IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GLAXOSMITHKLINE LLC (f/k/a SMITHKLINE BEECHAM CORPORATION),	:	C.A. 11-046-RGA
Plaintiff,	:	
v.	:	
ANCHEN PHARMACEUTICALS, INC; ANCHEN, INC.; BANNER PHARMACAPS, INC.; ROXANE LABORATORIES, INC; WATSON LABORATORIES, INC. – FLORIDA; MYLAN, INC.; MYLAN PHARMACEUTICALS, INC.; and IMPAX LABORATORIES, INC.,	:	
Defendants.	:	

CLAIM CONSTRUCTION OPINION

Jack B. Blumenfeld, Esq., Wilmington, Delaware; William F. Lee, Esq. (argued), Boston, Massachusetts; Attorneys for Plaintiff GlaxoSmithKline LLC.

John C. Phillips, Jr., Esq., Wilmington, Delaware; Christy G. Lea, Esq. (argued), Irvine, California; C. Kyle Musgrove, Esq. (argued), Washington, D.C.; Attorneys for Defendants.

November 15, 2012
Wilmington, Delaware

ANDREWS, UNITED STATES DISTRICT JUDGE:

Plaintiff GlaxoSmithKline LLC ("GSK") filed a patent infringement suit against Defendants Anchen Pharmaceuticals, Inc., Anchen, Inc., Banner Pharmacaps, Inc., Roxane Laboratories, Inc., Watson Laboratories, Inc. – Florida, Mylan, Inc., Mylan Pharmaceuticals, Inc., and Impax Laboratories, Inc. (collectively "Defendants"). GSK claims that Defendants infringed three of its patents: U.S. Patent No. 5,565,467, U.S. Patent No. 5,846,976, and U.S. Patent No. 5,998,427. This is a claim construction opinion.

INTRODUCTION

All three patents claim drug compounds related to the treatment of androgen responsive or mediated conditions, such as prostatic hyperplasia. The compound dihydrotestosterone ("DHT") plays an essential role in the development of the prostate, but also can cause undesired androgen action resulting in an enlarged prostate. DHT is formed when testosterone is catalyzed by 5-α reductase enzymes. The asserted patents claim a compound known as dutasteride, which inhibits 5-α reductase enzymes and thus the conversion of testosterone to DHT. An important feature of dutasteride is that it does not inhibit a compound known as 3βHSD, as the inhibition of 3βHSD by a non-selective 5-α reductase inhibitor has been shown to cause liver toxicity.

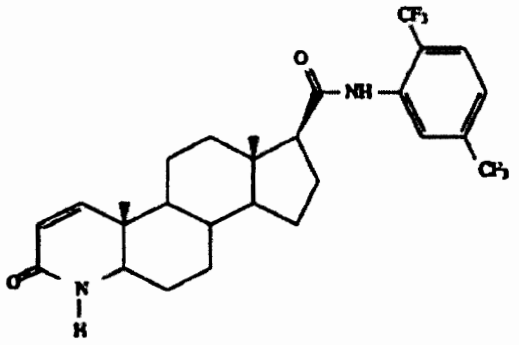
Each Defendant has filed at least one Abbreviated New Drug Application ("ANDA") seeking to market generic versions of GSK products containing dutasteride. GSK alleges that each Defendant infringes one or more of the asserted patents. Specifically, GSK has asserted claims 1–5 of the '467 Patent against Anchen and Watson; claims 1–3 of the '467 Patent, claims 1–3 of the '976 Patent, and claim 10 of the '427 Patent against Mylan and Banner; claims 1–3 of the '467 Patent, claims 1–3 of the '976 Patent, and claim 10 of the '427 Patent against Roxane;

and claims 1–5 of the '467 Patent, claims 1–4 of the '976 Patent, and claim 10 of the '427 Patent against Impax. The parties agree upon the construction of one claim term and dispute the construction of two claim terms.

