

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 IPR2024-00313
Patent No. RE47,045

PETITIONER'S UPDATED EXHIBIT LIST

Exhibit No.	Description
1001	U.S. Patent No. RE47,045 to Washington et al.
1002	Declaration of Dr. F. Peter Guengerich.
1003	<i>Curriculum Vitae</i> of Dr. F. Peter Guengerich.
1004	Declaration of Dr. Andrew Calman, M.D., Ph.D.
1005	<i>Curriculum Vitae</i> of Dr. A. Calman
1006	Robert Bergen, H., Furr, H. C., & Olson, J. A., Synthesis of Tri-, Tetra-, and Penta-deuterated Forms of Vitamin A, <i>Journal of Labelled Compounds and Radiopharmaceuticals</i> , 25(1), 11-21 (1988) (“Olsen 1988”).
1007	Furr, H. C., Amedee-Manesme, O., Clifford, A. J., Bergen 3rd, H. R., Jones, A. D., Anderson, D. P., & Olson, J. A., Vitamin A concentrations in liver determined by isotope dilution assay with tetradeuterated vitamin A and by biopsy in generally healthy adult humans, <i>The American Journal of Clinical Nutrition</i> , 49(4), 713-716 (1989) (“Olson 1989”)
1008	DE202006014588U1 (English Translation) (“Ortho Pharma”)
1009	WO 2006/007314 to Widder et al. (“Widder”)
1010	Mata, N. L. et al., Biosynthesis of a major lipofuscin fluorophore in mice and humans with ABCR-mediated retinal and macular degeneration, <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 97(13), 7154-7159 (2000) (“Mata”)
1011	Fishkin et al., Isolation and Characterization of a Retinal Pigment Epithelial Cell Fluorophore: An All-trans-retinal Dimer Conjugate, <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 102(20), 7091-7096 (2005) (“Fishkin”)

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1012	Haskins, N. J., The Application of Stable Isotopes in Biomedical Research, <i>Biomedical Mass Spectrometry</i> , 9(7), 269-277 (1982) (“Haskins”)
1013	Baillie, T. A., The Use of Stable Isotopes in Pharmacological Research, <i>Pharmacological Reviews</i> , 33(2), 81-132 (1981) (“Baillie”)
1014	Van Langenhove, A., Isotope Effects: Definitions and Consequences for Pharmacologic Studies, <i>The Journal of Clinical Pharmacology</i> , 26(6), 383-389 (1986) (“Langenhove”)
1015	Roth and König, Kinetic Isotope Effect of the 1.5-Hydrogen Displacement in <i>cis</i> -Pentadiene-(1.3), <i>Justus Liebigs Annalen Der Chemie</i> (1966) (“Roth”).
1016	Itou et al., Quantum Treatment of Hydrogen Nuclei in Primary Kinetic Isotope Effects in a Thermal [1, 5]-Sigmatropic Hydrogen (or Deuterium) Shift from (Z)-1, 3-Pentadiene. <i>The Journal of Physical Chemistry A</i> , 111(2), 261-267 (2007) (“Itou”)
1017	Remington: The Science and Practice of Pharmacy, 19th ed. (1995) (chs. 80 & 89) (“Remington”)
1018	Parish et al., Isolation and One-step Preparation of A2E and Iso-A2E, Gluorophores from Human Retinal Pigment Epithelium, <i>Proceedings of the National Academy of Sciences</i> , 95(25), 14609-14613 (1998) (“Parish”)
1019	Furr et al. Stable Isotope Dilution Techniques for Assessing Vitamin A Status and Bioefficacy of Provitamin A Carotenoids in Humans, <i>Public Health Nutrition</i> , 8(6), 596-607 (2005) (“Furr”)
1020	Shaban & Richter, A2E and Blue Light in the Retina: The Paradigm of Age-related Macular Degeneration, <i>Biol. Chem.</i> , 383(3-4), 537-45 (2002) (“Shaban & Richter”)
1021	Shaban et al., Phosphatidylglycerol Potently Protects Human Retinal Pigment Epithelial Cells Against Apoptosis Induced by A2E, a

