

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO. LTD.,
Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

Patent No. 10,888,601

Inter Partes Review No. IPR2023-00739

**PATENT OWNER'S OBJECTIONS TO EVIDENCE SUBMITTED WITH
THE PETITION FOR *INTER PARTES* REVIEW**

Regeneron Pharmaceuticals, Inc. (“Regeneron” or “Patent Owner”) hereby objects to the following evidence that was submitted by Petitioner Samsung, Bioepis Co. Ltd., (“Samsung” or “Petitioner”) with the Petition (“Pet.,” Paper 1) in the above-captioned proceeding.

A. Exhibit 1002 Expert Declaration of Dr. Edward Chaum in Support of Petition for *Inter Partes* Review of Patent No. 10,888,601, dated March 24, 2023 (“Chaum Decl.”)

Patent Owner objects to Exhibit 1002 under:

- FRE 801-804. The declaration constitutes hearsay to the extent that the declarant has not yet been made available for deposition.
- FRE 402-403. The declaration, including paragraphs 92, 96, 107-108, 137, 141-145, 185-201, is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder, to the extent it includes an opinion related to disclaimed claims.
- FRE 106 and/or FRE 1006.
 - The declaration relies on excerpts of documents identified below. In fairness, the full document ought to be considered at the same time.
 - For example, Paragraphs 54, 58, 59, 62-64, and 66-68 rely on incomplete evidence or improper summary and/or improperly cherry-picking selective passages of a reference, while ignoring other passages in the same reference.

- FRE 702, 703, and 705.
 - The declaration, including Paragraphs 113, 126, 146, 152-153, 156, 179, 204, and 210, is not based on sufficient facts or data, is not the product of reliable principles and methods, have not applied the proper principles to the facts of this proceeding.

B. Exhibit 1004 Regillo CD, Brown DM, Abraham P, et al. Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER Study year 1. Am J Ophthalmol. 2008; 145(2):239-248. (“PIER Study”).

Patent Owner objects to Exhibit 1004 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

C. Exhibit 1005 Heier JS, et al., CLEAR-IT 2 Investigators. The 1-year results of CLEAR-IT 2, a phase 2 study of vascular endothelial growth factor trap-eye dosed as-needed after 12-week fixed dosing. Ophthalmology. 2011 Jun;118(6):1098-106. (“Heier 2011”)

Patent Owner objects to Exhibit 1005 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit because it is offered for the truth of its content without satisfying any of the hearsay exceptions.

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

D. Exhibit 1006 Elman MJ, et al., Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. Ophthalmology. 2010 Jun;117(6):1064-1077.e35. (“Elman 2010”)

Patent Owner objects to Exhibit 1006 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit because it is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

E. Exhibit 1007 Heier JS, et al., Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012;119(12):2537-2548. (“Heier 2012”)

Patent Owner objects to Exhibit 1007 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.

- FRE 802. The exhibit because it is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

F. Exhibit 1009 Press Release, Enrollment Completed in Regeneron and Bayer Healthcare Phase 3 Studies of VEGF Trap-Eye in Neovascular Age-Related Macular Degeneration (Wet AMD) (September 14, 2009), <https://newsroom.regeneron.com/news-releases/news-releasedetails/enrollment-completed-regeneron-and-bayer-healthcare-phase-3> (“2009 Press Release”)

Patent Owner objects to Exhibit 1009 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

G. Exhibit 1010 WO 2006/047325 A1 (“Shams”)

Patent Owner objects to Exhibit 1010 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

H. Exhibit 1014 Elman MJ, et al., Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. Ophthalmology. 2010 Jun;117(6):1064-1077.e35, published April 28 2010, available at [https://www.aaojournal.org/article/S0161-6420\(10\)00243-5/fulltext](https://www.aaojournal.org/article/S0161-6420(10)00243-5/fulltext) (“Elman AAO Website)

Patent Owner objects to Exhibit 1014 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

I. Exhibit 1015 Lucentis ® Original Approved Labeling (2006), available at:https://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/125156s000_Lucentis_Prntlbl.pdf

Patent Owner objects to Exhibit 1015 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the document. It is not clear where the exhibit came from or how it was compiled.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

**J. Exhibit 1016 Eylea Label 2023 available at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125387s0751bl.pdf)**

Patent Owner objects to Exhibit 1016 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the document.

It is not clear where the exhibit came from or how it was compiled.

- FRE 106. The document appears to start at page 4. The remainder of this document has not been introduced or filed by Petitioner, but in fairness ought to be considered at the same time as those pages that were provided.

**K. Exhibit 1017 Comparison of Age-related Macular Degeneration Treatments Trials: Lucentis-Avastin Trial (NCT00593450), available at:
<https://clinicaltrials.gov/ct2/show/NCT00593450>**

Patent Owner objects to Exhibit 1017 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

**L. Exhibit 1018 Web Archive of the CATT Patient Eligibility Criteria (July 13, 2010), available at
https://web.archive.org/web/20100713035617/http://www.med.upenn.edu/cpob/studies/documents/CATTEligibilityCriteria_000.pdf (“CATT Study”)**

Patent Owner objects to Exhibit 1018 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues

and misleading the fact finder.