AGREED UPON CONSTRUCTION

A. 17β-N-(2,5-bis(Trifluoromethyl)) phenylcarbamoyl-4-aza-5α-androst-1-en-3-one

The parties agree that the term "17β-N-(2,5-bis(Trifluoromethyl)) phenylcarbamoyl-4-aza-5α-androst-1-en-3-one" should be construed to mean "A compound having the following chemical structure:



(i.e., dutasteride)."

DISPUTED CONSTRUCTIONS

A. Term 1 - "solvate thereof"

GSK's Proposed Construction (as used in claims 1-5, '467 Patent; claims 1-4, '976 Patent):	A complex formed by dutasteride with a solvent in which dutasteride is reacted or from which it is precipitated or crystallized.
Defendants' Proposed Construction (as used in claims 1-5, '467 Patent; claims 1-4, '976 Patent):	A complex of dutasteride molecules and solvent molecules, wherein the complex is in crystalline form such that the dutasteride molecules and solvent molecules are part of the same crystal structure.
Court's Construction (as used in claims 1-5, '467 Patent; claims 1-4, '976 Patent):	A complex formed by dutasteride with a solvent in which dutasteride is reacted or from which it is precipitated or crystallized.
GSK's Proposed Construction (as used in claim 10, '427 Patent):	A complex formed by a compound of formula (I) (as defined in claim 1) with a solvent in which that compound is reacted or from which it is precipitated or crystallized.
Defendants' Proposed Construction (as used in claim 10, '427 Patent):	A complex of molecules of a compound of formula (IB) and solvent molecules, wherein the complex is in crystalline form such that the molecule of a compound of formula (IB) and solvent molecules are part of the same crystal structure.
Court's Construction (as used in claim 10, '427 Patent):	A complex formed by a compound of formula (I) (as defined in claim 1) with a solvent in which that compound is reacted or from which it is precipitated or crystallized.

The parties dispute the construction of the term "solvate thereof" as used in claims 1-5 of the '467 Patent, claims 1-4 of the '976 Patent and claim 10 of the '427 Patent. The parties agree that "solvate" as used therein is a complex of dutasteride and a solvent. They disagree over whether "solvate" is limited to the crystalline form or whether it can also be reacted or precipitated. GSK argues that the specifications explicitly define "solvate" as a complex that may be reacted, precipitated, or crystallized, i.e., a complex not limited to the crystalline form. Defendants counter that the specifications call for "solvate" to be defined by its generally

accepted meaning in organic chemistry. They contend that this generally accepted meaning does in fact limit "solvate" to the crystalline form.

The parties debate the significance of the following passage from the '467 Patent's specification, both arguing that it supports their respective constructions:

> Those skilled in the art of organic chemistry will appreciate that many organic compounds can form complexes with solvents in which they are reacted or from which they are precipitated or crystallized. These complexes are known as "solvates."

'467 Patent, ll. 3:58-4:02. GSK argues that this passage is definitional as it expressly states that "solvates" may not only be crystallized, but also reacted or precipitated. Defendants disagree, arguing that the specification never suggests that "solvates" are reacted or precipitated. Instead, the reacted, precipitated, or crystallized characteristics refer to characteristics of solvents that may be combined with the organic compound to form the "solvates," rather than the characteristics of the "solvates" themselves. (D.I. 217, p. 18). Defendants further argue that "solvates" is due its ordinary meaning as understood by those skilled in the art of organic chemistry, which is limited to the crystalline form.

"It is well-established that the patentee can act as his own lexicographer, so long as he clearly states any special definitions of the claim terms in the patent specification or file history." *Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1300 (Fed. Cir. 2004). Even when guidance is not provided in explicit definitional format, "the specification may define claim terms 'by implication' such that the meaning may be 'found in or ascertained by a reading of the patent documents.'" *Id.* Here, the most natural reading of the specification confirms that "solvates" are defined as complexes that may be reacted, precipitated, or crystallized. The sentence begins by introducing complex formation and naming the corresponding formation ingredients (organic compounds combined with solvents). The sentence then names the specific

chemical processes at work in accomplishing complex formation (reacted, precipitated, or crystallized). Defendants argue that these reactions pertain to the solvents used in forming the complexes rather than the complexes themselves,[1] but complex formation is the passage's entire concern. There is no reason to believe that a switch in focus has occurred from complexes to solvents. If such a switch in focus occurred, assuredly there would be a signal from the patentee.