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	Compound Suspected to Cause Age-related Macula Degeneration, <i>Experimental eye research</i> , 75(1), 99-108 (2002) (“Shaban”)
1022	Age-Related Eye Disease Study Research Group, A Randomized, Placebo-controlled, Clinical Trial of High-dose Supplementation with Vitamins C and E, Beta Carotene, and Zinc for Age-related Macular Degeneration and Vision Loss: AREDS report no. 8. <i>Archives of Ophthalmology</i> , 119(10), 1417-1436 (2001) (“AREDS”)
1023	First Declaration of Irinia Hinrichs
1024	Second Declaration of Irina Hinrichs
1025	McCullough FS, Northrop-Clewes CA, Thurnham DI. The Effect of Vitamin A on Epithelial Integrity, <i>Proc Nutr Soc.</i> 58(2):289-93 (1999) (“McCullough”)
1026	J. A. Olson, The Biosynthesis and Metabolism of Carotenoids and Retinol (Vitamin A). <i>J. Lipid Res.</i> 5(3):281-99 (1964) (“Olson 1964”)
1027	Del Priore LV, Kuo YH, Tezel TH. Age-related Changes in Human RPE Cell Density and Apoptosis Proportion <i>in situ</i> , <i>Invest Ophthalmol Vis Sci.</i> 43(10):3312-8 (2002) (“Del Priore”)
1028	Wolf, G., A History of Vitamin A and Retinoids. <i>The FASEB Journal</i> , 10: 1102-1107 (1996) (“Wolf”)
1029	Sommer, A., Effects of Vitamin A Deficiency on the Ocular Surface, <i>Ophthalmology</i> 90(6):592-600 (1983) (“Sommer”)
1030	Radu, Roxana A. et al., Reductions in Serum Vitamin A Arrest Accumulation of Toxic Retinal Fluorophores: A Potential Therapy for Treatment of Lipofuscin-Based Retinal Diseases, <i>Invest. Ophthalmol. Vis. Sci.</i> 46(12):4393-4401 (2005) (“Radu 2005”)
1031	File History of U.S. Patent Application No. 12/733,631
1032	File History of U.S. Patent Application No. 14/510,975
1033	Sparrow JR, Fishkin N, Zhou J, Cai B, Jang YP, Krane S, Itagaki Y, Nakanishi K, A2E, a Byproduct of the Visual Cycle, <i>Vision Res.</i> 43(28):2983-90 (2003) (“Sparrow”)
1034	Wolf G., Lipofuscin and Macular Degeneration., <i>Nutr Rev.</i> 61(10):342-6 (2003) (“Wolf 2003”)

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1035	Radu, Roxana A. et al. "Treatment with Isotretinoin Inhibits Lipofuscin Accumulation in a Mouse Model of Recessive Stargardt's Macular Degeneration." <i>Proceedings of the National Academy of Sciences of the United States of America</i> 100:4742-4747 (2003) ("Radu")
1036	Fishkin N, Jang YP, Itagaki Y, Sparrow JR, Nakanishi K. A2-Rhodopsin: A New Fluorophore Isolated from Photoreceptor Outer Segments. <i>Org Biomol Chem.</i> 1(7):1101-5. (2003) ("Fishkin 2003")
1037	Law WC & Rando RR, The Molecular Basis of Retinoic Acid Induced Night Blindness, <i>Biochem Biophys Res Commun.</i> 161(2):825-9 (1989) ("Law")
1038	Sieving PA, Chaudhry P, Kondo M, Provenzano M, Wu D, Carlson TJ, Bush RA, Thompson DA. Inhibition of the Visual Cycle in vivo by 13-cis Retinoic Acid Protects from Light Damage and Provides a Mechanism for Night Blindness in Isotretinoin Therapy, <i>Proc Natl Acad Sci USA.</i> (2001) ("Sieving")
1039	Chopdar A, Chakravarthy U, Verma D, Age Related Macular Degeneration. <i>BMJ</i> (2003) ("Chopdar")
1040	Berson EL, Rosner B, Sandberg MA, Hayes KC, Nicholson BW, Weigel-DiFranco C, Willett W. A Randomized Trial of Vitamin A and Vitamin E Supplementation for Retinitis Pigmentosa. <i>Arch Ophthalmol.</i> 111(6):761-72. (1993) ("Berson")
1041	Jacobson SG, Cideciyan AV, Regunath G, Rodriguez FJ, Vandenburgh K, Sheffield VC, Stone EM. Night Blindness in Sorsby's Fundus Dystrophy Reversed by Vitamin A. <i>Nat Genet.</i> 11(1):27-32. (1995) ("Jacobson")
1042	Alberts D et al., Safety and Efficacy of Dose-intensive Oral Vitamin A in Subjects with Sun-damaged Skin. <i>Clin Cancer Res.</i> (2004) ("Alberts")
1043	Ross DA, Recommendations for Vitamin A Supplementation. <i>J Nutr.</i> 132(9 Suppl):2902S-2906S (2002) ("Ross")
1044	Haskell MJ et al., Use of the Deuterated-retinol-dilution Technique to Assess Total-body Vitamin A Stores of Adult Volunteers Consuming Different Amounts of Vitamin A. <i>Am J Clin Nutr.</i> 70(5):874-80 (1999) ("Haskell")

