

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GENE COMPANY PTY LTD,
Petitioner,

v.

THE TRUSTEES OF COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK,

Patent Owner.

Case No. IPR2024-00313
U.S. Patent No. RE47,045

PATENT OWNER'S UPDATED EXHIBIT LIST

Pursuant to 37 C.F.R. § 42.63(e), Patent Owner The Trustees of Columbia University in the City of New York hereby submits a current listing of Patent Owner exhibits. Exhibits 2048-2050, 2203, and 2210 are being filed today.

Exhibit	Description	Served Not Filed
2001	Guangwen Tang et al., <i>Deuterium enrichment of retinol in humans determined by gas chromatography electron capture negative chemical ionization mass spectrometry</i> , 9 J. Nutr. Biochem. 408-14 (1998)	
2002	J.A. Pardoen et al., <i>Synthesis of retinals isotopically labelled at positions 11, 12, 14 and 20</i> , 105 Recl. Trav. Chim. Pays-Bas 92-98 (1986)	
2003	Gabriel H. Travis et al., <i>Diseases Caused by Defects in the Visual Cycle: Retinoids as Potential Therapeutic Agents</i> , published in final edited form in 47 Annu Rev Pharmacol Toxicol 469-512 (2007)	
2004	WO 2005/065669 A1 (Lang)	
2005	U.S. Patent Application Pub. No. 2007/0015827 A1 (Widder 2007)	
2006	Yardana Kaufman et al., <i>Deuterium Enrichment of Vitamin A at the C20 Position Slows the Formation of Detrimental Vitamin A Dimers in Wild-type Rodents</i> , 286 J. of Biological Chem. 7958-65 (2011)	
2007	Allan B. Foster, <i>Deuterium Isotope Effects in the Metabolism of Drugs and Xenobiotics: Implications for Drug Design</i> , 14 Advances in Drug Research 1-40 (1985)	

Exhibit	Description	Served Not Filed
2008	Declaration of F. Peter Guengerich Ph.D. in Support of Petition for <i>Inter Partes</i> Review of Claims 1-15 of U.S. Patent No. 9,249,149, <i>Incyte Corp. v. Concert Pharmaceuticals, Inc.</i> , IPR2017-01256, Ex. 1002 (PTAB Apr. 7, 2017)	
2009	Videotaped Deposition of F. Peter Guengerich, Ph.D., <i>Incyte Corp. v. Concert Pharmaceuticals, Inc.</i> , IPR2017-01256, Ex. 2047 (PTAB Jun. 23, 2018)	
2010	Videoconference Deposition of Peter Guengerich, Ph.D., <i>Alzheon, Inc. v. Risen (Suzhou) Pharma Tech Co., Ltd.</i> , IPR2021-00347, Ex. 2041 (PTAB Sept. 28, 2021)	
2011	U.S. Patent Application Pub. No. 2006/0135460 A1 (Widder 2006)	
2012	U.S. Patent No. 7,973,079 (Mata 2011)	
2013	U.S. Patent Application Pub. No. 2012/0202885 A1 (Widder 2012)	
2014	Di Huang et al., <i>Stargardt disease and progress in therapeutic strategies</i> , 43(1) Ophthalmic Genetics 1-26 (2022)	
2015	Rehan M. Hussain et al., <i>Stargardt macular dystrophy and evolving therapies, published in final edited form in</i> 18(10) Expert Opinion on Biological Therapy 1049-59 (2018)	
2016	Jana Zernant, <i>ABCA4 as a Model for Complex Genetics in Monogenic Diseases</i> , Tallinn University of Technology Doctoral Thesis (2019)	
2017	Thomas A. Ciulla, <i>Seeking Therapies for Stargardt Macular Dystrophy: Clinical research teams are working toward a treatment for Stargardt disease. How far have they come?</i> , Retina Today 26-30 (July/August 2019)	

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2018	Robert Thornton Morrison & Robert Neilson Boyd, <i>Organic Chemistry</i> 858-59 (3d ed. 1973)	
2019	So R. Kim et al., <i>Characterization of dihydro-A2PE: an Intermediate in the A2E Biosynthetic Pathway, published in final edited form in</i> 46(35) <i>Biochemistry</i> 10122-29 (2007)	
2020	Nicolas J. Saettel & Olaf Wiest, <i>Ab Initio Studies of [1,5]-H Shifts: Pentadiene and Beyond</i> , 65(8) <i>J. Org. Chem.</i> 2331-36 (2000)	
2021	Kersey A. Black et al., <i>Alkynes, Allenes, and Alkenes in [3,3]-Sigmatropy: Functional Diversity and Kinetic Monotony. A Theoretical Analysis</i> , 120 <i>J. Am. Chem. Soc.</i> 5622-27 (1998)	
2022	Kenneth A. Connors, <i>Chemical Kinetics: The Study of Reaction Rates in Solution</i> , 1-15, 187-243 (1990)	
2023	Omitted	
2024	Rory A. More O’Ferrall, <i>Substrate Isotope Effects, Proton-Transfer Reactions</i> 201-61 (Edward Caldin & Victor Gold eds., 1975)	
2025	William von E. Doering & Xin Zhao, <i>Effect on Kinetics by Deuterium in the 1,5-Hydrogen Shift of a Cisoid-Locked 1,3(Z)-Pentadiene, 2-Methyl-10-methylenebicyclo[4.4.0]dec-1-ene: Evidence for Tunneling?</i> , 128 <i>J. Am. Chem. Soc.</i> 9080-85 (2006)	
2026	National Institutes of Health Office of Dietary Supplements, Vitamin D Fact Sheet for Health Professionals, https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/ (Updated Sept. 18, 2023)	
2027	Charles DeBoer et al., <i>Oral Drug Pipeline for Retinal Disease</i> , 19 <i>Retinal Physician</i> 27-28, 20, 32 (July 1, 2022)	

