UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SUN PHARMACEUTICAL INDUSTRIES LTD.
AND SUN PHARMACEUTICAL INDUSTRIES, INC.,

Petitioners,

v.

NOVO NORDISK A/S,

Patent Owner.

U.S. Patent No. 10,335,462 to Jensen
Issue Date: July 2, 2019
Title: Use of Long-Acting GLP-1 Peptides

Inter Partes Review IPR2024-00107

PETITIONERS' REPLY TO PATENT OWNER'S FURTHER AUTHORIZED REPLY

TABLE OF EXHIBITS

EXHIBIT	DESCRIPTION
1001	U.S. Patent No. 10,335,462
1002	Prosecution history excerpts for U.S. Patent No. 10,335,462
1003	Declaration of John Bantle, MD
1004	CV of John Bantle MD
1005	Declaration of William J. Jusko, Ph.D.
1006	CV of William J. Jusko, Ph.D.
1007	Declaration of Paul Dalby, Ph.D.
1008	CV of Paul Dalby, Ph.D.
1009	Intentionally Left Blank
1010	Intentionally Left Blank
1011	WO 2011/138421
1012	Lovshin, *Incretin-Based Therapies for Type 2 Diabetes Mellitus*, 5 NATURE REV. ENDOCRINOLOGY 262 (2009)
1013	Clinical Trial No. NCT00696657
1014	Clinical Trial No. NCT00851773
1015	WO 2006/097537
1016	U.S. Patent Application Pub. No. US2007/0010424
1017	U.S. Patent No. 5,512,549
1018	Banting, *The Internal Secretion of the Pancreas,* 7 J. LAB. CLINICAL MED. 251 (1922)

EXHIBIT	DESCRIPTION
1019	Bell, *Hamster Preproglucagon Contains the Sequence of Glucagon and Two Related Peptides*, 302 NATURE 716 (1983)
1020	Bydureon prescribing information (Jan. 2012)
1021	Byetta prescribing information (Oct. 2009)
1022	Drab, *Incretin-Based Therapies for Type 2 Diabetes Mellitus: Current Status and Future Prospects*, 30 PHARMACOTHERAPY 609 (2010)
1023	Drucker, *Enhancing Incretin Action for the Treatment of Type 2 Diabetes*, 26 DIABETES CARE 2929 (2003)
1024	Drucker, *The Incretin System: Glucagon-Like Peptide-1 Receptor Agonists and Dipeptidyl Peptidase-4 Inhibitors in Type 2 Diabetes*, 368 LANCET 1696 (2006)
1025	Glaesner, *Engineering and Characterization of the Long-Acting Glucagon-Like Peptide-1 Analogue LY2189265, an Fc Fusion Protein*, 26 DIABETES/METABOLISM RSCH. & REV. 287 (2010)
1026	HARRISON'S PRINCIPLES OF INTERNAL MED., Chapter 338 (Fauci et al. eds. 17th ed. 2008)
1027	Holst, *Truncated Glucagon-like Peptide I, an Insulin-Releasing Hormone from the Distal Gut*, 211 (2) FEBS LETTERS 169 (1987)
1028	Holst, *Glucagon-Like Peptide 1 and Inhibitors of Dipeptidyl Peptidase IV in the Treatment of Type 2 Diabetes Mellitus*, 4 CURRENT OP. IN PHARMACOLOGY 589 (2004)
1029	Jimenez-Solem, *Dulaglutide, a Long-Acting GLP-1 Analog Fused with an Fc Antibody Fragment for the Potential Treatment of Type 2 Diabetes*, 12 CURRENT OP. IN MOLECULAR THERAPEUTICS 790 (2010)

