

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

IN RE OZEMPIC (SEMAGLUTIDE) PATENT
LITIGATION

C.A. No. 22-md-3038-CFC

CONFIDENTIAL

NOVO NORDISK INC. AND NOVO
NORDISK A/S,

Plaintiffs/Counterclaim Defendants,

v.

RIO BIOPHARMACEUTICALS INC., et al.,

Defendants/Counterclaim Plaintiffs.

C.A. No. 22-294-CFC

NOVO NORDISK INC. AND NOVO
NORDISK A/S,

Plaintiffs/Counterclaim Defendants,

v.

MYLAN PHARMACEUTICALS INC.,

Defendants/Counterclaim Plaintiffs.

C.A. No. 22-cv-1040-CFC

**Opening Expert Report of Dr. Paul Dalby
Regarding Invalidity of U.S. Patent No. 10,335,462**

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TABLE OF ABBREVIATIONS

Full Name of Cited Reference	Abbreviation
U.S. Patent No. 5,164,366	'366 patent
U.S. Patent No. 10,335,462	'462 patent
U.S. Patent No. 7,022,674	'674 patent
U.S. Patent No. 6,284,727	'727 patent
U.S. Patent No. 8,114,833	'833 patent
U.S. Patent No. 6,458,924	'924 patent
Deposition of Christine Jensen, M.D., Ph.D. (Nov. 8, 2023)	Jensen Dep.
Knudsen, <i>Glucagon-Like Peptide-1: The Basis of a New Class of Treatment for Type 2 Diabetes</i> , 47 J. MED. CHEM. 4128 (2004)	Knudsen 2004
U.S. Patent No. 6,268,343	Knudsen patent
Lovshin, <i>Incretin-Based Therapies for Type 2 Diabetes Mellitus</i> , 5 NATURE REVIEWS ENDOCRINOLOGY 262 (2009)	Lovshin
Lund, <i>Emerging GLP-1 Receptor Agonists</i> , 16 EXPERT OPINION ON EMERGING DRUGS 607 (2011)	Lund
Madsbad et al., <i>An Overview of Once-Weekly Glucagon-Like Peptide-1 Receptor Agonists—Available Efficacy and Safety Data and Perspectives for the Future</i> , 13 DIABETES, OBESITY & METABOLISM, 394 (2011)	Madsbad 2011
Boylan, <i>Parenteral Products</i> , in MODERN PHARMACEUTICS (Gilbert S. Banker et al. eds., 3d ed. 1996)	Modern Pharmaceuticals
Clinical Trial No. NCT00696657	NCT657
Ozempic prescribing information (Oct. 2022)	Ozempic label
REMINGTON: THE SCIENCE AND PRACTICE OF PHARMACY (Alfonso R. Gennaro ed., 20th ed. 2000)	Remington
<i>Victoza</i> , PHYSICIANS' DESK REFERENCE (65th ed. 2010)	Victoza label
WO 00/37098	WO '098
WO 03/002136	WO '136
WO 2011/058193	WO '193

TABLE OF ABBREVIATIONS
(continued)

Full Name of Cited Reference	Abbreviation
WO 2011/073328	WO '328
WO 2011/138421	WO '421
WO 2006/097537	WO '537

1. My name is Paul Dalby, Ph.D. I have been retained by Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. ("DRL"), Rio Biopharmaceuticals Inc. and EMS S/A (collectively "Rio"), Sun Pharmaceutical Industries Ltd. and Sun Pharmaceutical Industries, Inc. (collectively "Sun"), Zydus Worldwide DMCC, Zydus Pharmaceuticals (USA) Inc., and Zydus Lifesciences Limited, (collectively "Zydus"), and Mylan Pharmaceuticals Inc. ("MPI") (collectively, "Defendants"). Defendants have asked me to provide my expert opinions regarding the invalidity of claims 4, 5, and 7 of U.S. Patent No. 10,335,462 ("462 patent"). I understand Novo Nordisk, Inc. and Novo Nordisk A/S (collectively, "Plaintiffs" or "Novo") assert that Defendants infringe claims 1, 3, 4, 5, and 7 of the '462 patent ("the asserted claims"). Because claims 1 and 3 of the '462 patent relate only to subject matter outside my area of expertise, I have not been asked to opine on those claims. I therefore address only claims 4, 5, and 7 of the '462 patent, which relate to my technical area of expertise. I reserve the right to address the invalidity of any additional claims later asserted by Plaintiffs.

