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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CELLTRION, INC.,
Petitioner,

v.

GENENTECH, INC.,
Patent Owner.

Case IPR2017-01373
Patent 6,407,213

DECLARATION OF DR. PAUL J. CARTER

I, Dr. Paul J. Carter, declare as follows:

I. Background

1. I am a research scientist with over 30 years of experience working in the biotechnology field.

2. I obtained my B.A. degree in Natural Sciences in 1982 from Cambridge University, with a focus in Biochemistry. I obtained my Ph.D. in Molecular Biology in 1986 at the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge University, UK. My Ph.D. dissertation research, which I carried out in the laboratory of Dr. Gregory Winter, related to the site-directed mutagenesis of a particular enzyme, tyrosyl tRNA synthetase, from the bacteria, *Bacillus stearothermophilus*.

3. I first joined Genentech as a Postdoctoral Fellow in 1986 researching protein engineering. In the spring of 1989, I started my own laboratory as a Scientist in the Protein Engineering Department. From 1989 to 1995, I focused on engineering antibodies for therapy and helped initiate Genentech's antibody humanization program.

4. One of the early projects in my laboratory at Genentech was to humanize an antibody. Dr. Leonard Presta and I collaborated on this project, and the specific methodology we used to perform this work involved the creation of widely-applicable human consensus sequences. We successfully created human

consensus sequences and humanized the murine 4D5 antibody, which was known to inhibit proliferation of human tumor cells overexpressing $p185^{HER2}$ found in certain breast cancers. For this work, Dr. Presta and I were awarded U.S. Patent No. 6,407,213 ("the '213 patent). This work also resulted in Herceptin® and other humanized antibodies that use the techniques of the '213 patent, such as Perjeta®, Xolair®, Avastin®, and Lucentis®. In addition to the '213 patent, this work is also described 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, which I co-authored. (Ex. 2020.)

5. In 1995, I was promoted to Senior Scientist in Molecular Oncology, and from 1995 to 2000, I led teams that focused on developing antibodies for treating cancer.

6. From 2000 to 2010, I held antibody research positions at several other biotechnology companies. For example, from 2000 to 2002, I was the Director of Protein Engineering at Immunex, Inc. in Seattle, Washington, where I helped develop and implement strategy to establish human antibody therapeutics as a major part of the drug pipeline. From 2002 to 2003, I was Associate Director then Director of Research of Antibody Technologies at Amgen, Inc., in Seattle, Washington. From 2003 to 2008, I was at Seattle Genetics, Inc., first as Senior Director of Antibody Technologies, and then as Vice President of Antibody

Technologies. And from 2008 to 2009, I was Chief Scientific Officer and Senior Vice President of Research and Development at VLST, Inc.

7. In 2010, I rejoined Genentech as a Staff Scientist and Senior Director of Antibody Engineering. Since then, I have led my department's research focusing on developing antibody therapeutics.

8. I have published over 100 scientific articles, with over 14,800 total citations. I am a listed inventor on 43 issued United States patents and 48 published United States applications, including several related to humanized antibodies. I have co-organized 13 international conferences on protein or antibody engineering and therapeutics, and delivered over 100 conference presentations and invited lectures, including keynote presentations. In 2006, I was short-listed by the journal *Nature Biotechnology* as a nominee for the most significant contributor to biopharmaceuticals in the past decade. In 2013, I was named as the second-most influential person in the antibody field by *Terrapinn*.

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

II. Overview of Invention and Documentation

10. Below, I describe my contribution to the invention of the '213 patent. In the course of that work, I: (1) proposed, with Dr. Presta, the concept of creating and using widely-applicable human consensus sequences to humanize an antibody;

(2) created the actual DNA sequences encoding for several different versions of heavy and light chain variable regions of a humanized 4D5 antibody; (3) created plasmids and vectors containing these DNA sequences; (4) expressed the DNA sequences that correlate to the sample referred to in the '213 patent as huMAb4D5-5 in *E. coli* to create fragment antigen-binding, or "Fabs," and full length IgG1 antibodies; (5) demonstrated that both the Fab and full-length antibody of huMAb4D5-5 showed binding specificity and affinity to HER2; and (6) supervised and directed others to create different versions of humanized 4D5 antibodies (also described in the '213 patent) and to perform comparative binding analyses. By [redacted], I had expressed the Fab of huMAb4D5-5 and established its binding specificity and affinity to HER2. By [redacted], I had expressed the full-length antibody of huMAb4D5-5 and confirmed that it bound to HER2 with specificity and high affinity. By [redacted], others at my direction produced and determined binding affinity for other variants of humanized 4D5 antibodies labeled huMAb4D5-3 to huMAb4D5-8 in the '213 patent.

11. My work is documented in my laboratory notebooks and records. I am familiar with Genentech's practices regarding the creation and maintenance of laboratory notebooks. Genentech's library provides Genentech scientists with laboratory notebooks, each of which is given a unique number and filmed when completed. As was the general practice with all scientists at Genentech, I

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