IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: SITAGLIPTIN PHOSPHATE ('708 & '921) PATENT LITIGATION	MDL No. 19-2902-RGA C.A. Nos. 19-310-RGA, 19-311-RGA, 19-312-RGA, 19-313-RGA, 19-314-RGA, 19-317-RGA, 19-318-RGA, 19-319-RGA, 19-347-RGA, 19-1489-RGA,

REPLY DECLARATION OF PROFESSOR ALLAN S. MYERSON, Ph.D.
REGARDING CLAIM CONSTRUCTION

TABLE OF CONTENTS

I, Allan S. Myerson, declare as follows:

I. BACKGROUND

1. I have reviewed the Declaration of Dr. Graham Buckton, dated May 4, 2020, ("Buckton Dec.") and the attached exhibits, submitted on behalf of Teva Pharmaceuticals USA and Watson Laboratories, Inc.; Sandoz Inc.; Lupin Limited and Lupin Pharmaceuticals, Inc.; Anchen Pharmaceuticals, Inc. and Par Pharmaceutical, Inc.; and Wockhardt Bio AG and Wockhardt USA LLC; Sun Pharmaceutical Industries Ltd; Apotex Inc. and Apotex Corp.; and Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Limited (collectively, "Defendants"). In this declaration, I will respond to the opinions set forth in Dr. Buckton's declaration.

2. In reaching the opinions I express herein, I have considered the '708 patent and its prosecution history, the materials cited in this declaration, my previous Declaration Regarding Claim Construction dated March 20, 2020 ("Opening Dec.") and the materials cited therein, as well as my training, general knowledge, basic principles, and experience in the relevant scientific disciplines.

II. THE PERSON OF ORDINARY SKILL IN THE ART

3. I understand that Dr. Buckton provided a slightly different definition of the person of ordinary skill in the art ("POSA"). *See* Buckton Dec. ¶24. My opinions would not change under his definition of the POSA.

III. CLAIM CONSTRUCTION

A. "the salt of claim 1 [or 2] . . ." (claims 2, 3, and 21 of the '708 patent)

4. Dr. Buckton did not provide an opinion on this term. Particularly, he did not rebut my opinion that a hydrate is a type of salt, and that the POSA would understand the reference to the "salt of claim 1" in the '708 patent claims 2, 3 and 21 to include all forms of salts, including hydrates. *See* Opening Dec. ¶61.

5. As discussed in my previous declaration, salts are electrically neutral compounds that consist of atoms or molecules held together via bonds that include some degree of ionic transfer between the acid and the base. *See* Opening Dec. ¶29.

6. Pharmaceutical salts can sometimes exist as crystalline solids, which in turn can potentially take different crystalline forms. Different crystalline forms have different arrangements in their three dimensional crystalline lattice. One type of crystalline form is known as a hydrate. A hydrate is a crystalline form of a given compound in which water is part of the crystalline lattice. The POSA would understand that hydrates are a type of pharmaceutical salt. J.A. 37 (Giron),[1] 73 (using tetracaine hydrochloride to describe a monohydrate, tetrahydrate, and hemihydrate); J.A. 38 (Bastin),[2] 432 ("The methanesulfonate salt, however, was a stable monohydrate form . . . .").

7. Consistent with this general understanding, the '708 patent repeatedly refers to hydrates as being a type of salt. J.A. 1 ('708 Patent), 4:13–18 ("the dihydrogenphosphate salt drug substance is substantially phase pure monohydrate"); 4:24–26 ("In particular, the enhanced chemical and physical stability of the crystalline dihydrogenphosphate salt monohydrate constitutes advantageous properties . . . "); 5:12–13 ("crystalline dihydrogenphosphate salt monohydrate"); 5:15–16 (same); 6:27 (same); 6:52–53 (same); 14:64–65 (same); 14:66–67 (same); 15:5–6 (same); 15:16 (same); 15: 31 (same); Example 8; 13:30–31 ("crystalline monohydrate form of the dihydrogenphosphate salt"); 13:37–38 (same); 13: 65–66 (same); 14:14–15 (same); 14:30–31 (same); 14:48–49 (same); 15:47–48 (same).

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[1] D. Giron and D.J.W. Grant, "Evaluation of Solid-State Properties of Salts," in HANDBOOK OF PHARMACEUTICAL SALTS, P.H. Stahl, C.G. Wermuth (Eds.) (2002).

[2] R.J. Bastin, M.J. Bowker, B.J. Slater, "Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities," *Organic Process Research & Development* 4:427-35 (2000).

8. Claim 1 of the '708 patent covers "a dihydrogenphosphate salt [of sitagliptin] of structural formula I or a hydrate thereof." The "dihydrogenphosphate salt … " limitation recites a compound "of structural formula I" that is and must be present in any polymorphic form, without specifying which form. For example, the "dihydrogenphosphate salt … of structural formula I" is present in the hydrate form. *Id*. at 2:63–65 ("In particular, the instant invention provides a crystalline monohydrate of the dihydrogenphosphate salt of formula I"); 3:53–55 ("In a further embodiment of the present invention, the dihydrogenphosphate salt of structural formulae I-III is a crystalline hydrate."); 3:57–60 ("A further embodiment of the present invention provides the dihydrogenphosphate salt drug substance of structural formulae I-III that comprises the crystalline monohydrate present in a detectable amount."); 6:26–29 ("The solubility of the crystalline dihydrogenphosphate salt monohydrate of formula I in water has been found to be about 72 mg/mL."); 6:56–60 ("General Methods for Crystallizing the Monohydrate of the Dihydrogenphospahte Salt of Structural Formula I."); 15:47-50 ("An intravenous (i.v.) aqueous formulation is defined as the monohydrate of dihydrogenphosphate salt of formula I in 10mM sodium acetate/0.8% saline solution at pH 4.5±0.2."). I do not understand these points to be in dispute. Further, the image of the compound in structural formula I indicates that there are no restrictions on the chirality of the compound; claim 1 does not speak at that level of specificity with respect to chirality.

9. As discussed in my previous declaration (Opening Dec. ¶62), claims 2 and 3 of the '708 patent limit the compound in structural formula I by imposing a chirality requirement, effectuated by replacing structural formula I with structural formulas II and III, respectively. This is illustrated using the wedge-dash notation to recite the (R)- and (S)- configurations, respectively, of the salt of claim 1. As with structural formula I, the written description of the

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