1. My name is ~~Dr. Eduardo A. Padlan~~Lutz Riechmann, Ph.D. Counsel for ~~Mylan Pharmaceuticals~~Celltrion Inc. ("~~Mylan~~Celltrion") retained me to provide my ~~opinion~~opinions regarding U.S. Patent No. 6,407,213 (the "'213 patent) [Ex. 1001], which is assigned to Genentech, Inc. I understand that ~~Mylan~~Celltrion intends to file a petition for inter partes review of the "'213 patent, and will request that the United States Patent and Trademark Office cancel certain claims of the "'213 patent as unpatentable in the petition. My opinions in this expert declaration supports ~~Mylan's~~Celltrion's request for inter partes review of the "'213 patent, and cancellation of the claims.

I. QUALIFICATIONS AND BACKGROUND

A. Education and Experience

2. I received my Ph.D. in Biology at the University of Bremen in Germany in 1986, and subsequently worked as a postdoctoral fellow in Sir Gregory Winter's laboratory at the Medical Research Council Laboratory of Molecular Biology (MRC-LMB) in Cambridge in the United Kingdom from 1986—1988. During this time the principle ideas of antibody humanization were conceived and put into practice in the Winter group, where I myself extended these ideas from antibodies against model antigens onto a therapeutic antibody against human lymphocyte surface antigen CD52. For me this was the first time I experienced recombinant DNA technology and I was keen to learn and practice all aspects of antibody engineering including cloning of the rodent antibody genes, their transformation into the genes for their humanized counterparts using site-directed mutagenesis, the transfer of those genes into and expression in eukaryotic cells as well as the purification and analysis of the expressed antibodies. I furthermore learned the computer graphic analysis of antibody structures, which I applied to design changes to my initially poorly binding humanized antibody into an improved version, which was then immediately used to treat

two patients at the adjacent Cambridge University Hospital. My project was helped by the cutting edge research undertaken at the MRC-LMB, which combined the groups of Drs. Michael Neuberger and Cesar Milstein with their experience in monoclonal and recombinant antibody technology, the groups of Chothia and Lesk providing their insight into antibody variable domain structure with the equally world leading research in site-directed mutagenesis and protein engineering undertaken by the Winter group. To this, the closeness of the Department of Pathology added the experience with the rodent antibody that I humanized and enabled both the fast characterization and then the immediate clinical use of the humanized antibody to help patients. More generally the MRC-LMB is a world-class research laboratory and one of the birthplaces of modern molecular biology. Many techniques have been pioneered at the laboratory, including DNA sequencing, methods for determining the three-dimensional structure of proteins and the development of monoclonal antibodies.

3. In 1988 I received a Leukemia Society fellowship for a research position to work until late 1989 with Professor Richard Lerner at the Scripps Research Institute in La Jolla, California, where I helped with the cloning of total antibody repertoire gene libraries from spleen cells after immunization. I also started the heteronuclear, multidimensional Nuclear Magnetic Resonance (NMR) analysis of antibody fragments within the group of Professor Peter Wright at the Scripps Institute. I moved back to Cambridge as a Group Leader at the MRC-LMB facility from 1989-1997, where I expanded my NMR studies of human antibody variable domain structures and their interaction with antigen and Protein A, a bacterial super-antigen frequently used to purify antibodies. I also made antigen specific single domain human antibody fragments from designed antibody heavy chain variable domain libraries using phage display and characterized their binding and folding properties with various biophysical methods. Together with Dr. Phil Holliger

I furthermore elucidated the mechanism, with which bacteriophage (as used for phage display experiments) infect bacteria - a vital step both for the natural life cycle of the bacteriophage and for in vitro phage selection experiments with displayed proteins and peptides, and determined its structural basis by both NMR and X-Ray crystallography.

4. Between 1997-2008 I acted as Senior Scientific Officer with Sir Gregory Winter at the MRC-LMB, during which time I, as my personal project, made proteins with novel folds from randomly rearranged gene fragments using proteolytic phage selection and analyzed their structures in the context of early protein evolution. I also acted as a guide for postdocs and Ph.D. students in the Winter group to help with various antibody projects. From 2008-2009 I was Director of Display Technology at F-star in Cambridge, where I set up and led a laboratory for the design and selection of antibodies with an additional antigen binding site in their constant domain, and was then re-appointed Senior Scientific Officer with Sir Gregory Winter at the MRC-LMB from 2009-2011.