I. QUALIFICATIONS AND BACKGROUND

A. Education and Experience; Prior Testimony

2. I earned my doctorate at Cambridge University, UK, in 1998 where I studied protein folding mechanisms, using protein engineering to alter the relative stabilities of the native, denatured, intermediate and transition states, and evaluating

B. Claims 4, 5, and 7 of the '462 patent would have been obvious over WO '421, NCT657, WO '537, and/or Lovshin, optionally in view of one or more of the '833 Patent and Madsbad, in view of the knowledge of a POSA

140. In my opinion, claims 4, 5, and 7 of the '462 patent would have been obvious over WO '421, NCT657, WO '537 and/or Lovshin, optionally in view of one or more of the '833 Patent and Madsbad 2011, in view of the knowledge of a person of ordinary skill in the art.

141. In light of the prior art disclosures described here, a POSA would have been further motivated to formulate this subcutaneous injection as an isotonic aqueous solution, including a phosphate buffer at a pH in the range of 7.0-9.0, as required by dependent claim 4. The prior art disclosed semaglutide formulations having pH ranges within, or that substantially overlap with, the pH values recited in the dependent claims of the '462 patent. A POSA would have had a reasonable expectation of success in making such a formulation using conventional techniques known in the pharmaceutical industry as stated in the '833 patent. '833 patent at 12:64–13:3.

142. As explained here, it is my opinion that a POSA would have been further motivated to formulate the isotonic aqueous solution to include propylene glycol and phenol, as required by dependent claims 5 and 7, and would have

reasonably expected such a formulation to have desirable properties based on the teachings of the '833 patent. *See id.*

143. Finally, a POSA would have had a reasonable expectation of success in making such a formulation using conventional techniques based on the disclosures of the '833 patent. *Id.* at 12:64–13:3.

1. The dependent limitations of claim 4 would have been obvious

144. Claim 4 depends from claim 1 and adds the limitation “wherein the semaglutide is administered in the form of an isotonic aqueous solution comprising phosphate buffer at a pH in the range of 7.0-9.0.” '462 patent at 35:49-52. In my opinion, claim 4 of the '462 patent would have been obvious in view of the prior art.

145. As explained above, NCT657 and Lovshin both disclosed that semaglutide had been administered via subcutaneous injection, and therefore taught that semaglutide could be formulated as an injectable solution. NCT657 at 15; Lovshin at 263-264. Further, WO '421 disclosed that GLP-1 analogues, including semaglutide specifically, could be “prepared according to known formulation techniques, e.g. using suitable liquid carriers, which usually comprise sterile water, and, optionally, further additives e.g. for aiding solubility or for preservation or the like, to obtain injectable solutions or suspensions.” WO '421 at 39:23-26, 43:13. Thus, a POSA would have been motivated by WO '421 to formulate semaglutide as an injectable solution with a reasonable expectation of success. Further, as explained

above, a POSA would have been aware that “known formulation techniques” as of the priority date included preparing injectable formulations as isotonic aqueous solutions with a pH in the range of 7.0-9.0, and that phosphate buffers were commonly used. *Supra* Sections VII.A, VII.D.

