The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 1/2016

Duesseldorf/Munich, **17 February 2016** The times they are a'changing – particularly in the Biopatent discipline. Biopatent professionals live in a quickly developing world, which is sometimes hard to keep pace with. Michalski • Huettermann & Partner Patent Attorneys have decided to produce relief to this situation, and are proud to present a new information service related to Patent issues in Biotechnology. This newsletter issues on an irregular basis in order to provide information with respect to actual events, as well as in-depth-analyses of long-term developments. Patent Attorneys from our firm explain the meaning of recent developments and decisions affecting the Biopatent community, and provide expert insight into what's going on behind the scenes. In this issue, we refer to earlier issues of the Rhineland Biopatent Gazette, and provide an update to the Infliximab biosimilar story (Dr. Christoph Volpers), as well as the patent disputes regarding the Cabilly patent, the anti-PD-1 antibodies Nivolumab and Pembrolizumab and the antibody drug conjugate ado-trastuzumab emtansine (Dr. Ulrich Storz).

Infliximab biosimilar on the home stretch in the US

FDA panel gave prefinal nod, but IP debate is going on

In Issue 4/2013 of the Rhineland Biopatent Gazette, we reported about the approval of the first (and still only) antibody biosimilar in Europe, Inflectra®/Remsima®, on September 10, 2013.

Inflectra/Remsima, is a biosimilar to J&J's infliximab (Remicade®), a chimeric IgG targeting TNFα. It was developed by Celltrion and approved for Hospira and Celltrion, respectively, in tandem.

In 2012, J&J's Remicade reached global sales of more than 9.1 bn US-$ according to business intelligence provider pmlive, which despite the appearance of Inflectra/Remsima in Europe rose to 10.2 bn US-$ in 2014.

On Thursday, February 11, 2016, the FDA's advisory committee recommended to approve Celltrion's biosimilar, which goes by the working title CT-P13, for each of Remicade's indications.

FDA approval would make this drug the first approved biosimilar antibody in the United States, outranked only by Sandoz' Zarxio®, a biosimilar to Amgen's Neupogen® (filgrastim), which was approved March 6, 2015, but is a small biologic, with a molecular weight of 19 Kd (vs. 150 kd of an antibody), and essentially no glycosylation.

Should Remsima eventually be approved, this would create a milestone that would affect the entire pharmaceutical industry.

Not surprisingly, an IP debate is ongoing in the background. Janssen Biotech, a J&J subsidiary, and the NY State University have sued Celltrion and Hospira on March 6, 2015, in the District of Massachusetts (1:15 cv 10698), for violation of regulation set forth in the Biologics Price Competition and Innovation Act (BCPIA), plus infringement of U.S. Patent No. 6,284,471 and five other patents. U.S. Patent No. 6,284,471 protects infliximab per se. Claim 1 reads as

Recent updates in Antibody IP

New IPR against Cabilly patent, Merck lost PD-1 case in UK; and no opposition filed against Genentech's ADCs patent

On Feb 5, 2015, the USPTO instituted an IPR review of the Cabilly II patent (US Patent No 6,331,415). See Issue 5/2011 of the Rhineland Biopatent Gazette, and an article in mAbs (get a reprint here). The IPR was filed by Sanofi/Genzyme. The Cabilly family of patents reportedly has ~70 licensees.

A deadline for 3rd parties to join the IPR and become a party to the proceeding will end March 5. Such joinder would be an effective measure to ensure that the proceeding does not get settled by the two parties while leaving the patent validity unresolved. The joinder is relatively simple but does require filing fees and some attorney work. Any party, not necessarily a licensee, may join.

We are in contact with our US colleagues. Should you be interested to join that IPR please let us know.

In a recent article in mAbs, we discussed the patent dispute between Bristol Myers Squibb and Merck & Co. Get a reprint here. See also Issue 3/2015 of the Rhineland Biopatent Gazette for a summary thereof.

The dispute focuses on infringement of US patents assigned to Ono, which are in-licensed by BMS, and protect BMS's anti-PD1 antibody Opdivo® (Nivolumab).

Merck has been sued by BMS for infringement of their patents through the sale of the competing antibody Keytruda® (Pembrolizumab).

Merck has challenged the validity of Ono's patent EP1537878B1 not only by means of an opposition at the EPO (which was rejected in 1st instance on Sept 10, 2014, appeal pending),

+ from our firm +

MH Partner to speak at the 15. Duesseldorfer Patentrechtstage 2016

MH Partner Ulrich Storz will speak at the 15. Düsseldorfer Patentrechtstage 2016, which take place March 10 and 11, 2016, in the Industrieclub.

This meeting, which is one of the most prestigious IP meetings in Germany, is organized by Dr. Jan Busche, who is a Professor at the Duesseldorf University, and Peter Meier-Beck, chief judge at the federal Supreme Court (BGH).

Ulrich will discuss the changes over time that 2nd medical use claims went through in the last decade. He will also address the transfer of this concept to medical devices, where 2nd medical use claims are still relatively novel.

Further, Ulrich will discuss a phenomenon that is sometimes disrespectfully called "nonsense indications".

If you want to attend the Patentrechtstage find more information here.

follows:

> 1. A chimeric antibody comprising at least part of a human immunoglobulin constant region and at least part of a non-human immunoglobulin variable region, said antibody capable of binding an epitope specific for human tumor necrosis factor TNFα, wherein the non-human immunoglobulin variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

The case thus nicely combines patent issues with regulatory issues nicknamed "patent dance" (see Issues 3/2015 and 6/2015 of the Rhineland Biopatent Gazette).