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2028	Griffith News, <i>Griffith University and Gene Company partner to create exciting RNA-based COVID anti-viral</i> , https://news.griffith.edu.au/2023/07/26/griffith-university-and-gene-company-partner-to-create-exciting-rna-based-covid-anti-viral/ (July 26, 2023)	
2029	Tawain News, <i>Queensland treasurer visits Taiwan to further trade, business, education, cultural links</i> , https://www.taiwannews.com.tw/news/4979623 (Aug. 24, 2023)	
2030	John-Paul Langbroek, <i>Report to Queensland Parliament On a Queensland Parliamentary Delegation to Republic of China (Taiwan)</i> (Apr. 26-May 1, 2023) (Parliament Report 2)	
2031	Cameron Dick, <i>Report to Parliament: Indonesia and Taiwan Trade and Investment Mission</i> (Aug. 9-16, 2023)(Parliament Report)	
2032	U.S. Securities and Exchange Commission Amendment No. 2 to Form F-1 for Belite Bio, Inc. (Apr. 22, 2022)	
2033	Michael B. Smith & Jerry March, <i>March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure</i> 98-105 (6th ed. 2007)	
2034	Jerry Huang LinkedIn Page, www.linkedin.com/in/jerry-huang-60a98051	
2035	Wilson Sonsini Press Release, <i>Firm Advises Belite Bio on IP Matters Related to \$36 million IPO</i> , https://www.wsgr.com/en/insights/firm-advises-belite-bio-on-ip-matters-related-to-dollar36-million-ipo.html (May 3, 2022)	
2036	Declaration of Jonathan L. Sessler Ph.D.	
2037	Curriculum Vita of Jonathan L. Sessler Ph.D.	

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2038	Eric V. Anslyn & Dennis A. Dougherty, <i>Modern Physical Organic Chemistry</i> 421-41 (2006)	
2039	Gene Company Pty Ltd LinkedIn Post	
2040	So R. Kim et al., <i>Characterization of Dihydro-A2PE: An Intermediate in the A2E Biosynthetic Pathway</i> , ACS Publications, https://pubs.acs.org/doi/10.1021/bi7009635 (last visited July 18, 2024)	X
2041	Log in with your ACS ID, ACS Publications, https://pubs.acs.org/action/addToCart?id=PPVJOURNALSE-ELECTRONIC-USD-10.1021%2FBI7009635-137903 (last visited July 18, 2024)	X
2042	Order form, ACS Publications, https://pubs.acs.org/action/addToCart?id=PPVJOURNALSE-ELECTRONIC-USD-10.1021%2FBI7009635-137903 (last visited July 18, 2024)	X
2043	ACS Publications purchase confirmation email, dated July 18, 2024	X
2044	So R. Kim et al., <i>Characterization of Dihydro-A2PE: An Intermediate in the A2E Biosynthetic Pathway</i> , 46(35) <i>Biochemistry</i> 10122-29 (2007)	X
2045	Michael B. Smith & Jerry March, <i>March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure</i> (6th ed. 2007)	X
2046	Omitted	
2047	Eric V. Anslyn & Dennis A. Dougherty, <i>Modern Physical Organic Chemistry</i> 421-88 (2006)	

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2048	Rehan M. Hussain et al., <i>Stargardt macular dystrophy and evolving therapies, published in final edited form in 18(10) Expert Opinion on Biological Therapy 1049-59 (2018)</i> , ScholarWorks, https://scholarworks.indianapolis.iu.edu/items/e4bfc377-999d-4940-bf07-ddf429b33b38 (last visited July 17, 2024)	
2049	Rehan M. Hussain et al., <i>Stargardt macular dystrophy and evolving therapies, published in final edited form in 18(10) Expert Opinion on Biological Therapy 1049-59 (2018)</i>	
2050	Declaration of Shauna L. Wiest	
2051	Shimon Ben-Shabat et al., <i>Biosynthetic Studies of A2E, a Major Fluorophore of Retinal Pigment Epithelial Lipofuscin</i> , 277(9) J. Biological Chem. 7183-90 (2002)	
2052	Declaration of Dr. Glenn Prestwich, Ph.D.	
2053	Curriculum Vitae of Dr. Glenn Prestwich , Ph.D.	
2054	F. Peter Guengerich, <i>Metals in Biology 2016: Molecular Basis of Selection of Metals by Enzymes</i> , 291(40) J. Biological Chem. 20838-39 (2016)	
2055	Omitted	
2056	Email dated September 21, 2010 from F. Guengerich to Ilyas Washington regarding JBC/2010/178640 – Manuscript Decision	
2057	Email dated September 24, 2010 from F. Guengerich to Ilyas Washington regarding JBC/2010/178657 – Manuscript Decision	