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1045	Haskell MJ, et al., Assessment of Vitamin A Status by the Deuterated-retinol-dilution Technique and Comparison with Hepatic Vitamin A Concentration in Bangladeshi Surgical Patients, <i>Am J Clin Nutr.</i> 66(1):67-74 (1997) (“Haskell 1997”)
1046	Kushner DJ, Baker A, Dunstall TG, Pharmacological Uses and Perspectives of Heavy Water and Deuterated Compounds, <i>Can J Physiol Pharmacol.</i> 77(2):79-88 (1999) (“Kushner”)
1047	Blake MI, Crespi HL, Katz JJ, Studies with Deuterated Drugs, <i>J Pharm Sci.</i> 64(3):367-91 (1975) (“Blake”)
1048	McCarty LP, Malek RS, Larsen ER. The Effects of Deuteration on the Metabolism of Halogenated Anesthetics in the Rat, <i>Anesthesiology</i> 51(2):106-10 (1979) (“McCarty”)
1049	Bull E. What is a Nutraceutical? <i>Pharm J.</i> 265:57-58 (2000) (“Bull”)
1050	Kuksa V, Imanishi Y, Batten M, Palczewski K, Moise AR. Retinoid Cycle in the Vertebrate Retina: Experimental Approaches and Mechanisms of Isomerization, <i>Vision Res.</i> 43(28):2959-81 (2003) (“Kuksa”)
1051	Miwa, GT & Lu, AY, Kinetic Isotope Effects and ‘Metabolic Switching’ in Cytochrome P450-catalyzed Reactions, <i>BioEssays</i> , 7(5), 215-219 (1987) (“Miwa”)
1052	WO 95/04018 to Marcus F. Boehm (“Boehm”)
1053	Ribaya-Mercado et al., “Dietary vitamin A intakes of Filipino elders with adequate or low liver vitamin A concentrations as assessed by the deuterated-retinol-dilution method: implications for dietary requirements,” <i>The American Journal of Clinical Nutrition</i> , 79(4), 633-641 (“Ribaya-Mercado”)
1054	Kemp, C. Visual Function and Rhodopsin Levels in Humans with Vitamin A Deficiency. 46 <i>Experimental Eye Research</i> (1988) (“Kemp”)
1055	Rosenfeld, P.J. et al. Ranibizumab for Neovascular Age-Related Macular Degeneration. 355 <i>New England Journal of Medicine</i> 1419-31 (October 5, 2006) (“Rosenfeld”)
1056	Sommer, A. Oral Versus Intramuscular Vitamin A in the Treatment of Xerophthalmia. 8168 (Part 1) <i>Lancet</i> (1980) (“Sommer 1980”)

Exhibit No.	Description
1057	File History resulting in U.S. Reissue Patent No. RE47,045
1058	Duszka, et al., Rat Intestinal β -Carotene Dioxygenase Activity Is Located Primarily in the Cytosol of Mature Jejunal Enterocytes. <i>Nutrient Metabolism</i> 2550-2556 (1996).
1059	American Optometric Association, "Care of the Patient with Age-Related Macular Degeneration," Optometric Clinical Practice Guideline (2004).
1060	First Supplemental Declaration of Irina Hinrichs (supplemental evidence for EX1023) (SERVED NOT FILED)
1061	Second Supplemental Declaration of Irina Hinrichs (supplemental evidence for EX1024) (SERVED NOT FILED)
1062	Age-Related Eye Disease Study Research Group, A Randomized, Placebo-controlled, Clinical Trial of High-dose Supplementation with Vitamins C and E, Beta Carotene, and Zinc for Age-related Macular Degeneration and Vision Loss: AREDS report no. 8. <i>Archives of Ophthalmology</i> , 119(10), 1417-1436 (2001) (supplemental evidence for EX1022) (SERVED NOT FILED)
1063	Wolf, G., A History of Vitamin A and Retinoids. <i>The FASEB Journal</i> , 10: 1102-1107 (1996) (supplemental evidence for EX1028) (SERVED NOT FILED)
1064	Bull E., What is a Nutraceutical? <i>Pharm J.</i> 265:57-58 (2000) (supplemental evidence for EX1049) (SERVED NOT FILED)
1065	Centrum Silver Adults Label (200 Tablets) Multivitamin
1066	Glenn J. Jaffee, et al., " <i>C5 Inhibitor Avacincaptad Pegol for Geographic Atrophy Due to Age-Related Macular Degeneration, Ophthalmology</i> ", Volume 128, Issue 4, 576 - 586
1067	Jeffrey S. Heier, et al., " <i>Pegcetacoplan for the treatment of geographic atrophy secondary to age-related macular degeneration (OAKS and</i>