The '471 patent claims a priority date of Jan 29, 1993, but will be in force until Sept 4, 2018, while the European counterparts have already expired.

Further patents that Janssen relied on are US 7,223,396 (methods to treat Crohn's disease), US 5,807,715 (methods of producing antibodies), US 7,598,083 and US 6,900,056 (chemical cell growth media) and US 6,773,600 (purifying biological products).

On Feb 12, 2015, Celltrion and Hospira managed to receive a favorable decision in that they successfully invalidated the patent in an ex-parte reexamination for obviousness-type double patenting over two expired U.S. patents.

Shortly after their DC complaint, Janssen therefore also demanded to stay the proceedings in view of the pending reexamination.

Janssen and NYU appealed the revocation on July 23, 2015, arguing that the obviousness-type double patenting rejection would be improper for formal reasons, plus the claims would be patentably distinct from the claims of the two expired patents that Celltrion and Hospira had referred to in their request.

In a status conference of the ongoing trial at the District Court following the FDA recommendation, Celltrion stated that they would not launch their product until after June 29, 2016, which is the expiration date of the patent covering the Crohn's disease indication of infliximab.

It will be exciting to see how this case, which nicely illustrates how tightly patent issues and issues of regulatory law are interrelated, will turn out.

In the meantime, European drug maker Sandoz, a Novartis subsidiary, has declared on Feb 12, 2016, that they have acquired rights from Pfizer to PF-06438179, Pfizer's infliximab biosimilar, and plan to make 10 biosimilar regulatory filings over a three-year period (2015-2017).

Pfizer had committed to the European Commission beforehand to divest its infliximab biosimilar program after having acquired Hospira.

but also with respect to its UK part at the UK Patents Court.

On October 22, 2015, the UK patents court Court has also upheld the validity of the patent, thus confirming the EPO decision. The Court came to the conclusion that the raised prior art did not plausibly enable the claimed therapeutic effect, and could thus not be construed to be novelty relevant.

Interestingly, during the proceedings, Merck accepted that if the patent was valid, its product fell within the scope of the claims, while Ono admitted that if priority was lost, the claims were invalid.

Another case we have recently discussed concerns Genentech's antibody drug conjugate Kadcyla® (ado-Trastuzumab emtansine). See issue 4/2015 of the Rhineland Biopatent Gazette, and our respective article in mAbs, reprint of which can be ordered here.

Phigenix has filed requests for Inter Partes Review (IPR) in 2014 against Genentech's US Patent 7575748 (IPR2014-00842) and Immunogen's US patent 8337856 (IPR2014-00676), which both protect Kadcyla.

Further, Phigenix has sued Genentech on Jan 31, 2014 for patent infringement of their own US patent 8080534 in the Georgia Northern District Court (1:14-cv-00287).

The infringement action is ongoing, while the first IPR was not instituted (Dec 9, 2014), and the second was rejected on Oct 27, 2015 because the Board was not convinced that by a preponderance of evidence the claims would have been obvious over the provided prior art.

Phigenix has also filed an opposition against Immunogen's EP counterpart of US patent No 8,337,856, EP2283867, on Feb 19, 2015. Claim 1 has essentially the following language:

> 1. Conjugate comprising Herceptin, or an antigen binding fragment thereof, and a maytansinoid, for use in treating cancer in a human patient, wherein the cancer is characterized by the overexpression of the ErbB2 receptor.

The proceedings are ongoing, the oral hearing is scheduled for Nov 17, 2016. A preliminary opinion from the Office can be expected by May 2016. Interestingly, Genentech got another EP application of the same family granted, EP2283866, with an almost identical claim scope. Claim 1 has essentially the following language:

> 1. Conjugate comprising Herceptin, or an antigen binding fragment thereof, and a maytansinoid, or a pharmaceutical formulation (…) for (…) treating a tumor (…) characterized by overexpression of ErbB2 and does not respond or responds poorly to treatment with Herceptin.

The opposition term of this patent ended November 2015, but neither Phigenix nor any other party filed an opposition.

Feedback please !

What do you think about this newsletter? Let us have your comments here.

Archive

To obtain a neat overview of the quickly changing world of Biopatents, find prior issues of the Rhineland Biopatent Gazette here.

Michalski · Huettermann & Partner are getting personal... Today: Dariush Hourfar

Dr.-Ing. Dariush Hourfar was born in Halle (Westfalen) in 1958. He studied energy and power plant technology at the University of Essen. After completing his degree in 1984, he worked at the Institute of System Research and Technological Development of the Nuclear Research Centre Jülich in the field of nuclear engineering, and completed his doctorate there in 1989. Until 2015 he was in the power industry, where he held various management positions, and was responsible for numerous national and international projects, from concept finding to realization. In the recent years, he was responsible for technology and innovation (photovoltaic, biomass, flexibility, energy storage, nuclear ...). Dariush Hourfar has authored more than 200 publications and was represented in national and international committees. In addition, he has worked at the power plant school and at Haus der Technik in Essen as a lecturer. Since January 2016 he has been working freelance for Michalski Hüttermann & Partner as a consultant.

MICHALSKI · HÜTTERMANN & PARTNER

Imprint: Michalski · Hüttermann & Partner Patent Attorneys, c/o: Dr. Ulrich Storz - email: st@mhpatent.de

Hafenspitze - Speditionstrasse 21 - 40221 Düsseldorf - Tel.: +49 (0)211 159 249 0 - Fax: +49 (0)211 159 249 20
Nymphenburger Strasse 4 - 80335 München - Tel.: +49 (0)89 208 027 274 - Fax: +49 (0)89 208 027 275