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2058	So Ra Kim et al., <i>Rpe65 Leu450Met variant is associated with reduced levels of the retinal pigment epithelium lipofuscin fluorophores A2E and iso-A2E</i> , 101(32) PNAS 11668-72 (2004)	
2059	Robert R. Rando, <i>The Biochemistry of the Visual Cycle</i> , 101 Chem. Rev. 1881-96 (2001)	
2060	John C. Saari et al., <i>Reduction of all-trans-retinal limits regeneration of visual pigment in mice</i> , 38 Vision Research 1325-33 (1998)	
2061	Li Ma et al. <i>C20-D₃-vitamin A Slows Lipofuscin Accumulation and Electrophysiological Retinal Degeneration in a Mouse Model of Stargardt Disease</i> , 286(10) J. Biological Chem. 7966-74 (2011)	
2062	Małgorzata Rózanowska & Tadeusz Sarna, <i>Light-induced Damage to the Retina: Role of Rhodopsin Chromophore Revisited</i> , 81 Photochemistry and Photobiology 1305-30 (2005)	
2063	Deviprasad R. Gollapalli & Robert R. Rando, <i>The specific binding of retinoic acid to RPE65 and approaches to the treatment of macular degeneration</i> , 101(27) PNAS 10030-35 (2004)	
2064	Akiko Maeda et al., <i>Effects of Potent Inhibitors of the Retinoid Cycle on Visual Function and Photoreceptor Protection from Light Damage in Mice</i> , 70(4) Molecular Pharmacology 1220-29 (2006)	
2065	Omitted	
2066	Pranab Maiti et al., <i>Small Molecule RPE65 Antagonists Limit the Visual Cycle and Prevent Lipofuscin Formation</i> , 45 Biochem. 852-860 (2006)	

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2067	Omitted	
2068	E.F. Greene & A. Kuppermann, <i>Chemical Reaction Cross Sections and Rate Constants</i> , 45(6) J. Chem. Educ. 361-69 (1968)	
2069	Shimon Ben-Shabat et al., <i>Fluorescent Pigments of the Retinal Pigment epithelium and Age-Related Macular Degeneration</i> , 11 Bioorganic & Med. Chem. Letters 1533-40 (2001)	
2070	Gabriel H. Travis et al., <i>Diseases Caused by Defects in the Visual Cycle: Retinoids as Potential Therapeutic Agents</i> , published in final edited form in 47 Annu Rev Pharmacol Toxicol 469-512 (2007)	
2071	Document from web page titled <i>Andrew F. Calman, M.D., Ph.D. Contact this Expert Witness</i>	
2072	Oxford Dictionary of Biochemistry and Molecular Biology Revised Edition (2006)	
2073	Laura E. Lamb & John D. Simon, <i>A2E: A Component of Ocular Lipofuscin</i> , 79(2) Photochemistry and Photobiology 127-36 (2004)	
2074	Amir Rattner & Jeremy Nathans, <i>Macular degeneration: recent advances and therapeutic opportunities</i> , 7 Nature Reviews 860-72 (2006)	
2075	Tracey Pirali et al., <i>Applications of Deuterium in Medicinal Chemistry</i> , 62 J. Med. Chem. 5276-97 (2019)	

Exhibit	Description	Served Not Filed
2076	Michael B. Fisher et al., <i>The complexities inherent in attempts to decrease drug clearance by blocking sites of CYP-mediated metabolism</i> , 9(1) Current Op. in Drug Discovery & Dev. 101-09 (2006)	
2077	Patrick C. Mowery & Walther Stoeckenius, <i>Mechanistic Aspects of the Thermal Equilibration of Retinylidene Imines and Immonium Salts</i> , 101(2) J. Am Chem. Soc. 414-17 (1979)	
2078	Peter J. E. Verdegem et al., <i>Condensation of All-E-Retinal</i> , 38(30) Tetrahedron Letters 5355-58 (1997)	
2079	Naomi Sakai et al, <i>Ocular Age Pigment "A2-E": An Unprecedented Pyridinium Bisretinoid</i> , 118 J. Am. Chem. Soc. 1559-60 (1996)	
2080	Dean Bok, <i>The retinal pigment epithelium: a versatile partner in vision</i> , Supp. 17 J. Cell Sci. 189-95 (1993)	
2081	Omitted	
2082	Jian Weng et al., <i>Insights into the Function of Rim Protein in Photoreceptors and Etiology of Stargardt's Disease from the Phenotype in abcr Knockout Mice</i> , 98 Cell 13-23 (1999)	
2083	Joel A. Krauser & F. Peter Guengerich, <i>Cytochrome P450 3A4-catalyzed Testosterone 6β-Hydroxylation Stereochemistry, Kinetic Deuterium Isotope Effects, and Rate-limiting Steps</i> , 280(20) J. Biological Chem. 19496-506 (2005)	
2084	F.H. Westheimer, <i>The Magnitude Of The Primary Kinetic Isotope Effect For Compounds Of Hydrogen And Deuterium</i> , 61(3) Chem. Reviews 265-73 (1961)	