146. In addition, WO '537 expressly disclosed pharmaceutical formulations comprising GLP-1 compounds, such as semaglutide, along with excipients:

The term “pharmaceutical composition” as used herein means a product comprising an active compound or a salt thereof together with pharmaceutical excipients such as buffer, preservative, and optionally a tonicity modifier and/or a stabilizer. Thus a pharmaceutical composition is also known in the art as a pharmaceutical formulation.

WO '537 at 5:32-35. As explained above, WO '537 disclosed a pharmaceutical formulation comprising a compound in a concentration from 0.1 mg/ml to 25 mg/ml, and wherein said formulation has a pH from 3.0 to 9.0. *See supra* Section VIII.C.

147. Exemplary pH ranges were also provided in WO '537, include examples of formulations having a pH from about 7.0 to about 9.5, about 3.0 to about 7.0., about 5.0 to about 7.5. and from about 7.5 to about 9.0. WO '537 at 24:30 – 25:2; *see also* '833 patent at 15:66–22:21; Knudsen patent at 42:59–43:4; *supra* Section VIII.C.

148. WO '537 also disclosed:

In a further embodiment of the invention the buffer is selected from the group consisting of sodium acetate,

sodium carbonate, citrate, glycylglycine, histidine, glycine, lysine, arginine, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium phosphate, and tris(hydroxymethyl)-aminomethan, bicine, tricine, malic acid, succinate, maleic acid, fumaric acid, tartaric acid, aspartic acid or mixtures thereof.

WO '537 at 25:4-8; *see also* '833 patent at 10:47-57; Knudsen patent at 168:1-6

149. WO '537 also provided a specific example of a pharmaceutical formulation comprising semaglutide, propylene glycol, phenol, and a phosphate buffer, where the pH is 8.15.

Pharmaceutical formulation:

A compound of the invention may be formulated as:

Compound of example 4	6,25 mg/ml
Propyleneglycol	14,0 mg/ml
Phenol	5.5 mg/ml

Phosphate Buffer pH 8.15

WO '537 at 63:10-15; *see also* '833 patent at 16:5-20:41; Knudsen patent at 98:1-8.

150. Accordingly, WO '057 taught that semaglutide could be formulated exactly as it is claimed in the '462 patent. In particular, a POSA would have been motivated by WO '537, including in view of WO '421, Lovshin, and NCT657, to formulate a 1.0 mg dose of semaglutide in the form of an isotonic aqueous solution comprising a phosphate buffer at a pH in the range of 7.0-9.0. And a POSA would

have had a reasonable expectation of success that semaglutide could be formulated in this way in view of the express teachings of at least WO '057.

151. Further, the '833 patent claimed “[a] pharmaceutical formulation comprising at least one GLP-1 agonist, a disodium phosphate dihydrate buffer and propylene glycol, wherein said propylene glycol is present in said formulation in a final concentration of from about 1 mg/ml to about 100 mg/ml and wherein said formulation has a pH of from about 7.0 to 10.0.” ’833 patent at 22:48-54 (claim 1). The ’833 patent explains that disodium phosphate dihydrate is a buffer. *Id.* at 10:47-57.

152. The ’833 patent further claimed “[t]he formulation according to claim 1, wherein the pH of said formulation is about 7.0 to about 8.3.” *Id.* at 22:66-67 (claim 6). As described above in Section VIII.E., Examples 1-6 of the ’833 patent disclosed the use of a phosphate buffer at pH within the range of 7.0-9.0. ’833 patent at 15:66–22:21.

153. The ’833 patent further disclosed:

Where a buffer is to be included in the formulations of the invention, the buffer is selected from the group consisting of sodium acetate, sodium carbonate, citrate, glycylglycine, histidine, glycine, lysine, arginin, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium phosphate, and tris(hydroxymethyl)-aminomethan, or mixtures thereof. . . . In a preferred embodiment of the invention, the buffer is glycylglycine,

sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium phosphate or mixtures thereof.

Id. at 10:47-57.