Any doubt as to whether these reactions apply to the complexes themselves is eliminated by the next sentence: "These complexes are known as solvates." The demonstrative adjective "these" emphasizes that complexes were always the passage's focus. The "known as" language also makes clear that "solvates" was intended to be defined by the preceding description of complexes. The specification naturally read thus states that "solvates" may be in the reacted, precipitated, or crystalline form.

Defendants unsuccessfully counter that the specification's subsequent paragraph rebuts any inference that "solvates" extend to non-crystalline forms:

> It will also be appreciated by those skilled in organic chemistry that many organic compounds can exist in more than one crystalline form. For example, crystalline form may vary from solvate to solvate. Thus, all crystalline forms of the compounds of formula (I) or the pharmaceutically acceptable solvates thereof are within the scope of the present invention.

'467 Patent, ll. 4:05-12. According to Defendants, the statements that crystalline forms vary from "solvate" to "solvate" and that all crystalline forms are within the scope of the invention supports limiting "solvates" to crystalline forms. Although the passage does discuss examples of crystalline "solvates," it never explicitly states that crystalline forms represent the entire universe of "solvates." The Court will not read in such a limitation

[1] Their argument relies upon disfavored extrinsic evidence, in particular, the reports of their retained expert. (D.I. 217, p. 18; D.I. 218, Exh. 500, ¶102; Exh. 501, ¶20).

into the claims, especially considering that the earlier paragraph suggests the opposite conclusion.

This brings the Court to the Defendants' argument that the specification's recognition that "those skilled in the art" will "appreciate" the formation of "solvates" requires the Court to adopt the generally understood scientific meaning of "solvates." They then cite extrinsic evidence in support of limiting the definition of "solvate" to crystalline forms. Defendants cite two cases where courts construed terms according to their ordinary meanings when the respective specifications stated that the terms were either "well known" or "understood" by those "skilled in the art."[2] These cases, however, have limited applicability to the construction here. In neither case did courts adopt the extrinsic generally understood meaning in direct contradiction to the specification. This is what Defendants ask the Court to do here. Here, the patentee did not end the discussion of the "solvates" with the acknowledgment that it had a generally understood scientific meaning. Instead, the patentee elaborated upon his statement that a generally understood meaning existed with examples illustrating his understanding of this meaning. This understanding was that "solvates" can be reacted, precipitated, or crystallized. Accepting Defendants' construction would require the Court to abandon this text of the specification, eliminating two out of three of these defined "solvate" forms on the basis of extrinsic evidence. This would violate the rule that intrinsic evidence is the most important evidence in claim construction. *See, e.g.*, *MBO Labs., Inc. v. Becton, Dickinson & Co.*, 474 F.3d 1323, 1329 (Fed. Cir. 2007) ("Extrinsic evidence—testimony, dictionaries, learned treatises, or other material not part of the public record associated with the patent—may be helpful but is less significant than the intrinsic record in determining the legally operative meaning of claim

[2] These cases are *Accolade System v. Citrix System*, 634 F. Supp. 2d 738, 756 (E.D. Tex. 2009) and *Brocade Communications System, Inc. v. A10 Networks, Inc.*, 2012 WL 33251, at *9 (N.D. Cal. 2012).

language."). To the extent there is a conflict between the specification and the ordinary meaning, the Court must side with the specification, as the specification is the single best guide to the meaning of a disputed term. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005). Defendants may cite considerable extrinsic evidence in disagreement with the patentee's definition, but the patentee is free to define the invention how he pleases. *See Irdeto Access*, 383 F.3d at 1300. The Court thus holds that the patentee defined "solvate thereof" to include non-crystalline forms and adopts GSK's constructions of the term.