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2085	Sidney D. Nelson & William F. Trager, <i>The Use Of Deuterium Isotope Effects To Probe The Active Site Properties, Mechanism Of Cytochrome P450-Catalyzed Reactions, And Mechanisms Of Metabolically Dependent Toxicity</i> , 31(12) Drug Metabolism and Disposition 1481-98 (2003)	
2086	Hendrik P. Scholl et al., <i>TEASE: a phase 2 clinical trial assessing the tolerability and effects of oral once-a-day ALK-001 on Stargardt disease</i> , ARVO Annual Meeting Abstract (2016)	
2087	Hendrik P. Scholl et al., <i>Stargardt disease ALK-001 phase 2 clinical trial: 12-month interim data</i> , ARVO Annual Meeting Abstract (2019)	
2088	Hendrik P. Scholl et al., <i>ALK-001 (C20-D3-Vitamin A) slows the growth of atrophic lesions in ABCA4-related Stargardt Disease: Results of a Phase 2 placebo-controlled clinical trial (TEASE study)</i> , ARVO Annual Meeting Abstract (2022)	
2089	Christine Nichols Kay et al., Abstract Id: 30069593 - <i>ALK-001 (C20-D3-Vitamin A) Slows the Growth of Atrophic Lesions in aBCA4-related Stargardt Disease: Results of a Randomized Placebo-Controlled Clinical Trial (TEASE study)</i> , Am. Academy of Ophthalmology (2002)	
2090	Hendrick P. Scholl et al., <i>Gildeuretinol Enables the Vitamin A Cycle</i> , ARVO Annual Meeting Abstract (2024)	
2091	Michael B. Gorin et al., Abstract: <i>Gildeuretinol Arrested Stargardt Disease, The TEASE-3 Study: IOVS</i> , iovs.arvojournals.org/article.aspx (2024)	
2092	Alkeus Press Release: <i>Alkeus Pharmaceuticals Announces Presentation of a TEASE-3 Study Update Showing Progression Stalled in Early-Stage Stargardt Disease Patients Treated with Gildeurentinol</i> (July 18, 2024)	

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2093	Alkeus Press Release: <i>Alkeus Pharmaceuticals Presents Positive Interim Data Showing Gildeuretinol Halted Stargardt Disease Progression</i> (January 10, 2024)	
2094	Boyer DS et al., Abstract: <i>Gildeuretinol in Geographic Atrophy: Results from SAGA, a 2-year, Randomized, Double-masked, Placebo-controlled Study</i> (2024) (CONFIDENTIAL – PROTECTIVE ORDER MATERIAL)	
2094	Boyer DS et al., Abstract: <i>Gildeuretinol in Geographic Atrophy: Results from SAGA, a 2-year, Randomized, Double-masked, Placebo-controlled Study</i> (2024)	
2095	Alkeus Press Release: <i>Alkeus Pharmaceuticals Announces Results from the SAGA Study of Oral Gildeuretinol in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration</i> (September 17, 2024)	
2096	Alkeus Press Release: <i>FDA Grants Alkeus Pharmaceuticals Breakthrough Therapy Designation for ALK-001 (C20-D3-vitamin A) for the Treatment of Stargardt Disease</i> (July 14, 2021)	
2097	Alkeus Press Release: <i>Alkeus Announces \$150 Million Series B Financing, Supporting Rapid Registration Path for gildeuretinol (ALK-001) in the Treatment of Stargardt Disease</i> (June 5, 2023)	
2098	ClinicalTrials.gov ID NCT02402660, <i>Phase 2 Tolerability and Effects of ALK-001 on Stargardt Disease (TEASE)</i> (last update posted June 21, 2024)	
2099	ClinicalTrials.gov ID NCT03845582, <i>Phase 3 Study of ALK-001 in Geographic Atrophy (SAGA)</i> (last update posted January 30, 2024)	

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2100	Rupert W. Strauss et al., <i>Progression of Stargardt Disease as Determined by Fundus Autofluorescence Over a 12-Month Period: ProgStar Report No. 11</i> , 137(10) JAMA Ophthalmol. 1134-45 (2019)	
2101	Avery E. Sears et al., <i>Towards Treatment of Stargardt Disease: Workshop Organized and Sponsored by the Foundation Fighting Blindness</i> , 6(5) TVST 1-12 (2017)	
2102	Kimberly J. Cocce et al., <i>Visual function metrics in early and intermediate dry age-related macular degeneration for use as clinical trial endpoints, published in final edited form in</i> 189 Am. J. Ophthalmol. 127-38 (2018)	
2103	Deposition Transcript of Peter Guengerich, Ph.D. (August 16, 2024)	
2104	Deposition Transcript of Andrew Calman, M.D., Ph.D. (August 27, 2024)	
2105	ClinicalTrials.gov ID NCT02230228, <i>Phase 1 Safety Study of ALK-001 in Healthy Volunteers</i> (last update posted March 24, 2015)	
2106	ClinicalTrials.gov ID NCT04239625, <i>Phase 3 Study of ALK-001 in Geographic Atrophy (SAGA)</i> , (last update posted January, 30, 2024)	
2107	FDA Breakthrough Therapy	
2108	Alkeus Website, <i>Pursuing a Rapid Path to Market</i> , http://alkeuspharma.com	
2109	Harper's Illustrated Biochemistry 60-71 (26th ed. 2003)	

