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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2016-01694
Patent 6,407,213

DECLARATION OF DR. LEONARD G. PRESTA

I, Dr. Leonard G. Presta, declare as follows:

I. Background

1. I have over thirty years of experience in the biotechnology industry, focusing on antibody and protein engineering.

2. In 1976, I obtained my Bachelors of Science degrees in chemistry and biology from the University of Arizona. In 1985, I obtained my Ph.D. in biochemistry from Texas A&M University where the emphasis of my research was on x-ray crystallography and molecular modeling. My thesis was titled, "Studies of the interaction of peptide and non-peptide substrates and inhibitors with serine proteases by computer modeling, molecular mechanics calculations and X-ray crystallography."

3. After obtaining my Ph.D., I took a post-doctoral position in the group of Dr. George Rose at Hershey Medical Center, Penn State University. In that role, I continued to work on molecular modeling and focused specifically on modeling of alpha-helix start/stop signals in protein sequences.

4. In 1988, I joined Genentech as a molecular modeler in the Protein Engineering Department. My initial role was to create computer models representing proteins (whether actual or hypothetical) by using known information about the proteins' amino acid sequences and the crystal structures of related proteins.

5. [redacted] I began to apply my modeling skills and knowledge to create a human consensus sequence for an antibody, with the idea that such a consensus sequence could be used as a broadly-applicable framework to create humanized antibodies. My efforts were successful, and I, along with my co-inventor, Dr. Paul J. Carter, were awarded U.S. Patent No. 6,407,213 ("the '213 patent) in connection with that work. As described in the '213 patent, I created a human consensus sequence, and in turn used it to "humanize" the murine 4D5 antibody, which inhibits proliferation of human tumor cells overexpressing $p185^{HER2}$ found in breast cancer. Our work led to Herceptin®, as well as other therapeutics that use the humanization techniques of the '213 patent, including Perjeta®, Xolair®, Avastin®, and Lucentis®. The work is also documented in the research paper, "Humanization of the anti-p185 antibody for human cancer therapy," published in Proc. Natl. Acad. Sci., Vol. 89, pp. 4285-4289, May 1992, that I co-authored. (Ex. 2019.)

6. I continued to work at Genentech as the Director of the Antibody Technology Group until 2001. I have since held a number of positions including Distinguished Fellow at Merck/Schering-Plough Biopharma, Executive Director of Protein Engineering at Zymeworks, Inc., and consultancy positions with several biotechnology companies.

7. I am a named inventor on more than 150 U.S. patents, have published extensively, and have served on the editorial boards of scientific journals, including the Journal of Biological Chemistry, PROTEINS, and MABS.

8. My *curriculum vitae*, which has a list of my publications and presentations, is attached as **Appendix A**.

II. Overview of Invention and Documentation

9. Below, I describe my contribution to the invention of the '213 patent. In connection with that work, I (1) created and proposed a human consensus sequence for humanized antibodies; (2) determined rules for identifying framework positions in the human consensus sequence that contribute to antibody binding affinity and conformation; and (3) applied these concepts to propose amino acid sequences for humanized 4D5 antibodies. By [redacted], I had completed each of these steps and provided to Dr. Carter proposed sequences for the heavy and light chains of humanized 4D5 antibodies.

10. My work is documented in my laboratory notebooks and records, which I kept in the ordinary course of my work at Genentech. Through my employment with Genentech, I am familiar with Genentech's practices regarding the creation and maintenance of laboratory notebooks. Genentech's library provides researchers with laboratory notebooks, each of which has a unique number and is filmed when completed. As was the general practice with

researchers at Genentech, I maintained laboratory notebooks to record progress on my projects, [redacted] when I worked on developing the human consensus sequence and proposing the humanized 4D5 sequences. Although much of my work involved computer modeling, it was my general practice to record in my notebooks significant steps I took on any project. I recorded those steps in my notebook on or around the time I took those steps—whether by printing out a page from the computer or writing my analyses—and signed and dated each page with that date. As a result, the dates recorded on my laboratory notebook entries were made at or near the time they occurred.

11. Exhibit 2001 is a true and correct copy of my laboratory Notebook 10098, [redacted]. Exhibit 2002 is a true and correct copy of my laboratory Notebook 10823, [redacted]. Other than when these notebooks were filmed by the Genentech library [redacted], they remained in my possession during my employment with Genentech. When I left Genentech, I provided Genentech's records department with the original notebooks. As I describe below, the steps I took to develop a human consensus sequence and proposed humanized 4D5 sequences are documented in my notebooks.

12. In addition to these notebooks, I also kept three-ring binders with materials relating to my projects. It was my general practice to print out emails

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