EXHIBIT	DESCRIPTION
1030	Kim, *Effects of Once-Weekly Dosing of a Long-Acting Release Formulation of Exenatide on Glucose Control and Body Weight in Subjects with Type 2 Diabetes*, 30 DIABETES CARE 1487 (2007)
1031	Knudsen, *GLP-1 Derivatives as Novel Compounds for the Treatment of Type 2 Diabetes: Selection of NN2211 for Clinical Development*, 26 DRUGS OF THE FUTURE 677 (2001)
1032	Knudsen, *Glucagon-like Peptide-1: The Basis of a New Class of Treatment for Type 2 Diabetes*, 47 J. MED. CHEMISTRY 4128 (2004)
1033	Knudsen, *Liraglutide, a GLP-1 Analogue to Treat Diabetes*, *in* ANALOGUE-BASED DRUG DISCOVERY II (Fischer & Ganellin eds. 2010)
1034	U.S. Patent No. 6,268,343 ("Knudsen patent")
1035	Lund, *Emerging GLP-1 Receptor Agonists*, 16 EXPERT OP. ON EMERGING DRUGS 607 (2011)
1036	Mojsov, *Insulinotropin: Glucagon-like Peptide I (7-37) Co-encoded in the Glucagon Gene is a Potent Simulator of Insulin Release in the Perfused Rat Pancreas*, 79 J. CLINICAL INVESTIGATION 616 (1987)
1037	Nielsen, *Pharmacology of Exenatide (Synthetic Exendin-4): A Potential Therapeutic for Improved Glycemic Control of Type 2 Diabetes*, 117 REGUL. PEPTIDES 77 (2004)
1038	Seino, *Dose-Dependent Improvement in Glycemia with Once-Daily Liraglutide without Hypoglycemia or Weight Gain: A Double-Blind, Randomized, Controlled Trial in Japanese Patients with Type 2 Diabetes*, 81 DIABETES RSCH. & CLINICAL PRACTICE 161 (2008)
1039	*Victoza*, PHYSICIANS' DESK REFERENCE (65th ed. 2010)

EXHIBIT	DESCRIPTION
1040	Vilsbøll, *Glucagon-Like Peptide-1 and Diabetes Treatment*, 21 INT'L DIABETES MONITOR 1 (2009)
1041	WO 03/002136
1042	WO 91/11457
1043	U.S. Patent App. Pub. 2004/0102486
1044	Rohatagi, *Model-Based Development of a PPARγ Agonist, Rivoglitazone, to Aid Dose Selection and Optimize Clinical Trial Designs*, 48 J. CLINICAL PHARMACOLOGY 1420 (2008)
1045	Shargel, APPLIED BIOPHARMACEUTICS & PHARMACOKINETICS (5th ed. 2005)
1046	Yun, *Pharmacokinetic and Pharmacodynamic Modelling of the Effects of Glimepiride on Insulin Secretion and Glucose Lowering in Healthy Humans*, 31 J. CLINICAL PHARMACY & THERAPEUTICS 469 (2006)
1047	Tamimi, *Drug Development: From Concept to Marketing!*, 113 NEPHRON CLINICAL PRACTICE c125 (2009)
1048	FDA Guidance for Industry, *Exposure-Response Relationships - Study Design, Data, Analysis, and Regulatory Applications* (Apr. 2003)
1049	*International Conference on Harmonisation; Dose-Response Information to Support Drug Registration; Guideline; Availability*, 59 Fed. Reg. 55972 (Nov. 9, 1994) ("ICH 1994")
1050	Garber, *Efficacy of Metformin in Type II Diabetes: Results of a Double-Blind, Placebo-Controlled, Dose-Response Trial*, 102 AM. J. MED. 491 (1997)
1051	Landersdorfer, *Pharmacokinetic/Pharmacodynamic Modelling in Diabetes Mellitus*, 47(7) CLINICAL PHARMACOKINETICS 417 (2008)