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2110	Robert K. Koenekoop, <i>the gene for Stargardt disease, ABDA4, is a major retinal gene: a mini-review</i> , 24 Ophthalmic Genetics 75-80 (2003)	
2111	Kimberly A. Howes et al., <i>Dry AMD: From Theory to Treatment</i> , https://www.reviewofophthalmology.com/article/dry-amd-from-theory-to-treatment (2006)	
2112	W. Gerald Robison, Jr. et al., <i>Deficiencies of vitamins E and A in the rat: Retinal damage and lipofuscin accumulation</i> , 19(9) Invest. Ophthalmol. Vis. Sci. 1030-37 (1980)	
2113	W. Gerald Robison, Jr. et al., <i>The Roles of Vitamin E and Unsaturated Fatty Acids in the Visual Process</i> , 2(4) Retina 263-81 (1982)	
2114	Martin L. Katz et al., <i>Relationship Between Dietary Retinol And Lipofuscin In The Retinal Pigment Epithelium</i> , 35 Mechanisms of Ageing and Development 291-305 (1986)	
2115	Martin L. Katz et al., <i>Lipofuscin Autofluorescence: Evidence For Vitamin A Involvement In The Retina</i> , 39 Mechanisms of Ageing and Development 81-90 (1987)	
2116	Martin L. Katz & Michael Norberg, <i>Influence of Dietary Vitamin A on Autofluorescence of Leupeptin-induced Inclusions in the Retinal Pigment Epithelium</i> , 54 Exp. Eye Res. 239-46 (1992)	
2117	Roxana A. Radu et al., <i>Accelerated Accumulation of Lipofuscin Pigments in the RPE of a Mouse Model for ABDA4-Mediated Retinal Dystrophies following Vitamin A Supplementation</i> , 49(9) IOVS 3821-29 (2008)	

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2118	C. Owsley & G. R. Jackson, <i>Aging and scotopic dysfunction</i> , Prof. Mulder lecture; Oral presentations: Motion mechanisms 80 (2000)	
2119	Cynthia Owsley et al., <i>Delays in Rod-mediated Dark Adaptation in Early Age-related Maculopathy</i> , 108(7) Ophthalmology 1196-1202 (2001)	
2120	Wolfgang Baehr et al., <i>The retinoid cycle and retina disease</i> , 43 Vision Research 2957-58 (2003)	
2121	Konstantin H. Dragnev et al., <i>The Retinoids and Cancer Prevention Mechanisms</i> , 5 The Oncologist 361-68 (2000)	
2122	Sarah J. Freemantle, et al., <i>Retinoids in cancer therapy and chemoprevention: promise meets resistance</i> , 22 Oncogene 7305-15 (2003)	
2123	Soriatan Drug Description, The Wayback Machine, https://web.archive.org/web/20080616120730/http://www.rxlist.com:80/cgi/generic/acitretin.htm (June 16, 2008)	
2124	Targretin Drug Description, The Wayback Machine, https://web.archive.org/web/20080615214054/http://www.rxlist.com:80/cgi/generic/bexarotene.htm (June 15, 2008)	
2125	Accutane Drug Description, The Wayback Machine, https://web.archive.org/web/20080902152402/http://www.rxlist.com:80/cgi/generic/isotret.htm (September 2, 2008)	
2126	Waun Ki Hong & Loretta M. Itri, <i>Retinoids and Human Cancer</i> , The Retinoids: Biology, Chemistry, and Medicine 597-630 (2nd ed. 1994)	
2127	Lorraine J. Gudas et al., <i>Cellular Biology and Biochemistry of the Retinoids</i> , The Retinoids: Biology, Chemistry, and Medicine 443-520 (2nd ed. 1994)	

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2128	K. Nason-Burchenal & E. Dmitrovsky, <i>The Retinoids: Cancer Therapy and Prevention Mechanisms</i> , 139 Handbook of Experimental Pharmacology 301-22 (1999)	
2129	Tiziana Camerini et al., <i>Safety of the Synthetic Retinoid Fenretinide: Long-Term Results From a Controlled Clinical Trial for the Prevention of Contralateral Breast Cancer</i> , 19 J. Clin. Oncol. 1664-70 (2001)	
2130	Judith G. Villablanca et al., <i>Phase I Trial of 13-cis-Retinoic Acid in Children With Neuroblastoma Following Bone Marrow Transplantation</i> , 13 J. Clin. Oncol. 894-901 (1995)	
2131	Isotretinoin, The Wayback Machine, https://web.archive.org/web/20080603203929/http://www.chemocare.com:80/BIO/isotretinoin.asp (June 3, 2008)	
2132	Vinay K. Puduvalli et al., <i>Phase II Study of Fenretinide (NSC 374551) in Adults With recurrent Malignant Gliomas: A North American Brain Tumor Consortium Study</i> , 22(21) J. Clin. Oncology 4282-89 (2004)	
2133	IreneVoo & Kent W. Small, <i>Update On The Genetics Of Macular Dystrophies</i> , 24(4) Retina, The Journal Of Retinal And Vitreous Diseases 591-601 (2004)	
2134	NEI Stargardt Disease, https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/stargardt-disease (2024)	
2135	UCSF Stargardt Disease, https://www.ucsfhealth.org/conditions/stargardt-disease# (2024)	

