UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

MERCK SHARP & DOHME CORP.,
Patent Owner.

Case IPR2020-00040
U.S. Patent 7,326,708

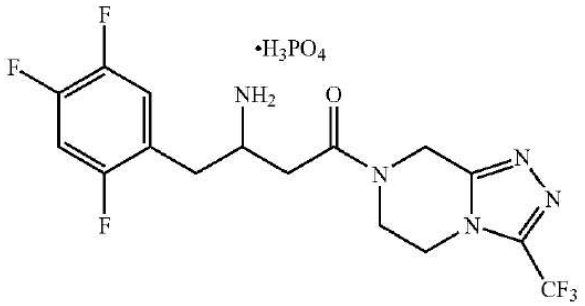
DECLARATION OF KARL B. HANSEN, PH.D.

I, Karl B. Hansen, Ph.D., hereby declare as follows:

I. INTRODUCTION

1. I am a named inventor of subject matter claimed in U.S. Patent No. 7,326,708 ("the '708 patent"). I understand that Merck Sharp & Dohme Corp. ("Merck") is the owner and assignee of the '708 patent.

2. I understand that claim 1 of the '708 patent recites a dihydrogenphosphate ("DHP") salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4] triazolo[4,3-a]pyrazine-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine, a compound also known as sitagliptin, in which the DHP counterion and the sitagliptin freebase are present in 1:1 stoichiometric ratio.



3. In this declaration, I provide facts about which I have first-hand knowledge regarding Merck's research and development of sitagliptin into the FDA-approved drug, Januvia®. In particular, I provide information related to my role in synthesizing and characterizing the claimed 1:1 DHP salt of sitagliptin, the timing of that synthesis and characterization, and my efforts to form and characterize its crystal polymorphs.

II. BACKGROUND

4. I received my doctorate in organic chemistry from Harvard University in 1998 and my B.S. in chemistry from the University of Delaware in 1993.

5. After receiving my Ph.D., I joined the Process Research department of Merck Research Laboratories ("MRL") as a Senior Research Chemist. My responsibilities principally focused on the development of robust chemical syntheses suitable for commercial scale-up of drug candidates under development by Merck. A significant portion of my work was devoted to the synthesis and identification of new salt forms, as well as their selection and optimization in terms of pharmaceutical properties, an area in which I have substantial experience.

6. In this declaration, I have cited certain documents from Merck's archives related to the research and development of sitagliptin and Januvia®, including several lab notebooks and weekly reports. I maintained several lab notebooks over the course of my career at Merck and am generally familiar with Merck's practices regarding lab notebooks during that time. In the usual and ordinary course of its business, Merck issued numbered lab notebooks to scientists for the purpose of recording their daily research activity. Each lab notebook page was numbered and individual entries typically included information regarding the project or compound for which the experiment was run. Entries in my lab notebooks were made by me at or near the time that I conducted each experiment.

It was also my customary practice (and one generally shared by my colleagues) to refer to particular lab notebook numbers and pages to track samples and/or experimental procedures (*e.g.*, "NB 70316-043"). I recorded my work regarding sitagliptin in several lab notebooks, true and correct excerpts of which may be found in EX2128 (Lab Notebook ("LNB") 70130), EX2129 (LNB 70316), and EX2130 (LNB 72471).

7. During my time at Merck, scientists in the Process Research department submitted weekly reports summarizing their activities at or near the time they submitted the report. These reports were generated in the usual and ordinary course of business to track the work of individual scientists. True and correct copies of weekly reports submitted by me in January, February, March, April and November of 2002 may be found in EX2131.

8. In 2006, I left Merck to join Amgen, where I was eventually promoted to Scientific Director for Process Development. While at Amgen, I led, participated, and was accountable for multi-disciplinary teams that discovered, developed and selected optimal salt forms and polymorph of drug candidates. In 2018, I joined Boston Pharmaceuticals where I became the Vice President for Chemistry, Manufacturing, and Controls ("CMC"). I am currently employed as the Senior Vice President for CMC at Praxis Precision Medicines.

III. SYNTHESIS AND CHARACTERIZATION OF SITAGLIPTIN SALTS

9. In or around January 2002, I joined the Merck team developing L-224715, the internal Merck designation for sitagliptin. I understood that L-224715 had been internally approved at Merck for clinical development as part of Merck's overall project to develop an inhibitor of the enzyme dipeptidyl-peptidase IV ("DPP-IV") into an oral treatment for type 2 diabetes. When I joined the DPP-IV project team, I joined the effort to develop sitagliptin into a dosage form suitable for administration to humans as part of clinical trials designed to investigate sitagliptin's safety and efficacy at inhibiting DPP-IV in patients, and eventually, for approval by the FDA for the treatment of type 2 diabetes.

10. In January 2002, a primary focus of the DPP-IV project team was to identify crystalline salts of L-224715 suitable for further research and development. The salt selection process for sitagliptin required both the synthesis and identification of candidate salts, as well as the development and scale-up of the synthesis reactions to produce quantities of the candidate salts sufficient to characterize their physical properties.

A. Initial Salt Formation Experiments

11. The initial synthesis and identification of sitagliptin salts was assigned to Vicky Vydra—a colleague of mine at Merck and a named co-inventor of the '708 patent. In December 2001, Ms. Vydra conducted a series of salt formation

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