- FRE 802. The exhibit because it is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

M. Exhibit 1020 History of Changes for Study: A Study of rhuFab V2 (Ranibizumab) in Subjects With Subfoveal Choroidal Neovascularization Secondary to Age-Related Macular Degeneration (AMD) (NCT00090623), available at: https://clinicaltrials.gov/ct2/history/NCT00090623?V_1=View#StudyPageTop.

Patent Owner objects to Exhibit 1020 under:

- FRE 402 and 403. The exhibit is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

N. Exhibit 1021 ClinicalTrials.gov Background, available at: <https://clinicaltrials.gov/ct2/about-site/background>

Patent Owner objects to Exhibit 1021 under:

FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

O. Exhibit 1022 ClinicalTrials.gov About the Results Database, available at: <https://clinicaltrials.gov/ct2/about-site/results>

Patent Owner objects to Exhibit 1022 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

P. Exhibit 1023 Do DV et al., Incorporating the Latest Findings From Clinical Trials Into the Management of Diabetic Retinopathy for the Comprehensive Ophthalmologist (October 25, 2009), available at: <https://aao.scientificposters.com/epsView.cfm?xvTgEJiNo9X9FYlsrbBjRKZ9ICSVGWMJbEunzn9LGZqaMHKIw4tNfg%3D%3D> (“Do workshop 2009”)

Patent Owner objects to Exhibit 1023 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

Q. Exhibit 1024 Pai A, El Shafei MM, Mohammed OA, Al Hashimi M., Current concepts in intravitreal drug therapy for diabetic retinopathy. Saudi J Ophthalmol. 2010 Oct;24(4):143-9. (“Pai 2010”).

Patent Owner objects to Exhibit 1024 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

R. Exhibit 1026 U.S. Dep’t Health & Human Servs., Nat’l Inst. Health, Nat’l Eye Inst., Diabetic Retinopathy: What You Should Know (Sept. 2015), https://www.nei.nih.gov/sites/default/files/healthpdfs/Diabetic_Retinopathy_What_You_Should_Know.pdf (“NIH DR”).

Patent Owner objects to Exhibit 1026 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit because it is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

S. Exhibit 1027 U.S. Dep’t Health & Human Servs., Nat’l Inst. Health, Nat’l Eye Inst., Age-Related Macular Degeneration: What You Should Know (Sept. 2015), https://www.nei.nih.gov/sites/default/files/healthpdfs/WYSK_AMD_English_Sept2015_PRINT.pdf (“NIH AMD”).

Patent Owner objects to Exhibit 1027 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.
- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.

T. Exhibit 1028 Halpern MT, Schmier JK, Covert D, Venkataraman K. Resource utilization and costs of age-related macular degeneration. Health Care Financ Rev. 2006;27(3):37-47. (“Halpern 2006”).

Patent Owner objects to Exhibit 1028 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.

U. Exhibit 1029 Holash J, Davis S, Papadopoulos N, et al. VEGF-Trap: a VEGF blocker with potent antitumor effects. Proc Natl Acad Sci U S A. 2002;99(17):11393-11398. (“Holash”)

Patent Owner objects to Exhibit 1029 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder. The exhibit is also irrelevant, and its probative value is substantially outweighed by the danger of

confusion of the issues and misleading the fact finder, to the extent it relates only to claims that have been disclaimed.

V. Exhibit 1030 Rudge JS, Thurston G, Davis S, et al. VEGF trap as a novel antiangiogenic treatment currently in clinical trials for cancer and eye diseases, and VelociGene- based discovery of the next generation of angiogenesis targets. Cold Spring Harb Symp Quant Biol. 2005;70:411-418 (“Rudge 2005”)

Patent Owner objects to Exhibit 1030 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder. The exhibit is also irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder, to the extent it relates only to claims that have been disclaimed.

W. Exhibit 1031 Gomez-Manzano C, Holash J, Fueyo J, et al. VEGF Trap induces antiglioma effect at different stages of disease. Neuro Oncol. 2008;10(6):940-945. (“Gomez-Manzano”)

Patent Owner objects to Exhibit 1031 under:

- FRE 402 and 403. The exhibit is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder, to the extent it relates only to claims that have been disclaimed.

X. Exhibit 1032 U.S. Patent No. 7,531,173 (“173 patent”)

Patent Owner objects to Exhibit 1032 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.

Y. Exhibit 1033 Rudge JS, Holash J, Hylton D, et al. VEGF Trap complex formation measures production rates of VEGF, providing a biomarker for predicting efficacious angiogenic blockade. Proc Natl Acad Sci U S A. 2007;104(47):18363-18370. (“Rudge 2007”)

Patent Owner objects to Exhibit 1033 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.