EXHIBIT	DESCRIPTION
1052	Madsbad, *An Overview of Once-Weekly Glucagon-Like Peptide-1 Receptor Agonists—Available Efficacy and Safety Data and Perspectives for the Future*, 13 DIABETES, OBESITY & METABOLISM 394 (2011)
1053	Møller, *Mechanism-Based Population Modelling for Assessment of L-Cell Function Based on Total GLP-1 Response Following an Oral Glucose Tolerance Test*, 38 J. PHARMACOKINETICS & PHARMACODYNAMICS 713 (2011)
1054	Landersdorfer, *Mechanism-Based Population Pharmacokinetic Modelling in Diabetes: Vildagliptin as a Tight Binding Inhibitor and Substrate of Dipeptidyl Peptidase IV*, 73 BRIT. J. CLINICAL PHARMACOLOGY 391 (2011) ("Landersdorfer 2011a")
1055	Landersdorfer, *Mechanism-Based Population Modelling of the Effects of Vildagliptin on GLP-1, Glucose and Insulin in Patients with Type 2 Diabetes*, 73 BRIT. J. CLINICAL PHARMACOLOGY 373 (2011) "(Landersdorfer 2011b")
1056	U.S. Patent No. 5,118,666
1057	WO 2011/073328
1058	Blonde, *Comparison of Liraglutide Versus Other Incretin-Related Anti-Hyperglycaemic Agents*, 14 (suppl. 2) DIABETES, OBESITY & METABOLISM 20 (2012)
1059	Murphy, *Review of the Safety and Efficacy of Exenatide Once Weekly for the Treatment of Type 2 Diabetes Mellitus*, 46 ANNALS OF PHARMACOTHERAPY 812 (2012)
1060	WO 2011/058193
1061	U.S. Patent App. Pub. No. 2011/0166321
1062	Zarin, *The ClinicalTrials.gov Results Database—Update and Key Issues*, 364 NEW ENGL. J. MED. 852 (2011)

EXHIBIT	DESCRIPTION
1063	Kirillova, *Results and Outcome Reporting in ClinicalTrials.gov, What Makes it Happen?*, 7(6) PLOS ONE 1 (2012)
1064	Monami, *Effects of Glucagon-Like Peptide-1 Receptor Agonists on Body Weight: A Meta-Analysis*, 2012 EXPERIMENTAL DIABETES RSCH. 1 (2012)
1065	Tasneem, *The Database for Aggregate Analysis of ClinicalTrials.gov (AACT) and Subsequent Regrouping by Clinical Specialty*, 7(3) PLOS ONE 1(2012)
1066	Knudsen, *Liraglutide: The Therapeutic Promise from Animal Models*, 64(suppl 167) INT'L J. CLINICAL PRACTICE 4 (2010) ("Knudsen 2010b")
1067	U.S. Patent No. 8,536,122
1068	U.S. Patent No. 8,129,343
1069	REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (Alfonso R. Gennaro ed., 20th ed. 2000)
1070	Boylan, *Parenteral Products*, *in* MODERN PHARMACEUTICS (Gilbert S. Banker et al. eds., 3d ed. 1996)
1071	U.S. Patent No. 6,284,727
1072	U.S. Patent No. 5,164,366
1073	U.S. Patent No. 6,458,924
1074	WO 00/37098
1075	U.S. Patent No. 7,022,674
1076	*ClinicalTrials.gov Background*, *CLINICALTRIALS.GOV, https://clinicaltrials.gov/ct2/about-site/background (*last visited Mar. 10, 2023)

EXHIBIT	DESCRIPTION
1077	Award: *ClinicalTrials.gov*, https://ash.harvard.edu/news/clinicaltrials.gov (last visited Mar. 10, 2023)
1078	U.S. Patent App. Pub. No. 2004/0102486
1079	*NCT00167115*, *CLINICALTRIALS.GOV,* https://www.clinicaltrials.gov/ct2/show/NCT00167115 (last visited Mar. 10, 2023)
1080	*NCT01933490*, *CLINICALTRIALS.GOV,* https://www.clinicaltrials.gov/ct2/show/NCT01933490 (last visited Mar. 10, 2023)
1081	Ozempic prescribing information (Oct. 2022)
1082	Scheduling Order, *Novo Nordisk Inc. v. Rio Biopharmaceuticals Inc.*, No. 22-294 (CFC) (D. Del. June 30, 2022), ECF No. 22
1083	Transfer Order, *In re: Ozempic (Semaglutide) Patent Litigation*, No. 3038 (MDL Aug. 5, 2022)
1084	EMA, *ICH Topic S 7 A Safety Pharmacology Studies for Human Pharmaceuticals* (June 2001)
1085	ACS Publications, https://pubs.acs.org/toc/jmcmar/47/17; https://pubs.acs.org/doi/10.1021/jm030630m
1086	"Last Update Posted" definition from ClinicalTrials.gov https://clinicaltrials.gov/ct2/show/NCT00696657
1087	Prosecution history excerpts for U.S. Patent No. 9,764,003
1088	Intentionally Left Blank
1089	Intentionally Left Blank
1090	Intentionally Left Blank

