IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA AB, Plaintiff, v. AUROBINDO PHARMA LTD. and AUROBINDO PHARMA U.S.A., INC, Defendants.	)	C.A. No. 14-cv-664-GMS (CONSOLIDATED)

DEFENDANTS' JOINT INITIAL INVALIDITY CONTENTIONS
REGARDING U.S. PATENT NO. RE 44,186

Defendants (i) Aurobindo Pharma Ltd. and Aurobindo Pharma U.S.A., Inc. ("Aurobindo"); (ii) Wockhardt Ltd. and Wockhardt USA LLC ("Wockhardt"); (iii) Actavis Laboratories FL, Inc. and Watson Laboratories, Inc. ("Actavis"); (iv) Mylan Pharmaceuticals Inc. ("Mylan); (v) Sun Pharma Global FZE and Sun Pharmaceutical Industries Ltd. ("Sun"); and (vi) Amneal Pharmaceuticals LLC ("Amneal") (collectively, Aurobindo, Wockhardt, Actavis, Mylan, Sun and Amneal are referred to herein as "Defendants"), through their undersigned counsel, hereby provide the following Joint Initial Invalidity Contentions Regarding U.S. Patent No. RE 44,186 ("the RE '186 patent") to Plaintiff AstraZeneca AB ("Plaintiff" or "AstraZeneca"). Defendants contend that each of the asserted claims of the RE '186 patent are invalid under at least 35 U.S.C. §§ 103 and/or 251. Defendants reserve the right to supplement these Initial Invalidity Contentions pursuant to the Federal Rules of Civil Procedure, Local Rules, Default Guidelines and/or Court's Orders.

Discovery and investigation regarding the RE '186 patent and potential grounds for

invalidity is ongoing. This disclosure is made in good faith and based upon Defendants' present understanding of the claims being asserted by Plaintiff in Plaintiff's initial infringement contentions directed to each Defendant. In the absence of a claim construction order from the Court, Defendants have based their Initial Invalidity Contentions on their preliminary constructions of the asserted claims of the RE '186 patent. Further, Defendants object to any attempt to imply claim construction from their identification or discussion of prior art in the attached exhibits. In addition, if Plaintiff revises those contentions to add additional claims, then Defendants reserve the right to amend their contentions to include invalidity contentions for those newly added claims. Defendants reserve the right, without prejudice, to supplement these Initial Invalidity Contentions as additional research is conducted, prior art is discovered, discovery is obtained, supplements or modifications are made to the infringement theories advanced by Plaintiff, claim construction positions are taken or orders issued, expert discovery is obtained, and for any other reason permitted under the Federal Rules of Civil Procedure, Local Rules, and/or the Court's Orders.

INVALIDITY OF ASSERTED CLAIMS OF THE RE '186 PATENT

Plaintiff has asserted claims 8, 9, 25 and 26 of the RE '186 patent (the "Asserted Claims") against each of the Defendants. Each of the Asserted Claims is invalid as obvious under 35 U.S.C. § 103, or alternatively, as invalid under 35 U.S.C. § 251. Claim charts demonstrating Defendants' invalidity contentions for the Asserted Claims are provided in Exhibit A.

The RE '186 patent, entitled "Cyclopropyl Fused Pyrrolidine-Based Inhibitors of Dipeptidyl Peptidase IV and Method," issued on April 20, 2013 from U.S. Patent Application No. 13/308,658 ("the '658 application). The '658 application, filed on December 1, 2011 is a reissue application of U.S. Patent No. 6,395,767 ("the '767 patent"), which issued on May 28,

2002 to Bristol-Myers Squibb Company. The '767 patent issued from the U.S. Patent Application No. 09/788,173 ("the '173 application") which was filed on February 16, 2001. The '173 application claims priority to U.S. Provisional Application No. 60/188,555 filed on March 10, 2000. Therefore, the earliest possible priority date for the RE '186 patent is March 10, 2000.[1]

The RE '186 patent generally relates to cyclopropyl-fused pyrrolidine-based inhibitors of dipeptidyl peptidase IV, pharmaceutical combinations, and methods of treatment involving such inhibitors and/or pharmaceutical combination. All of the Asserted Claims of the RE '186 patent recite compounds including saxagliptin or pharmaceutically acceptable salts thereof.

I. The Asserted Claims of the RE '186 Patent are Invalid as Obvious

Each of Asserted claims 8, 9, 25 and 26 of the RE '186 patent would have been obvious to a person of ordinary skill in the art at the time of the invention. The obviousness inquiry takes into account the following factors: (1) the level of ordinary skill in the art at the time the invention was made; (2) the scope and content of the prior art; (3) the differences between the prior art and the claims at issue; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Each of these factors is discussed below.