Z. Exhibit 1034 Li E, Donati S, Lindsley KB, Krzystolik MG, Virgili G. Treatment regimens for administration of anti-vascular endothelial growth factor agents for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2020;5(5):CD012208. (“Li 2020”)

Patent Owner objects to Exhibit 1034 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

AA. Exhibit 1035 Brown DM, Michels M, Kaiser PK, et al. Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: Two-year results of the ANCHOR study. Ophthalmology. 2009;116(1):57-65.e5. (“Brown 2009”)

Patent Owner objects to Exhibit 1035 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

BB. Exhibit 1036 Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE, et al, Comparison of Age-Related Macular Degeneration Treatments Trial (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology 2012; 119(7):1388-98 (“Martin”)

Patent Owner objects to Exhibit 1036 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

CC. Exhibit 1037 Chakravarthy U, Harding SP, Rogers CA, Downes SM, Lotery AJ, Wordsworth S, et al, Inhibition of VEGF in Age-related choroidal Neovascularization (IVAN) Study Investigators. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology 2012; 119(7):1399-411 (“Chakravarthy 2012”)

Patent Owner objects to Exhibit 1037 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

DD. Exhibit 1043 Using the Wayback Machine, available at: <https://help.archive.org/help/using-the-wayback-machine/>

Patent Owner objects to Exhibit 1043 under:

- FRE 402 and 403. The exhibit is not relevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

EE. Exhibit 1045 Do DV et al., The DA VINCI Study: phase 2 primary results of VEGF Trap-Eye in patients with diabetic macular edema. Ophthalmology. 2011 Sep;118(9):1819-26 (published online on May 5, 2011). (“Do 2011”)

Patent Owner objects to Exhibit 1045 under:

- FRE 402 and 403. The exhibit is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder, to the extent it relates only to claims that have been disclaimed.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from or how it was compiled.

FF. Exhibit 1047 Eylea Label 2011 available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125387lbl.Pdf

Patent Owner objects to Exhibit 1047 under:

- FRE 901. Petitioner has not demonstrated the authenticity of the document. It is not clear where the exhibit came from or how it was compiled.

GG. Exhibit 1049 Steps for a Safe Intravitreal Injection Technique (2009), available at: <https://www.retinalphysician.com/issues/2009/july-aug/steps-for-a-safe-intravitreal-injection-technique>

Patent Owner objects to Exhibit 1049 under:

- FRE 402 and 403. The exhibit is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from, how it was compiled, or what methods, materials, or metrics were used to arrive at the information in the document.

HH. Exhibit 1050 Eylea Label May 2016, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125387s051lbl.pdf (“Eylea 2016 Label”)

Patent Owner objects to Exhibit 1050 under:

- FRE 402 and 403. The exhibit is irrelevant, and its probative value is substantially outweighed by the danger of confusion of the issues and misleading the fact finder.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from, how it was compiled, or what methods, materials, or metrics were used to arrive at the information in the document.
- FRE 106. The document appears to start at page 4. The remainder of this document has not been introduced or filed by Petitioner, but in

fairness ought to be considered at the same time as those pages that were provided.

II. Exhibit 1054 Institution Decision in Mylan Pharmaceuticals Inc. v. Regeneron Pharmaceuticals, Inc., IPR2022-01225 (Paper 21) (“’681 ID”)

Patent Owner objects to Exhibit 1054 under:

- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.

JJ.Exhibit 1055 Do DV et al., The DA VINCI Study: phase 2 primary results of VEGF Trap-Eye in patients with diabetic macular edema. Ophthalmology. 2011 Sep;118(9):1819-26, available at: [https://www.aaojournal.org/article/S0161-6420\(11\)00177-1/fulltext](https://www.aaojournal.org/article/S0161-6420(11)00177-1/fulltext) (“Do 2011 AAO Website”)

Patent Owner objects to Exhibit 1055 under:

- FRE 802. The exhibit is offered for the truth of its content without satisfying any of the hearsay exceptions.
- FRE 901. Petitioner has not demonstrated the authenticity of the exhibit. It is not clear where the exhibit came from, how it was compiled, or what methods, materials, or metrics were used to arrive at the information in the document.

To the extent the exhibits are admitted, their scope should be restricted to the purpose for which they were originally submitted. FRE 105. Should Samsung rely on an exhibit for a different purpose than the one for which it has been offered,

Regeneron reserves the right to make additional objections.

In accordance with 37 C.F.R. § 42.64(b)(1), these objections are being timely filed and served within ten (10) business days of the institution of the trial by the Patent and Trial Appeal Board (“Board”), which is reflected in the Board’s Institution Decision dated October 20, 2023 (Paper 9).

Dated: November 3, 2023

Respectfully submitted,

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Certificate of Service (37 C.F.R. § 42.6(e)(4))

I hereby certify that the attached PATENT OWNER'S OBJECTIONS TO EVIDENCE SUBMITTED WITH THE PETITION FOR *INTER PARTES* REVIEW was served as of the below date via email on the Petitioner at the following correspondence address:

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Dated: November 3, 2023

By: /Adam R. Brausa/
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