154. The '833 patent stated that "[t]he inclusion of isotonicity agents in peptide-containing pharmaceutical formulations is widely known." *Id.* at 1:30-31. The POSA would have known that semaglutide is a GLP-1 analogue, which is a peptide.

155. Example 3 of the '833 patent disclosed that "[i]t is believed that similar results [i.e., 'no clogging of the needles'] to those obtained with the above-described propylene glycol-containing formulation would also be obtained if the pH was adjusted to 7.40, 7.70 or 7.90" and disclosed a pH of "7.40, 7.70, 7.90, or 8.15." *Id.* at 20:6-19. Example 4 disclosed a liraglutide composition with a pH of 7.40 containing sodium dihydrogen phosphate. *Id.* at 20:29-35. Example 5 of the '833 patent also disclosed a composition with a pH of 7.4. *Id.* at 20:67.

156. The '833 patent also disclosed:

The formulations of the invention may be prepared by conventional techniques, e.g. as described in Remington's *Pharmaceutical Sciences*, 1985 or in Remington: *The Science and Practice of Pharmacy*, 19th edition, 1995, where such conventional techniques of the pharmaceutical industry involve dissolving and mixing the ingredients as appropriate to give the desired end product.

'833 patent at 12:64–13:3.

157. Thus, as explained above, the '833 patent, like WO '537, expressly disclosed that injectable solutions of GLP-1 analogues could be formulated as an isotonic aqueous solution comprising phosphate buffer at a pH in the range of 7.0-9.0. In my opinion, when WO '421, NCT657, WO '537, and/or Lovshin are read in view of the '833 patent, a POSA would have been motivated to formulate the 1.0 mg semaglutide solution recited in the asserted claims as an isotonic aqueous solution comprising phosphate buffer at a pH in the range of 7.0-9.0. And, in my opinion, a POSA would have had a reasonable expectation of success in view of the prior art, which expressly taught that GLP-1 analogues could be formulated and administered consistent with the limitations of dependent claim 4.

158. For at least these reasons, it is my opinion that claim 4 is invalid as obvious over WO '421, NCT657, WO '537 and/or Lovshin optionally in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge of a POSA.

2. *The dependent limitations of claim 5 would have been obvious*

159. Claim 5 depends from claim 4 and adds the limitation “wherein the solution further comprises propylene glycol and phenol.” '462 patent at 35:53-54. For the same reasons discussed above, the elements of claim 4 would have been obvious over WO '421, NCT657, WO '537 and/or Lovshin, optionally in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge

of a POSA. Further, in my opinion, for many of the same reasons explained above, a POSA would have been motivated to use propylene glycol and phenol in an injectable semaglutide solution.

160. First, WO '537 expressly taught a pharmaceutical formulation that included semaglutide, propylene glycol, phenol, and a phosphate buffer, where the pH is 8.15.

Pharmaceutical formulation:

A compound of the invention may be formulated as:

Compound of example 4 6,25 mg/ml

Propyleneglycol 14,0 mg/ml

Phenol 5.5 mg/ml

Phosphate Buffer pH 8.15

WO '537 at 63:10-15. Indeed, WO '537 disclosed that phenol could be used as a preservative. *Id.* at 25:11-13. WO '537 further disclosed that propylene glycol could be used as an isotonicity agent. *Id.* at 25:34-35. Thus, in my opinion, a POSA would have been motivated to use propylene glycol and phenol in view of WO '537, and would have had a reasonable expectation of success.

161. Second, the '833 patent disclosed the use of propylene glycol as an isotonicity agent in aqueous solutions containing GLP-1 agonists. *See* '833 patent at 24:7-14 (claim 23); *see also id.* at 19:44 (disclosing the use of propylene glycol as

an isotonicity agent). A POSA would have known that semaglutide is a GLP-1 agonist. *Supra* Section VII.B.