[1] Less than one week before the March 12, 2015 deadline for Defendants' service of initial invalidity contentions regarding the RE '186 patent, on March 6, 2015, AstraZeneca served a supplemental response to Defendants' Joint Interrogatory No. 1 in which AstraZeneca has indicated that it may allege that the "assertable dates of invention for the asserted patents" may be prior to March 10, 2000. As of March 12, 2015, AstraZeneca has produced no documentation to support the claims set forth in its March 6, 2015 supplemental response to Defendants' Joint Interrogatory No. 1. Further, AstraZeneca has not formally asserted a date of invention for the asserted claims of the RE '186 patent prior to the March 10, 2000 earliest priority date of the RE '186 patent. Defendants reserve the right to supplement and revise their contentions based on AstraZeneca's possible future assertion of prior invention and identification of documents supporting any such claim or other reasons.

A. The Level of Ordinary Skill in the Art

The court conducts the obviousness analysis from the perspective of a person of ordinary skill in the art. The level of skill in the art is a fact-specific inquiry determined on a case-by-case basis. Based on the currently available facts, for purposes of these Initial Invalidity Contentions, Defendants assert that a person of ordinary skill in the art relevant to the RE '186 patent, is an organic chemist, a medicinal chemist, a pharmaceutical chemist or a related scientist with a Ph.D. or an equivalent advanced degree in their field of practice with several years' practical experience designing, discovering, testing and/or optimizing new pharmaceutical chemicals for potential and eventual human use. The person of ordinary skill also has familiarity with dipeptidyl-peptidase IV ("DPP-IV") inhibitors, as well as with amino acids and amino acid analogs as well as the chemistry of peptides and peptidomimetics, and enzyme-substrate interactions and chemical homology of substrates interacting with a given enzyme or protein.

Defendants' definition of a person of ordinary skill in the art may change, depending on what is discovered during litigation, including evidence related to the type of problems encountered in art; prior art solutions to those problems; rapidity with which innovations were made; sophistication of the technology; and educational level of active workers in the field. The conclusions set forth in these Initial Invalidity Contentions would not change even if this definition is changed substantially and significantly.

B. The Scope and Content of the Prior Art

Each asserted claim of the RE '186 patent would have been obvious to a person of ordinary skill in the art at the time of the invention, based on the collective teachings of the prior art.

The scope and content of the prior art generally is determined by examining "the field of the inventor's endeavor" and "the particular problem with which the inventor was involved" at

"the time the invention was made." *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 881 (Fed. Cir. 1998). In determining the scope and content of the prior art, the court first obtains an understanding of the asserted invention and claimed in the application or patent by reading the specification, including the claims, to understand what the applicant or patentee has invented. *Id.*; Manual of Patent Examination Procedure (MPEP) § 904.

Prior to the filing date of the RE '186 patent, there existed several oral anti-diabetic agents with different mechanism of action, such as hepatic glucose suppressors, insulin secretagogues, glucose absorption inhibitors, and insulin sensitizers. A person of ordinary skill knew, however, that each had significant limitations and side effects. Therefore, there existed a motivation to develop a new oral anti-diabetic agent that would not only provide an efficacious alternative mechanism for lowering blood glucose and glycosylated hemoglobin (HbA1c) levels, but also would have acceptable safety and tolerability profiles. A drug that worked through an alternative mechanism would also allow it to be combined with existing treatment agents for combined and synergistic effects. As of this time period, the use of multiple oral anti-diabetic agents was an emerging standard of treatment paradigm for type-2 diabetes therapy.

Also as of this time period, a person of ordinary skill in the art knew that glucagon like peptide-1 (GLP-1) was a desired target for diabetic patients. GLP-1 is a 30-amino acid peptide incretin hormone derived from processing of pro-glucagon, and is secreted by the L-cells of the intestinal mucosa in response to glucose stimulation. Since the early 1990's, the GLP-1 had been known to be a potent insulin secretagogue and glucagon suppressor, with robust anti-diabetic and pro-satiety effects in diabetic humans.[2] Parenteral versions of GLP-1 receptor agonists, such as Byetta (exenatide) and Victoza (liraglutide), have been developed.

[2] *See* M.A. Nauck et al., *Effects of subcutaneous glucagon-like peptide 1 (GLP-1 [7-36 amide]) in patients with NIDDM*, Diabetologia, 39 (12), 1546-53 (1996).

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