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2136	G. Karan et al., <i>Lipofuscin accumulation, abnormal electrophysiology, and photoreceptor degeneration in mutant ELOVL4 transgenic mice: A model for macular degeneration</i> , 102(11) PNAS 4164-69 (2005)	
2137	Barbara L. Brody et al., <i>Depression, Visual Acuity, Comorbidity, and Disability Associated with Age-related Macular Degeneration</i> , 108(10) Ophthalmology 1893-1900 (2001)	
2138	Barry W. Rovner et al., <i>Effect of Depression on Vision Function in Age-Related Macular Degeneration</i> , 120 Arch. Ophthalmol. 1041-44 (2002)	
2139	Robyn H. Guymer & Elaine Wei-Tinn Chong, <i>Modifiable risk factors for age-related macular degeneration</i> , 184 MJA 455-58 (2006)	
2140	Redmer van Leeuwen et al., <i>Dietary Intake of Antioxidants and Risk of Age-Related Macular Degeneration</i> , 294 JAMA 3101-07 (2005)	
2141	Jennifer S. L. Tan et al., <i>Dietary Antioxidants and the Long-term Incidence of Age-Related Macular Degeneration</i> , 115 Ophthalmology 334-41 (2008)	
2142	Johanna M. Seddon et al., <i>Dietary Carotenoids, Vitamins A, C, and E, and Advanced Age-Related Macular Degeneration</i> , 272 JAMA 1413-20 (1994)	
2143	Elizabeth J. Johnson, <i>The Role of Carotenoids in Human Health</i> , 5(2) Nutr. Clin. Care 56-65 (2002)	
2144	Elaine W-T Chong et al., <i>Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis</i> , BMJ 1-8 (2007)	

Exhibit	Description	Served Not Filed
2145	The Age-Related Eye Disease Study 2 (AREDS2) Research Group, <i>Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration: The Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial</i> , 309(19) JAMA 2005-15 (2013)	
2146	M. Michaelides et al., <i>The genetics of inherited macular dystrophies</i> , 40 J. Med. Genet. 641-50 (2003)	
2147	M. Goldstein et al., <i>Retinal pigment epithelial tear following photodynamic therapy for choroidal neovascularization secondary to AMD</i> , 19 Eye 1315-24 (2005)	
2148	Anita I. Miedziak et al., <i>Stargardt's macular dystrophy – a patient's perspective</i> , 71(3) Optometry: Journal of the American Optometric Association 165-76 (2000)	
2149	FDA Stargardt Disease, https://www.fda.gov/patients/learn-about-fda-patient-engagement/patient-listening-session-summaries (2022)	
2150	Kristina L. Penniston & Sherry A. Tanumihardjo, <i>The acute and chronic toxic effects of vitamin A¹⁻⁴</i> , 83 Am. J. Clin. Nutr. 191-201 (2006)	
2151	Andrew M. Glenn et al., <i>Effect Of Vitamin A Treatment On The Prolongation Of Dark Adaptation In Stargardt's Dystrophy</i> , 14 Retina 27-30 (1994)	
2152	Zeng Li et al., <i>TIMP3 mutation in Sorsby's fundus dystrophy: molecular insights</i> , 7(24) Expert Rev. Mol. Med. 1-15 (2005)	
2153	Michael F. Mamor and John W. Gamel, <i>A Randomized Trial of Vitamin A and Vitamin E Supplementation for retinitis Pigmentosa</i> , 111 Arch. Ophthalmol. 1460-63 (1993)	

Exhibit	Description	Served Not Filed
2154	Robret W. Massof, <i>Supplemental Vitamin A Retards Loss ERG Amplitude in Retinitis Pigmentosa</i> , 111 Arch. Ophthalmol. 751-54 (1993)	
2155	Brenda Cartmel et al., <i>Effects of long-term intake of retinol on selected clinical and laboratory indexes</i> ¹⁻³ , 69 Am. J. Clin. Nutr. 937-43 (1999)	
2156	Chris J. Kennedy et al., <i>Lipofuscin Of The Retinal Pigment Epithelium: A Reivew</i> , 9 Eye 763-71 (1995)	
2157	Christopher Hodge & Christopher Taylor, <i>Vitamin A Deficiency</i> , https://www.ncbi.nlm.nih.gov/books/NBK567744/?report=pr intable (2023)	
2158	Christian Hamel, <i>Retinitis pigmentosa</i> , 1 Orphanet Journal of Rare Diseases 40 (2006)	
2159	Foundation Fighting Blindness, <i>New Report: Vitamin A Supplementation Provides No Vision Benefit to RP Patients</i> , https://www.fightingblindness.org/news/new-report-vitamin-a-supplementation-provides-no-vision-benefit-to-rp-patients- 867 (2023)	
2160	Jason Comander et al., <i>Natural history of retinitis pigmentosa based on genotype, vitamin A/E supplementation, and an electroretinogram biomarker</i> , 8(15) JCI Insight e167546 (2023)	
2161	Konstantin Petrukhin, <i>Pharmacological Inhibition of lipofuscin accumulation in the retina as a therapeutic strategy for dry AMD treatment</i> , 10(1) Drug Discovery Today: Therapeutic Strategies e11-e20 (2013)	