162. The '833 patent disclosed that the use of a preservative in pharmaceutical compositions is well-known to the skilled artisan. '833 patent at 10:58-67. In particular, the '833 patent disclosed the use of “phenol (5.0 or 5.5 mg/ml)” as a preservative. *Id.* at 20:14. The '833 patent also disclosed that “[i]n a preferred embodiment of the invention the preservative is phenol or m-cresol.” *Id.* at 10:65-67.

163. The '833 patent further disclosed “that peptide formulations containing propylene glycol at certain concentrations exhibit reduced deposits in production equipment and in the final product and also exhibit reduced clogging of injection devices.” *Id.* at 1:53-57; *see also id.* at 13:43-45 (Disclosing “the ability of propylene glycol to reduce clogging of injection devices when compared to other isotonic agents and to mannitol in particular.”). The '833 patent also disclosed that “[t]he present invention further relates to a method for reducing the clogging of injection devices by a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.” *Id.* at 2:58-62.

164. Accordingly, in my opinion, a POSA would have been highly motivated to use propylene glycol in a semaglutide solution formulation in view of

the '833 patent. Further, it is my opinion that a POSA would have been motivated to use both phenol and propylene glycol in view of the '833 patent, and would have had a reasonable expectation of success.

165. For at least these reasons, and the reasons discussed above with respect to claim 4, claim 5 is invalid as obvious over WO '421, NCT657, WO '537 and/or Lovshin, optionally in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge of a POSA.

3. *The dependent limitations of claim 7 would have been obvious*

166. Claim 6 depends from claim 4 and adds the limitation “wherein the pH is 7.4.” '462 patent at claim 6. Claim 7 depends from claim 6 and adds the limitation “wherein the solution further comprises propylene glycol and phenol.” '462 patent at claim 7. Thus, I understand claim 7 of the '462 patent requires the solution of claim 4 to include propylene glycol and phenol, and to have a pH of 7.4.

167. For the same reasons set forth above, it is my opinion that a POSA would have been motivated to use both propylene glycol and phenol, and would have had a reasonable expectation of success, in view of WO '421, NCT657, WO '537 and/or Lovshin, optionally in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge of a POSA. *Supra* Section IX.B.2. Further, in my opinion, a POSA would have been motivated to prepare the semaglutide solution having a pH of 7.4 in view of the prior art.

168. First, WO '537 disclosed exemplary pH ranges for a semaglutide formulation:

In another embodiment of the invention the pH of the formulation is from about 7.0 to about 9.5. In another embodiment of the invention the pH of the formulation is from about 3.0 to about 7.0. In another embodiment of the invention the pH of the formulation is from about 5.0 to about 7.5. In another embodiment of the invention the pH of the formulation is from about 7.5 to about 9.0. In another embodiment of the invention the pH of the formulation is from about 7.5 to about 8.5. In another embodiment of the invention the pH of the formulation is from about 6.0 to about 7.5. In another embodiment of the invention the pH of the formulation is from about 6.0 to about 7.0. In another embodiment the pharmaceutical formulation is from 8.0 to 8.5.

Id. at 24:30–25:2. Accordingly, a POSA would have understood from WO '537 that one pH suitable for a semaglutide solution would be 7.4.

169. Second, as explained above, Example 3 of the '833 patent disclosed that “similar results [i.e., ‘no clogging of the needles’]” if the pH was adjusted to 7.40, 7.70 or 7.90 and disclosed a pH of “7.40, 7.70, 7.90, or 8.15.” '833 patent at 20:6-19. Example 4 disclosed a liraglutide composition with a pH of 7.40 containing sodium dihydrogen phosphate (20:29-35) and Example 5 disclosed a pH of 7.4 (20:67). Examples 1-6 of the '833 patent (each exemplary formulation) further disclosed the use of a phosphate buffer at pH within the range of 7.0-9.0. *Id.* at 15:66–22:21.