Exhibit No.	Description
	<i>DERBY</i>): two multicentre, randomised, double-masked, sham-controlled, phase 3 trials”, Lancet 2023; 402: 1434–48
1068	Liangbo L. Shen et al., “ <i>Natural History of Autosomal Recessive Stargardt Disease in Untreated Eyes</i> ”, Ophthalmology, Volume 126, Issue 9, 1288 - 1296
1069	Deposition Transcript of Lucian Del Priore (November 13, 2024)
1070	Deposition Transcript of Glenn D. Prestwich, Ph.D. (November 15, 2024)
1071	Alkeus Pharmaceuticals Inc - Transformation in Sight, https://alkeuspharma.com (last visited Oct. 25, 2024)
1072	Bain Capital - Current and former portfolio companies, available from https://www.baincapitalprivateequity.com/portfolio/current-and-former-portfolio-companies (last visited Nov. 21, 2024)
1073	Alkeus Pharmaceuticals Inc - Transformation in Sight, https://alkeuspharma.com (last visited Nov. 21, 2024)
1074	LinkedIn Profile for Michael Song (last visited Nov. 21, 2024)
1075	LinkedIn Profile for Monica Hennessey (last visited Nov. 20, 2024)
1076	LinkedIn Profile for Christine Xu (last visited Nov. 21, 2024)
1077	LinkedIn Profile for Cyriac Joyce (last visited Nov. 21, 2024)
1078	LinkedIn Profile for Runyao Tung (last visited Nov. 21, 2024)
1079	CONFIDENTIAL and PUBLIC REDACTED VERSIONS– Deposition Transcript of Leonide Saad Ph.D. (November 26, 2024)
1080	Rebuttal Declaration of Dr. F. Peter Guengerich
1081	Ben Fidler, “ <i>An unconventional drug startup lures Vertex founder Josh Boger back to biotech</i> ,” BioPharmaDive (Jun. 5, 2023), available

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	from https://www.biopharmadive.com/news/alkeus-biotech-startup-josh-boger-stargardt/651949/ (last visited Dec. 20, 2024)
1082	Jonathan Saltzman, “ <i>Cambridge biotech raises \$150 million and rehires founder of Vertex</i> ,” Boston Globe (Jun. 5, 2023) available from https://www.bostonglobe.com/2023/06/05/business/alkeus-pharmaceuticals-raises-150-million/ (last visited Dec. 19, 2024)
1083	Ilyas Washington, PubMed Publication Entries, 2001-2007, available from https://pubmed.ncbi.nlm.nih.gov/?term=Ilyas+Washington&filter=years.2001-2004&sort=pubdate (last visited Dec. 19, 2024)
1084	Rowan Walrath, “ <i>Vertex founder Josh Boger is back in biotech. Here’s why he ‘unretired.’</i> ” Boston Business Journal (Jun. 11, 2023), available from https://www.bizjournals.com/boston/news/2023/06/12/alkeus-vertex-josh-boger-un-retirement.html (last visited Dec. 19, 2024)
1085	Screenshot of https://timmermanreport.com/2023/06/alkeus-a-bootstrap-success-story-graduates-with-150m-series-b/ - Luke Timmerman, “ <i>Alkeus, A Bootstrap Success Story, Grows Up With \$150M Series B</i> ”, Timmerman Report (Jun. 2023), available from Timmerman Report.com (last visited Dec. 19, 2024)
1086	Luke Timmerman, “ <i>Alkeus, A Bootstrap Success Story, Grows Up With \$150M Series B</i> ”, Timmerman Report (Jun. 2023), available from Timmerman Report.com
1087	Christine N. Kay, MD; Leonide Saad; Gabrielle DeBartolomeo; Ilyas Washington; Philip J. Ferrone; Hendrik P. Scholl; Marc T. Mathias; “Gildeuretinol Slows Progression of Stargardt Disease The TEASE Program, Presented at the Annual Meeting of the American Academy of Ophthalmology (AAO), Chicago, IL (Oct. 20, 2024).
1088	CONFIDENTIAL and PUBLIC REDACTED VERSIONS–Petitioner’s Demonstratives

Respectfully submitted,

Dated: March 25, 2025

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CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing Petitioner's Updated Exhibit List and EX1088 were served March 25, 2025, on the Patent Owner at the electronic service addresses as follows:

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