UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFIZER, INC., and
SAMSUNG BIOEPIS CO., LTD.,[1]
Petitioners,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-01488
Patent 6,407,213

PETITIONERS' RESPONSES TO PATENT OWNER'S OBSERVATIONS ON CROSS-EXAMINATION OF JEFFERSON FOOTE, PH.D.[2]

[1] Samsung Bioepis Co. Ltd.'s IPR2017-02139 has been joined with this proceeding. (IPR2017-02139, Paper 42.)

[2] All emphases within are added.

Pursuant to the Joint Notice of Stipulation to Revise Schedule (Paper 53), Petitioners submit the following responses to Patent Owner's (PO's) observations on cross-examination of Jefferson Foote, Ph.D. ("Observations," Paper 64).

Responses to Foote (Ex. 2059) Observations

Response to Observation 1: Observation 1 is misleading and irrelevant. The observation is irrelevant because Petitioners and Dr. Foote do not rely on the Riechmann 1988 paper (Ex. 1069) as anticipating or rendering obvious the challenged claims of the '213 patent, but rather as forming part of the state of the art prior to that patent. Indeed, as described in Dr. Foote's opening and reply declarations, and during his first deposition, the humanized CAMPATH antibody described in Riechmann 1998 is an example of a prior art antibody in which murine CDR residues were incorporated into a human framework region including, in the case of the light chain, a human framework comprising a "consensus" sequence derived from the Kabat 1983 reference, with framework regions substitutions made back to the corresponding murine residue at several positions. Exs. 1003, ¶103; 1202, ¶¶12, 42-43, 82; 2039 (Foote Tr.) at 327:12–331:11. This reference is therefore relevant because it refutes PO's assertion that the so-called "consensus" approach described in the '213 patent was somehow novel and/or non-obvious. The fact that Riechmann *et al.* substituted framework residues at positions not listed in the '213 patent claims is also irrelevant, as Petitioners rely on other prior art

references that indisputably disclose the same criteria to identify framework residues to substitute as those in the '213 patent, and identify many of the same residues listed in the claims. *See, e.g.* Pet.1 at 11-13.

Response to Observation 2: Observation 2 is misleading and irrelevant. As Dr. Foote explains in his opening and reply declarations, Queen 1990 discloses the same criteria to identify framework residue to substitute as those in the '213 patent. *See, e.g.* Exs. 1003, ¶¶34-35; 120, 179-182, 188; 1202, ¶¶4, 6, 100-103. The fact that the specific residues positions of the claims are not substituted in the working example of Queen 1990 is irrelevant. As Dr. Foote explained in his reply declaration, and Dr. Presta confirmed at his deposition, the first step after identifying candidate positions for framework substitution based on any given criteria, including those in Queen 1990, is to determine whether the donor mouse and human acceptor sequences differ at those positions. Exs. 1202, ¶15; 1199 (Presta Tr.) at 98:25–99:5.

Response to Observation 3: Observation 3 is misleading and irrelevant, and takes Dr. Foote's testimony out of context. What Dr. Foote actually testified is that "Queen articulates principles of humanizing an antibody, Queen '90 and Queen '89. And those teachings about homology, proximity to the CDRs through sequence or through space, one using those would end up changing — well, may or may not, but very likely would end up substituting some of the claimed residues in '213. But I didn't give a specific example of how that would happen if that's what you were

asking." Ex. 2059 (Foote Tr.) at 32:22-33:9. He further clarified that he "didn't create a specific hypothetical example with sequence" and "didn't do an illustrative example the way someone might do as an example in a patent specification." *Id.* at 33:19-22. What he did do, however, in both his opening and reply declarations, is explain in detail how Queen 1989 and Queen 1990 disclose and/or render obvious the limitations of the '213 patent claims, and indeed how one skilled in the art following Queen's teachings would be led to the claimed invention of the '213 patent as a matter of course. Exs. 1003, ¶¶125-137; 155-349; 1202, ¶¶98-103, 122-181.

Response to Observation 4: Observation 4 is misleading and irrelevant. As Dr. Foote explained at his deposition, Queen 1990 presents testing showing that the binding affinity of the humanized anti-Tac antibody and its murine parent were "about the same, within a factor of three and four" and that "that could be on either side, less or more." Ex. 2059 (Foote Tr.) at 46:7-19. This testimony is consistent with the opinions in his declarations that, following prior art procedures including those in Queen 1990, one skilled in the art would expect to be able to achieve around the same binding affinity as the parent, including a moderate improvement in affinity, which would meet the "up to 3-fold more" binding affinity limitation of claim 65 of the '213 patent, which sets no lower limit. Exs. 1003, ¶¶247-251; 306-310; 1202, ¶¶176-178. That is also consistent with the testimony of PO's expert Dr. Wilson that it was known from the prior art that "using the humanization techniques

that were known prior to the '213 patent invention," a POSITA "could achieve about the same binding affinity as the parent" and that "in achieving around about the same binding affinity as the parent, that might include a little bit more or a little bit less." Ex. 1197 (Wilson Tr.) at 104:12-105:5.

Response to Observation 5: Observation 5 is misleading and irrelevant. Dr. Foote testified that "binding affinity is not a standard kind of entry when you submit a new crystal structure to the database" but that "each entry in the Protein Data Bank -- the main point of the entry is to give the [3D] coordinates, but they have subsidiary information -- including references which may give binding -- those would be literature references." Ex. 2059 (Foote Tr.) at 50:10-51:11. Moreover, PO does not identify the relevance of whether the PDB lists binding affinity to the validity issues in this IPR, including with respect to claim 65. Indeed, this observation is irrelevant because Petitioners rely on different references, Dr. Foote's expert opinion, the admissions of PO's own expert Dr. Wilson, and the admissions regarding the state of the art in the '213 patent, as showing that achieving "up to 3-fold more" binding affinity than the parent as required by claim 65 was either disclosed in, or obvious over, the prior art. *See* Pet. at 55-56; Reply at 21-23; *see also* Response to Observation 4, *supra*.

Response to Observation 6: Observation 6 is misleading and irrelevant. As Dr. Foote explained at his deposition, Kurrle discloses at least one humanized

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