170. Accordingly, in my opinion, a POSA would have been motivated to use a pH of 7.4 in view of the '833 patent, and would have had a reasonable expectation of success. In particular, it is my opinion that a POSA would have been motivated to use a pH of 7.4 in a semaglutide solution, and would have had a reasonable expectation of success, in view of WO '421, NCT657, WO '537 and/or Lovshin, optionally in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge of a POSA.

171. In my opinion, for at least these reasons, and the reasons discussed above with respect to claims 4 and 5, claim 7 is invalid as obvious over WO '421, NCT657, WO '537 and/or Lovshin in view of the '833 Patent, optionally in view of Madsbad 2011, and in view of the knowledge of a person of ordinary skill in the art.

4. Conclusion

172. For each of claims 4, 5, and 7 of the '462 patent, it is my opinion that a POSA would have been motivated to formulate the claimed semaglutide dose into an isotonic aqueous solution that includes a phosphate buffer, propylene glycol, and phenol, at a pH in the range of 7.0-9.0, specifically at a pH of 7.4. Indeed, the prior art expressly disclosed semaglutide formulations having these ingredients and properties (i.e., the claimed excipients, aqueous isotonic solutions, pH ranges within, or that overlap with, the claimed pH values recited in the dependent claims of the '462 patent). And a POSA would have had a reasonable expectation of success of

making such a formulation using conventional techniques known to a POSA. My opinions are limited to the formulation elements in claims 4, 5, and 7 of the '462 patent. However, Defendants' medical and clinical experts' opinions are that WO '537 disclosed all treatment-related elements of the asserted claims of the '462 patent. Thus, the asserted claims of the '462 patent would have been obvious over WO '421, NCT657, WO '537, and/or Lovshin, optionally in view of one or more of the '833 Patent and Madsbad, in view of the knowledge of a person of ordinary skill in the art.

C. Claims 4, 5, and 7 of the '462 patent would have been obvious over WO '421 alone or in view of the '833 patent

173. As explained above, claims 4, 5, and 7 of the '462 patent recite a method for treating type 2 diabetes, comprising once-weekly administration of 1.0 mg of semaglutide with the following properties and excipients: (1) as an isotonic aqueous solution for subcutaneous injection; (2) with propylene glycol and phenol; (3) with a phosphate buffer; and/or (4) with a pH in the range of 7.0-9.0, and at 7.4 specifically. In my opinion, a POSA would have been motivated to formulate the claimed dose of semaglutide with the claimed excipients and properties in view of WO '421 further in view of the '833 patent.

174. First, I explained above why the limitations of claims 4, 5, and 7 would have been obvious in view of the '833 patent. *Supra* Section IX.B. For those same

reasons, it is my opinion that a POSA would have been motivated by the '833 patent to formulate semaglutide with the excipients and properties recited in the formulation claims.

175. In addition, in my opinion, when WO '421 is read in view of the '833 patent, the formulations claims would have been obvious. WO '421 disclosed “methods for treating and/or preventing metabolic diseases, especially type 2 diabetes mellitus, obesity and/or conditions related thereto (e.g. diabetic complications) comprising the combined administration of a GLP-1 receptor agonist (e.g. exogenous GLP-1 or a GLP-1 analogue) and a certain DPP-4 inhibitor.” WO '421 at 1:4-7. WO '421 further disclosed that “[p]referred examples of GLP-1 receptor agonists (GLP-1 analogues) of this invention are exenatide, exenatide LAR, liraglutide, taspoglutide, *semaglutide*, albiglutide, lixisenatide and dulaglutide.” *Id.* at 33:20-22 (emphasis added).