EXHIBIT	DESCRIPTION
1091	Declaration of Melissa Weinberg, MD
1092	CV of Melissa Weinberg, MD
1093	Declaration of Craig Dyar, Ph.D.
1094	CV of Craig Dyar, Ph.D.
1095	Declaration of Alekha Dash, Ph.D.
1096	CV of Alekha Dash, Ph.D.
1097	*Mylan Pharmaceuticals Inc., v. Novo Nordisk A/S*, IPR2023-00724, Paper 10 (PTAB Oct. 4, 2023)
1098	Oral Order, *Novo Nordisk Inc. v. Rio Biopharmaceuticals Inc.*, No. 22-294 (CFC) (D. Del. March 13, 2024)
1099	Sun Pharmaceutical Industries Ltd. and Sun Pharmaceutical Industries, Inc.'s Stipulation of Invalidity Contentions

On May 1, 2024, Petitioners filed a *Sotera* stipulation in the parallel district court proceeding. EX1099. This filing was prompt and in good faith – within a week of the Board declining to exercise discretionary denial based on an identical stipulation in a related IPR because the Interim Procedure set forth by Director Vidal "does not condition or otherwise qualify the effect of a *Sotera* stipulation on our exercise of discretion to deny the Petition[.]" *Dr. Reddy's Labs. Inc. et al. v. Novo Nordisk A/S*, IPR2024-00009 (Paper No. 19, April 25, 2024, at 9) ("DRL Decision"). The operable facts in this case are now the same as those considered by the Board in the DRL Decision, and thus, the resolution should be the same.

Petitioners will comply with its *Sotera* stipulation and their rejection of Patent Owner's contrived "conditions" is not an admission of non-compliance. Patent Owner's conditions exceed the plain terms of the stipulation and questions about its scope are properly directed to the district court. *Shaw Indus. Grp., Inc. v. Automated Creel Sys., Inc.*, 817 F.3d 1293, 1305 (Fed. Cir. 2016), rev'd on other grounds by *California Inst. of Tech. v. Broadcom Ltd.*, 25 F.4th 976 (Fed. Cir. 2022) ("whether [conduct is] subject to estoppel must be determined in the first instance by the district court[.]"). Petitioner's *Sotera* stipulation and their arguments against discretionary denial are determinative in view of the Board's recent application of the Interim Procedure as set forth in the DRL Decision. Accordingly, the Board should decline to exercise discretionary denial, institute the Petition and grant the joinder motion.

Respectfully submitted,

Dated: May 22, 2024

/s/ Brian Sodikoff

Brian Sodikoff
Reg No. 54,697
KATTEN MUCHIN ROSENMAN LLP
525 West Monroe Street
Chicago, IL 60661

Counsel for Petitioners
Sun Pharmaceutical Industries Ltd. and
Sun Pharmaceutical Industries Inc.

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I hereby certify that on this 22nd day of May 2024, I caused to be served a true and correct copy of the foregoing by electronic delivery to Patent Owner's counsel of record:

J. Steven Baughman - steve.baughman@groombridgewu.com
Megan Raymond - megan.raymond@groombridgewu.com
Novo-Semaglutide-IPR@groombridgewu.com
GROOMBRIDGE, WU, BAUGHMAN & STONE LLP

Dated: May 22, 2024

/s/ Brian Sodikoff
Brian Sodikoff