5. Since 2011, I have been a consultant in the antibody engineering field for a variety of industries and legal entities.

6. My research interests include antibody and protein engineering, phage display and selection of proteins and peptides, protein evolution and folding as well as the structural analysis of proteins by Nuclear Magnetic Resonance spectroscopy.

7. I have published extensively in the field of antibody and protein engineering with over 40 publications and patents covering 25 years.

8. A full description of my background and qualifications can be found in my curriculum vitae. Ex. 1003A.

2. I completed my undergraduate studies in 1960 at the University of the Philippines, majoring in Physics. I obtained my Ph.D in Biophysics from Johns Hopkins University in 1968, working on X-ray crystallography of the hemoglobin protein from Glycera dibranchiata, a marine annelid worm, in the laboratory of Dr. Warner E. Love. I continued to work at Johns Hopkins University, first as a Research Associate from 1969 to 1971, then again as a Research Scientist from 1978 to 1983. I subsequently completed an M.S. in Computer Science at Johns Hopkins University in 1984.

3. I was also a scientist at the Laboratory of Molecular Biology, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (NIH) from 1971-1978, as a Visiting Associate and then a Visiting Scientist, where I first started working on antibodies in the laboratory of Dr. David R. Davies. I returned to the NIH in 1983, working as an Expert from 1983 to 1987, as a Visiting Scientist from 1987-1997, and then as a Research Physicist from 1997-2000. I received tenure-track status at the NIH in 1987, continuing my work on antibody structure and function. I retired from the NIH in 2000.

4. I have been an Adjunct and Visiting Professor for various academic institutions in the United States and the Philippines, teaching structural biology and protein engineering. From 1960-63, and again from 1968-1969, I was on the Faculty at the Department of Physics, College of Arts and Sciences, University of the Philippines, Diliman. I was on the Faculty for the Foundation for Advanced Education in the Sciences, NIH from 1984-1997. In 1992, I also served as an Adjunct Professor, Department of Biochemistry and Molecular Biology, Medical University of South Carolina. I served in various positions from 1998 to 2013, including as a Visiting Professor, College of Science, University of the Philippines (1998-2002), Affiliate Professor, School of Science and Engineering, Ateneo de Manila University (2000-2002),

Visiting Professor, Graduate School, University of Santo Tomas (2003) and as Adjunct Professor, Institute of Chemistry, College of Arts and Sciences, University of the Philippines, Los Banos (2002-2005). From 2002 to 2013, I was an Adjunct Professor at the Marine Science Institute, College of Science at the University of the Philippines, Diliman.

5. I have served as an editor or co-editor of several research journals, including ImmunoMethods (vol. 1, no. 2 (1992)), Protein Engineering Section, Current Opinion in Biotechnology (vol. 8 (1997)), Selected Essays on Science and Technology for Securing a Better Philippines (vol. 1 (2008)), and Philippine Science Letters (2008-2014). I served as a member on Advisory and Editorial Boards of Molecular Immunology (1980-1999), Macromolecular Structures (1993-1997) and Receptor (1990-1996). I have been a guest lecturer at many academic institutions both in the United States and in the Philippines throughout my career.

6. I have also worked as a consultant since 1989 (i.e., before my retirement from the NIH) up to the present. As a consultant, I helped to design humanized antibodies for various biotechnology companies, including Merck Sharpe and Dohme, Biogen Inc., MedImmune Inc., T Cell Sciences Inc., IDEC Pharmaceuticals Corp., SmithKline Beecham, Medarex Inc., Tanox Biosystems, System Research Inc., Biogen Idec, BioMedicas, Inc., NeoGenix Oncology, Inc., PharMab Inc., A&G Pharmaceutical Inc., Synthetic Biologics Inc., Bio-Technology General, Ltd. (Israel) and Tanabe Research Laboratories.

7. I was and currently am a member in several Professional and Academic Societies, including National Academy of Science and Technology, Philippines, Philippine-American Academy of Science and Engineering, Phi Kappa Phi, International Honor Society, Sigma Pi Sigma Physics Honor Society, Phi Sigma Biological Honor Society, American Crystallographic Association, American Society for Biochemistry and Molecular Biology, American Association

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