176. Further, as explained above, WO '421 disclosed that injectable formulations of GLP-1 receptor agonists “may be prepared according to known formulation techniques, e.g. using suitable liquid carriers, which usually comprise sterile water, and, optionally, further additives e.g. for aiding solubility or for preservation or the like, to obtain injectable solutions or suspensions.” WO '421 at 39:23-26. And WO '421 disclosed that injectable formulations of GLP-1 receptor agonists “may be prepared according to known formulation techniques, e.g. using

suitable liquid carriers, which usually comprise sterile water, and, optionally, further additives e.g. for aiding solubility or for preservation or the like, to obtain injectable solutions or suspensions.” *Id.* at 39:23-26. Thus, a POSA would have been motivated by WO ’421 to formulate semaglutide as an injectable solution with a reasonable expectation of success. Further, as explained above, a POSA would have been aware that “known formulation techniques” as of the priority date included preparing injectable formulations as isotonic aqueous solutions with a pH in the range of 7.0-9.0, and that phosphate buffers were commonly used. *Supra* Sections VII.A, VII.D, IX.A.

177. Accordingly, in my opinion, the formulation claims would have been obvious in view of WO ’421 and the ’833 patent. In my opinion, a POSA would have been motivated to formulate the claimed semaglutide dose into an isotonic aqueous solution that includes a phosphate buffer, propylene glycol, and phenol, at a pH in the range of 7.0-9.0, including at a pH of 7.4 specifically. Indeed, the prior art expressly disclosed semaglutide formulations having these ingredients and properties (i.e., the claimed excipients, aqueous isotonic solutions, pH ranges within, or that overlap with, the claimed pH values recited in the dependent claims of the ’462 patent). And a POSA would have had a reasonable expectation of success of making such a formulation using conventional techniques known to a POSA.

D. Claims 4, 5, and 7 of the '462 patent would have been obvious over WO '537 considering Lovshin

178. In my opinion, claims 4, 5, and 7 of the '462 patent would have been obvious over WO '537 considering Lovshin. I explain why the challenged claims would have been obvious in view of these references.

179. First, as explained above, claims 4, 5, and 7 of the '462 patent recite a method for treating type 2 diabetes, comprising once-weekly administration of 1.0 mg of semaglutide with the following properties and excipients: (1) as an isotonic aqueous solution for subcutaneous injection; (2) with propylene glycol and phenol; (3) with a phosphate buffer; and/or (4) with a pH in the range of 7.0-9.0, and at 7.4 specifically. In my opinion, a POSA would have been motivated to formulate the claimed dose of semaglutide with the claimed excipients and properties in view of WO '537 and Lovshin.

180. I also explained above why the formulation claims would have been obvious in view of WO '537. *Supra* Section IX.B. For those same reasons, it is my opinion that a POSA would have been motivated by WO '537 to formulate semaglutide with the excipients and properties recited in the formulation claims.

181. Further, as mentioned herein, Lovshin disclosed that NN9535 (i.e., semaglutide), was being investigated for once weekly dosing in the 0.1-1.6 mg dose range. Lovshin at 263. It would have been routine to a POSA to optimize the

formulation to contain a 1.0 mg dose of semaglutide. Accordingly, in view of WO '537 considering Lovshin, and in light of the state of the art, a POSA would have been motivated to formulate semaglutide as an isotonic aqueous solution for subcutaneous injection, with propylene glycol and phenol, a phosphate buffer, and a pH in the range of 7.0-9.0, including at a pH of 7.4, with a reasonable expectation of success.

X. RESERVATION OF RIGHTS

182. I reserve the right to supplement and/or expand on the opinions I have set forth in this report based on the information I have reviewed and/or based on any additional information produced in discovery, modifications of the Court's claim construction, in response to any expert reports submitted on behalf of Plaintiffs, or any other circumstances that may impact my opinions.

183. Moreover, at trial I may rely upon documents and/or other materials produced in this litigation, publicly available documents, and/or any documents the parties have exchanged, such as discovery responses. Additionally, I may rely on visual aids and/or demonstrative exhibits that I prepare or have been prepared on my behalf based upon my opinions.

I declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Dated: March 19, 2024

By: 

Dr. Paul Dalby