Exhibit	Description	Served Not Filed
2162	So R. Kim et al., <i>The all-trans-retinal dimer series of lipofuscin pigments in retinal pigment epithelial cells in a recessive Stargardt disease model</i> , 104(49) PNAS 19273-78 (2007)	
2163	Nisha Mukherjee & Stefanie Schuman, <i>Diagnosis and Management of Stargardt Disease</i> , Eysenet 29-31 (2014)	
2164	Irena Tsui et al., <i>A Practical Approach to Retinal Dystrophies</i> , Retinal Physician, https://retinalphysician.com/issues/2007/april/a-practical-approach-to-retinal-dystrophies/ (2007)	
2165	Jerome Sherman, <i>A Novel Biomarker for Stargardt Disease?</i> , Review of Optometry, https://www.reviewofoptometry.com/article/a-novel-biomarker-for-stargardt-disease (2013)	
2166	Peter Charbel Issa et al., <i>Rescue of the Stargardt phenotype in Abca4 knockout mice through inhibition of vitamin A dimerization</i> , 112(27) PNAS 8415-20 (2015)	
2167	Ji Eun Diana Han et al., <i>Association of sildenafil use with age-related macular degeneration: a retrospective cohort study</i> , 9 BMJ Open Ophth e001525 (2024)	
2168	ClinicalTrials.gov ID NCT00307398, Anecortave Acetate Risk-Reduction Trial (AART) (last update posted November 28, 2012)	
2169	ClinicalTrials.gov ID NCT00429936, <i>Study of Fenretinide in the Treatment of Geographic Atrophy Associated With Dry Age-Related Macular Degeneration</i> (last update posted June 22, 2010)	

Exhibit	Description	Served Not Filed
2170	ClinicalTrials.gov ID NCT00485394, <i>The OMEGA Study: Use of Eye Drops to Treat Geographic Atrophy Associated With Age-Related Macular Degeneration (Dry AMD) (OMEGA)</i> (last update posted April 2, 2008)	
2171	Lucian V. Del Priore, <i>To Treat or Not to Treat Geographic Atrophy – That is the Question</i> , 8(3) Ophthalmology Retina 207-09 (2024)	
2172	August F. Deutman, <i>Stargardt disease</i> , Orphanet Encyclopedia 1-3 (2003)	
2173	Kent L. Anderson et al., <i>A YAC Contig Encompassing the Recessive Stargardt Disease Gene (STGD) on Chromosome 1p</i> , 57 Am. J. Hum. Genet. 1351-63 (1995)	
2174	Cory Jurgensmeier et al., <i>Evaluation of 4-Methylpyrazole as a Potential Therapeutic Dark Adaptation Inhibitor</i> , 32 Current Eye Research 911-15 (2007)	
2175	ClinicalTrials.gov ID NCT00346853, <i>Phase I Pilor Study of 4-MP to Treat Stargardt Macular Dystrophy</i> (last update posted August 5, 2020)	
2176	Maurizio Battaglia Parodi et al., <i>Ranibizumab for subfoveal choroidal neovascularization associated with Stargardt disease</i> , 99 Br. J. Ophthalmol. 1268-70 (2015)	
2177	R. C. Caruso et al., <i>Docosahexaenoic Acid Does Not Improve Visual Function in Patients With Autosomal Recessive Stargardt Disease</i> , ARVO Annual Meeting Abstract (2008)	
2178	ClinicalTrials.gov ID NCT00060749, <i>Effect of DHA Supplements on Macular Function in Patients With Stargardt Macular Dystrophy and Stargardt-like Macular Dystrophy</i> (last update posted July 2, 2017)	

Exhibit	Description	Served Not Filed
2179	Aron Shapiro et al., <i>Funding Strategies for a Retina Program</i> , Retina Today 16-19 (2015)	
2180	Elena Piotter et al. <i>Therapy Approaches for Stargardt Disease</i> , 11 Biomolecules 1179 (2021)	
2181	Doina M. Mihai et al., <i>The retina rapidly incorporates ingested C20-D₃-vitamin A in a swine model</i> , 19 Molecular Vision 1677-83 (2013)	
2182	Lynda Charters, <i>TEASE-3 study: Positive interim data reported for Stargardt drug</i> , 4(1) Modern Retina Digital Edition, https://www.modernretina.com/view/tease-3-study-positive-interim-data-reported-for-stargardt-drug (2024)	
2183	FDA Patient Listening Sessions, https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-listening-sessions (2024)	
2184	Tomas S. Aleman et al., <i>Macular Pigment and Lutein Supplementation in ABCA4-Associated Retinal Degenerations</i> , 48 Invest. Ophthalmol. Vis. 1319-29 (2007)	
2185	Nathan L. Mata et al., <i>Investigation Of Oral Fenretinide For Treatment Of Geographic Atrophy In Age-Related macular Degeneration</i> , 33 Retina 498-507 (2013)	
2186	P. Sternberg et al., <i>Topical OT-551 for Treating Geographic Atrophy: Phase II Results</i> , ARVO Annual Meeting Abstract (2010)	
2187	Thomas J. Stokkermans, <i>What's New in Clinical Trials for Treatment of Dry AMD</i> , https://www.reviewofoptometry.com/article/whats-new-in-clinical-trials-for-treatment-of-dry-amd (2009)	

