Amgen responded by filing a patent infringement suit, which was eventually tossed by a federal judge in September 2016, a decision that was upheld by the Federal Circuit last month.

Apotex filed the instant request for inter partes review of the '138 patent in August 2016.

Neulasta and Neupogen generated nearly $4.6 billion in revenue last year.

The patent-in-suit is U.S. Patent No. 8,952,138.

Administrative Patent Judges James T. Moore, Michael J. Fitzpatrick and Christopher G. Paulraj sat on the panel for the PTAB.

Apotex is represented by Deborah Yellin, Teresa Rea, Vincent Galluzzo, Michael Jacobs and Shannon Lentz of Crowell & Moring LLP.

Amgen is represented by Arlene Chow of Hogan Lovells and Catherine Nyarady of Paul Weiss Rifkind Wharton & Garrison LLP.

The case is Apotex Inc. et al. v. Amgen Inc. et al., IPR number 2016-01542, at the Patent Trial and Appeal Board.

--Additional reporting by Matthew Bultman. Editing by Breda Lund.