UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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SAMSUNG BIOEPIS CO., LTD.

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.

Patent Owner.

Patent No. 11,253,572

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Inter Partes Review No. IPR2023-00884

DECLARATION OF GEORGE YANCOPOULOS, M.D., PH.D.

I, George Yancopoulos, M.D., Ph.D., declare as follows:

I. BACKGROUND

1. I have personal knowledge of the facts contained in this Declaration, and if called upon to do so, I could and would testify competently thereto.

2. I am the sole inventor on U.S. Patent No. 11,253,572 ("the '572 patent"). Ex.1001.

3. I was raised in New York City and attended its public schools, eventually being accepted to The Bronx High School of Science, where I graduated as valedictorian. I received my Bachelor of Arts degree in Biochemistry from Columbia College, where I also graduated as valedictorian. I received my M.D. from Columbia University's College of Physicians and Surgeons, and I received my Ph.D. in Biochemistry and Molecular Biophysics from Columbia University's Graduate School of Arts and Sciences. In 1989, I became the Co-Founder and founding scientist of Regeneron Pharmaceuticals, where I currently serve as President, Chief Scientific Officer, and Board Co-Chair of Regeneron.

4. Over the course of my career, I have received numerous honors and awards, including the Prix Galien USA Best Biotechnology Product in 2022, the Prix Galien Roy Vagelos Pro Bono Humanum Award in 2021, Fortune's World's 25 Greatest Leaders: Heroes of the Pandemic in 2020, Forbes America's 100 Most Innovative Leaders in 2019, the Legends in Leadership Award, Yale School of

Management, CEO Institute in 2017, and the Ernst & Young Life Sciences Entrepreneurs of the Year National Award in 2016. During the 1990's, I was among the ten most highly cited scientists in the world.

5. In addition to the '572 patent, I am also named as an inventor of more than 100 patents. I am the principal inventor of the aflibercept composition of matter and several other important medicines, such as the world's leading medicine for allergic diseases (DUPIXENT®) and the first antibody cocktail treatment for COVID (REGN-COV®) for which Regeneron received the U.S. Patent and Trademark Office Patents for Humanity Award in 2020.

6. I have personal knowledge of Exhibits 2005-2007, 2009-2011, 2015, 2017-2020, 2024, 2035, 2039-2045, and 2069-2075 cited in this declaration, which are true and correct copies or excerpts of documents I received, sent, or reviewed. They also are business records created during the ordinary course of Regeneron's business operations and documenting various activities and product development, as is and was our practice at Regeneron.

II. DEVELOPMENT TIMELINE OF EYLEA®

7. Aflibercept is a fusion protein, which I designed and led the clinical development of, that inhibits vascular endothelial growth factor. Aflibercept is the active ingredient in Regeneron's EYLEA® product, which is FDA-approved for the treatment of various angiogenic eye disorders. During clinical trials,

Regeneron used the name "VEGF Trap-Eye" for the drug later known as EYLEA® (aflibercept). I also use that terminology in this Declaration, and any reference to VEGF Trap-Eye below should be understood to refer to aflibercept.

8. Prior to FDA approval of EYLEA®, Regeneron conducted clinical trials to test the safety and efficacy of VEGF Trap-Eye for, among other indications, neovascular age-related macular degeneration ("wet AMD" or "AMD") and diabetic macular edema ("DME"). As I noted above, I led the scientific and clinical development of VEGF Trap-Eye, including overseeing the clinical trial programs directed to AMD and DME, key portions of which are briefly summarized below.

A. Phase I AMD Clinical Trial – CLEAR-IT-1

9. Regeneron conducted a Phase I clinical trial called CLEAR-IT-1 to test the safety and tolerability of VEGF Trap-Eye in patients with AMD. Ex.1027. In CLEAR-IT-1, a single intravitreal injection of 0.05, 0.15, 0.5, 1, 2, or 4 mg of VEGF Trap-Eye was administered to 21 subjects with AMD. Ex.1027. The CLEAR-IT-1 study detected improvements in both retinal and visual acuity in patients with AMD following a single intravitreal injection of VEGF Trap-Eye. In May 2006, Regeneron issued a press release announcing positive preliminary results at a population level. Ex.1027.

B. Phase I DME Clinical Trial – CLEAR-IT-DME

10. In April 2006, Regeneron began its Phase I clinical trial, CLEAR-IT-DME, to test the safety and tolerability of VEGF Trap-Eye in 5 subjects suffering from DME. Ex.2012, 4. As shown in Exhibit 2012, which is a printout from ClinicalTrials.gov summarizing the CLEAR-IT-DME protocol, each subject in the study received a single 4 mg intravitreal injection of VEGF Trap-Eye. Ex.2012. The single injection resulted in an increase in best corrected visual acuity (BCVA) of 6 to 10 letters for 4 of the subjects. Ex.1030. The study also observed regression in BCVA at 6 weeks. Ex.1009, 3.

C. Phase II AMD Clinical Trial – CLEAR-IT-2

11. On May 1, 2006, Regeneron also announced the start of a Phase II clinical trial. Ex.1027. The Phase II trial was called CLEAR-IT-2 and tested dosing on a fixed interval followed by dosing on an as-needed ("PRN") basis in 157 subjects. Ex.1009, 4. The fixed dosing period spanned the first 12 weeks—subjects received either monthly doses of 0.5 mg or 2 mg of VEGF Trap-Eye for a total of 4 injections (initial dose and weeks 4, 8, and 12) or quarterly doses of 0.5, 2, or 4 mg of VEGF Trap-Eye for a total of 2 injections (initial dose and week 12). Ex.2004. After the fixed dosing period, the subjects were treated on an as-needed basis with the same dose they received during the fixed dosing period. Ex.1009.

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