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2188	FDA News Release, <i>FDA awards 15 grants for clinical trials to stimulate product development for rare diseases</i> , https://www.fda.gov/news-events/press-announcements/fda-awards-15-grants-clinical-trials-stimulate-product-development-rare-diseases (October 6, 2017)	
2189	FDA News Release, <i>FDA awards 12 grants to fund new clinical trials to advance the development of medical products for the treatment of rare diseases</i> , https://www.fda.gov/news-events/press-announcements/fda-awards-12-grants-fund-new-clinical-trials-advance-development-medical-products-treatme... (September 24, 2018)	
2190	Belite Bio Company Presentation, <i>Early Intervention with an Oral Treatment for Macular Degeneration: Mission for Vision</i>	
2191	Declaration of Leonide Saad, Ph.D.	
2192	Declaration of Dr. Lucian V. Del Priore, MD, Ph.D.	
2193	Curriculum Vitae of Dr. Lucian V. Del Priore, MD, Ph.D.	
2194	Declaration of Kelley Hayes Greenhill	
2195	Declaration of Shauna Wiest	
2196	Declaration of Shauna L. Wiest Regarding <i>Greene & Kupperman 1968</i>	X
2197	Declaration of Shauna L. Wiest Regarding <i>Westheimer 1961</i>	X
2198	Declaration of Shauna L. Wiest Regarding <i>Howes 2006</i>	X
2199	Declaration of Shauna L. Wiest Regarding <i>Owsley 2000</i>	X
2200	Declaration of Shauna L. Wiest Regarding <i>Orphanet 2003</i>	X
2201	Declaration of Kelley M. Hayes Greenhill	X

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2202	E.F. Greene & A. Kuppermann, <i>Chemical Reaction Cross Sections and Rate Constants</i> , 45(6) J. Chem. Educ. 361-69 (1968)	X
2203	Patrick C. Mowery & Walther Stoeckenius, <i>Mechanistic Aspects of the Thermal Equilibration of Retinylidene Imines and Immonium Salts</i> , 101(2) J. Am Chem. Soc. 414-17 (1979)	
2204	F.H. Westheimer, <i>The Magnitude Of The Primary Kinetic Isotope Effect For Compounds Of Hydrogen And Deuterium</i> , 61(3) Chem. Reviews 265-73 (1961)	X
2205	Kimberly A. Howes et al., <i>Dry AMD: From Theory to Treatment</i> , https://www.reviewofophthalmology.com/article/dry-amd-from-theory-to-treatment (2006)	X
2206	Perception: ECVF 2000 abstract, C. Owsley & G. R. Jackson, <i>Aging and scotopic dysfunction</i> , https://web.archive.org/web/20010223080851/http://perceptionweb.com/ecvp00/0248.html	X
2207	August F. Deutman, <i>Stargardt's disease</i> , https://web.archive.org/web/20030712144018/http://www.orpha.net/data/patho/GB/uk-Stargardt.html	X
2208	Omitted	
2209	Deposition Transcript of Peter Guengerich, Ph.D. (January 24, 2025)	
2210	Patent Owner's Updated Exhibit List July 23, 2024	

Respectfully submitted,

Dated: March 11, 2025

By: /Drew D. Christie/

Drew D. Christie, Reg. No. 78,004
Finnegan, Henderson, Farabow,
Garrett & Dunner, LLP

Counsel for Patent Owner
The Trustees of Columbia University in the
City of New York

CERTIFICATE OF SERVICE

The undersigned certifies that a copy of the foregoing **Patent Owner's Updated Exhibit List and Exhibits 2048-2050, 2203, and 2210** were served electronically via email on March 11, 2025, in their entirety on the following:

Jad A. Mills
Michael T. Rosato
Wilson, Sonsini, Goodrich & Rosati
701 Fifth Avenue, Suite 5100
Seattle, WA 98104-7036
jmills@wsgr.com
mrosato@wsgr.com

Matthew Bresnahan
Wilson, Sonsini, Goodrich & Rosati
12235 El Camino Real
San Diego, CA 82130-3002
mbresnahan@wsgr.com

Petitioner has consented to service by electronic mail.

Dated: March 11, 2025

/William Esper/
William Esper
Legal Assistant and PTAB Coordinator
Finnegan, Henderson, Farabow,
Garrett & Dunner, LLP