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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFIZER, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-01488
Patent 6,407,213 B1

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

POLLOCK, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Pfizer, Inc. ("Petitioner") filed a Petition for an *inter partes* review of claims 1, 2, 4, 12, 25, 29–31, 33, 42, 60, 62–67, 69, and 71–81 of U.S. Patent No. 6,407,213 B1 ("the '213 patent," Ex. 1001). Paper 1 ("Pet."). Genentech, Inc. ("Patent Owner") timely filed a Preliminary Response. Paper 6 ("Prelim. Resp."). We review the Petition, Preliminary Response, and accompanying evidence under 35 U.S.C. § 314.

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Because Petitioner has demonstrated a reasonable likelihood that at least claim 1 of the '213 patent is unpatentable, we institute an *inter partes* review of the challenged claims.

A. Related Proceedings

According to Petitioner, the '213 Patent is at issue in *Amgen Inc. v. Genentech, Inc.*, No. 2-17-cv-07349 (C.D. Cal.); *Genentech, Inc. v. Amgen Inc.*, No. 1-17-cv-01407 (D. Del.); *Genentech, Inc. v. Amgen Inc.*, No. 1-17-cv-01471 (D. Del.). Paper 16, 1.

The '213 patent was the subject of two earlier IPR proceedings filed by Mylan Pharmaceuticals Inc., IPR2016–01693 and IPR2016–01694, which we terminated on March 10, 2017, in response to the parties' Joint Motion to Terminate. *See* IPR2016–01693, Paper 24; IPR2016–01694, Paper 23.

In addition to the present case, the '213 patent is presently the subject of seven pending matters: IPR2017-01489, brought by Pfizer, Inc.; IPR2017-01373 and IPR2017-01374, brought by Celltrion, Inc.; IPR2017-

02031 and IPR2017-02032 brought by Boehringer Ingelheim Pharmaceuticals, Inc.; and IPR2017-02139 and IPR2017-02140, brought by Samsung Bioepis Co., Ltd. Paper 4, 4; Paper 16, 1.

B. The '213 Patent and Relevant Background

The '213 patent relates to "methods for the preparation and use of variant antibodies and finds application particularly in the fields of immunology and cancer diagnosis and therapy." Ex. 1001, 1:12–14.

A naturally occurring antibody (immunoglobulin) comprises two heavy chains and two light chains. *Id.* at 1:18–20. Each heavy chain has a variable domain (V_H) and a number of constant domains. *Id.* at 1:21–23. Each light chain has a variable domain (V_L) and a constant domain. *Id.* at 1:23–24.

The variable domains are involved directly in binding the antibody to the antigen. *Id.* at 1:36–38. Each variable domain "comprises four framework (FR) regions, whose sequences are somewhat conserved, connected by three hyper-variable or complementarity determining regions (CDRs)." *Id.* at 1:40–43. The constant domains are not involved directly in binding the antibody to an antigen, but are involved in various effector functions. *Id.* at 1:33–34.

Before the '213 patent, monoclonal antibodies targeting a specific antigen, obtained from animals, such as mice, had been shown to be antigenic in human clinical use. *Id.* at 1:51–53. The '213 patent recognizes efforts to construct chimeric antibodies and humanized antibodies in the prior art. *Id.* at 1:59–2:52. According to the '213 patent, chimeric antibodies are "antibodies in which an animal antigen-binding variable

domain is coupled to a human constant domain" (*id.* at 1:60–62), whereas "humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies" (*id.* at 2:32–35).

The '213 patent also acknowledges the following as known in the prior art:

1. In certain cases, in order to transfer high antigen binding affinity, it is necessary to not only substitute CDRs, but also replace one or several FR residues from rodent antibodies for the human CDRs in human frameworks. *Id.* at 2:53–61.

2. "For a given antibody[,] a small number of FR residues are anticipated to be important for antigen binding" because they either directly contact antigen or "critically affect[] the conformation of particular CDRs and thus their contribution to antigen binding." *Id.* at 2:62–3:8.

3. In a few instances, a variable domain "may contain glycosylation sites, and that this glycosylation may improve or abolish antigen binding." *Id.* at 3:9–12.

4. The function of an antibody is dependent on its three-dimensional structure, and amino acid substitutions can change the three-dimensional structure of an antibody. *Id.* at 3:40–43.

5. The antigen binding affinity of a humanized antibody can be increased by mutagenesis based upon molecular modelling. *Id.* at 3:44–46.

Despite such knowledge in the field, according to the '213 patent, at the time of its invention, humanizing an antibody with retention of high affinity for antigen and other desired biological activities was difficult to

achieve using then available procedures. *Id.* at 3:50–52. The '213 patent purportedly provides methods for rationalizing the selection of sites for substitution in preparing humanized antibodies and thereby increasing the efficiency of antibody humanization. *Id.* at 3:53–55.

C. Illustrative Claims

Among the challenged claims, claims 1, 30, 62–64, 66, 79, and 80 are independent. Claim 1 is illustrative and is reproduced below:

> 1. A humanized antibody variable domain comprising non-human Complementarity Determining Region (CDR) amino acid residues which bind an antigen incorporated into a human antibody variable domain, and further comprising a Framework Region (FR) amino acid substitution at a site selected from the group consisting of: 4L, 38L, 43L, 44L, 58L, 62L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, and 92H, utilizing the numbering system set forth in Kabat.[1]

D. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability (Pet. 6–7):

Ground	Claim(s)	Basis	Reference(s)
1	1, 2, 25, 29, 63, 66, 67, 71, 72, 75, 76, 80, and 81	§ 102	Kurrle[2]
2	1, 2, 4, 29, 62–64, 80, and 81	§ 102	Queen 1990[3]

[1] *See* Ex. 1001, 10:45–56 (indicating that the Kabat numbering scheme for antibodies "assign[s] a residue number to each amino acid in a listed sequence").
[2] Kurrle, et al., European Patent Application Publication No. 0403156, published December 19, 1990. Ex. 1071.
[3] Queen, et al., International Publication No. WO 1990/07861, published July 26, 1990. Ex. 1050.

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