B. Term 2 - "pharmaceutically acceptable"

GSK's Proposed Construction:	Not deleterious to the recipient thereof when administered as a pharmaceutical.
Defendants' Proposed Construction:	Suitable for use in a finished drug product to be administered to a patient.
Court's Construction:	Suitable for use when administered to the recipient thereof as a pharmaceutical.

The parties dispute the construction of the term "pharmaceutically acceptable" as used in claims 1-5 of the '467 Patent, claims 1-4 of the '976 Patent, and claim 10 of the '427 Patent. "Pharmaceutically acceptable" is used to modify both the claimed dutasteride solvates as well as the claimed carriers of the dutasteride. For example, claim 1 of the '467 Patent claims, "[dutasteride] or a pharmaceutically acceptable solvate thereof." Claim 2 of the '467 Patent claims, "a pharmaceutical formulation comprising the compound of claim 1 and a pharmaceutically acceptable carrier thereof."

GSK argues that the specification expressly defines "pharmaceutically acceptable" as "not deleterious to the recipient thereof when administered as a pharmaceutical." Defendants argue that "suitable for use in a finished drug product to be administered to a patient" is consistent with the ordinary meaning of the term and that ordinary meaning applies here. At oral

argument, Defendants allowed that "finished drug product" was not a necessary element of their construction. (D.I. 226, p. 56). This narrowed the focus of the dispute to whether "pharmaceutically acceptable" means "not deleterious" or "suitable for use," as there was agreement that all other differences of the proposed constructions were not substantive.

GSK relies on a statement from the '467 Patent's specification for its construction: "The carrier must be pharmaceutically acceptable in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof." '467 Patent, 11:1-4. According to GSK, this is an express definition of "pharmaceutically acceptable" and justifies defining it as "not deleterious." Defendants disagree, arguing that this definition only applies to characteristics of a "pharmaceutically acceptable carrier" and makes no sense as to what defines a "pharmaceutically acceptable [dutasteride] solvate."

The Court agrees with Defendants. "Pharmaceutically acceptable" must be construed to accurately encompass its scope as a modifier of both suitable carriers and suitable dutasteride solvates. GSK's proffered passage may expressly define a "pharmaceutically acceptable carrier," but does not sensibly apply to a "pharmaceutically acceptable solvate." As the drug's active ingredient, the dutasteride solvate's acceptability would depend on far more than being "not deleterious" or harmful. It would be expected to provide some sort of therapeutic effect. "Not deleterious" would thus be an inadequate construction of "pharmaceutically acceptable" as used in the claims.

GSK's argument is further weakened by GSK's unwillingness to adopt the supposed definitional language in its entirety. This specification defines "pharmaceutically acceptable carrier" as "compatible with the other ingredients of the formulation." Yet GSK omits this "compatible" characteristic from its definition. GSK's omission is understandable, as the

"compatible" limitation cannot sensibly apply to a "pharmaceutically acceptable solvate," as it makes no sense to require the active ingredient of the drug to be adjusted for compatibility with its carrier. The carrier must be compatible with the active ingredient, not vice-versa. GSK's omission thus makes sense from a practical standpoint, but the omission is inconsistent with the position that the patentee intended the "not deleterious" language from this same sentence to serve as an express definition. If the content of this sentence was intended to be an express definition, the sentence would not need to be sliced and diced in order to fit the term's usage within the claims. Thus, the Court rejects GSK's argument that the specification provides for an express definition of "pharmaceutically acceptable."

"Pharmaceutically acceptable" should be construed as it applies to modify both a carrier and the active ingredient dutasteride solvate. Because the term modifies both the active ingredient and the carrier of the invention, a flexible construction must be given that accurately encompasses the general scope of the term. Thus, the Court agrees with Defendants that "suitable for use" is an appropriate limitation of the construction. The Court thus construes "pharmaceutically acceptable" as "suitable for use when administered to the recipient thereof as a pharmaceutical."

This concludes the Court's construction of the disputed terms.