NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

CELGENE CORPORATION, Plaintiff, v. NATCO PHARMA LIMITED, ARROW INTERNATIONAL LIMITED, AND WARSON LABORATORIES, INC. Defendants.	Civil Action No. 10-5197 (SDW) **MARKMAN OPINION** May 27, 2014

WIGENTON, District Judge.

Before the Court are the briefs and supporting materials of Plaintiff Celgene Corporation ("Celgene") and Defendants Natco Pharma Limited ("Natco"), Arrow International Limited ("Arrow"), and Watson Laboratories, Incorporated ("Watson") (collectively "Defendants") regarding the request for a patent claim construction pursuant to Local Patent Rule 4.5(a).

This Court has jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a). Venue is proper under 28 U.S.C. §§ 1391(b) and 1400(b). This Court held a Markman hearing on May 15, 2014 regarding patent claims in Plaintiff's United States Patent Nos. 6,281,230 ("the '230 Patent"), 6,555,554 ("the '554 Patent"), 7,465,800 ("the '800 Patent"), 7,977,357 ("the '357 Patent"), 8,193,219 ("the '219 Patent"), and 8,431,598 ("the '598 Patent"). After carefully considering the parties' written and oral arguments regarding five claim terms in dispute

covering the six patents listed above, this Court has construed several claim terms, as discussed below.

FACTUAL AND PROCEDURAL BACKGROUND[1]

The drug at issue in this case is called lenalidomide. Lenalidomide is a chemical that decreases the concentration of tumor necrosis factor ("TNFa") in cells. Elevated TNFa concentrations have been linked to various malignant diseases. As a result, lenalidomide has been found to be an effective treatment to these diseases.

Plaintiff markets lenalidomide under the brand name Revlimid®. Revlimid® is approved by the United States Food and Drug Administration ("FDA") to treat multiple myeloma, mantle cell lymphoma, and myelodysplastic syndrome.[2] The patents at issue cover the pharmaceutical compositions containing lenalidomide, the medical uses of lenalidomide, and crystal forms of lenalidomide.

Defendants are generic pharmaceutical makers. Defendants filed an Abbreviated New Drug Application ("ANDA") with the FDA seeking approval to market a generic version of Revlimid®.

On October 8, 2010, Plaintiff filed a Complaint against Natco claiming that the generic version of Revlimid® infringed on Plaintiff's patents. On January 7, 2011, Plaintiff filed an Amended Complaint adding Arrow as a defendant. On March 25, 2011, Plaintiff filed a Second Amended Complaint adding Watson as a defendant.

On October 18, 2013, the parties filed a Joint Claim Construction and Prehearing Statement for the patents at issue. A Markman hearing was held before this Court on May 15, 2014.

[1] Unless otherwise noted, the facts are taken from the parties' submissions.

[2] Use of Revlimid® to treat mantle cell lymphoma is not currently relevant to this litigation because Defendants have not sought FDA approval to market its generic product for this indication.

LEGAL STANDARD

Markman Hearing and Claim Construction

Patent claim construction is a matter of law for the court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995). When interpreting a claim, courts should initially look to intrinsic evidence, namely "the patent claims, the specification and the prosecution history if in evidence." Bristol-Myers Squibb Co. v. Immunex, 86 F. Supp. 2d 447, 448 (D.N.J. 2000). "[I]ntrinsic evidence is the most significant source of the legally operative meaning of disputed claim language." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). "The court should presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms." Bristol-Myers Squibb Co., 86 F. Supp. 2d at 448. A person of ordinary skill in the art "is deemed to read the claim term . . . in the context of the entire patent." Phillips v. AWH Corp., 415 F.3d 1303, 1313 (Fed. Cir. 2005); see Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) ("We cannot look at the ordinary meaning of the term . . . in a vacuum. Rather, we must look at the ordinary meaning in the context of the written description and the prosecution history.") (citation omitted); see also Markman, 52 F.3d at 979.

If the intrinsic evidence alone will not resolve the ambiguity, the court may rely on extrinsic evidence, which includes expert testimony, treatises, dictionaries and articles. Bristol-Myers Squibb Co., 86 F. Supp. 2d at 448-49. Extrinsic evidence may not be used to vary or contradict the meaning established by the intrinsic evidence. Phillips, 415 F.3d at 1318-19,

1324. "The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be . . . the correct construction." Id. at 1316.

A key aspect of claim construction is to assist the jury in understanding complicated language and concepts. See Encap LLC v. Oldcastle Retail, Inc., No. 11-cv-808, 2012 WL 2339095, at *9 (E.D. Wis. June 19, 2012) ("Claim construction is not intended to allow for needless substitution of more complicated language for terms easily understood by a lay jury."); see also C.R. Bard, Inc. v. United States Surgical Corp., 388 F.3d 858, 863 (Fed. Cir. 2004) ("[M]erely rephrasing or paraphrasing the plain language of a claim by substituting synonyms does not represent genuine claim construction."); AFG Indus., Inc. v. Cardinal IG Co., Inc., 239 F.3d 1239, 1247 (Fed. Cir. 2001) ("It is critical for trial courts to set forth an express construction of the material claim terms in dispute, in part because the claim construction becomes the basis of the jury instructions, should the case go to trial. It is also the necessary foundation of meaningful appellate review.") (internal citation omitted).

DISCUSSION

1. "[S]aid compound has the R-configuration" and "said compound has the S-configuration"

Plaintiff and Defendants disagree on the construction of "said compound has the R-configuration" as used in claims 15 and 24 of the '230 Patent and claims 2 and 14 of the '554 Patent. Similarly, the parties dispute the construction of "said compound has the S-configuration" as used in claims 16 and 25 of the '230 Patent and claims 3 and 15 of the '554 Patent. Plaintiff contends that "said compound has the R-configuration" means "said compound has the R-isomer" and that "said compound has the S-configuration" means "said compound has the S-isomer." Defendants define "said compound has the R-configuration" as "the stereochemical configuration of the compound is all or substantially all the R-isomer, thus

excluding a compound that is a racemic mixture" and they define "said compound has the S-configuration" as "the stereochemical configuration of the compound is all or substantially all the S-isomer, thus excluding a compound that is a racemic mixture."

The references to "R-configuration" and "S-configuration" relate to different "enantiomers" of the lenalidomide molecule. (Defs. Op. Br. 26.) "Enantiomers are different versions of the molecule that have the same chemical formula and structural formula, but differ in the three-dimensional orientation of their atoms in space." (Id.) When a compound is made up of both "R" and "S" isomers, it is said to be a "racemic mixture," or a "racemate." (See id. at 27.)

This Court finds that "said compound has the R-configuration" means "the stereochemical configuration of the compound is all or substantially all the R-isomer, thus excluding a compound that is a racemic mixture" and "said compound has the S-configuration" to mean "the stereochemical configuration of the compound is all or substantially all the S-isomer, thus excluding a compound that is a racemic mixture." These constructions are supported by the intrinsic evidence. The claim language at issue expressly requires that the compound being administered have the "R-configuration" or the "S-configuration." A person of ordinary skill in the art ("POSA") would focus on the particular enantiomer and not the racemic mixture. See e.g., Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 348 F. Supp. 2d 713, 724 (N.D.W. Va. 2004) (noting that "chemists skilled in the art regard levorotatory enantiomers as distinct from racemic compounds or the dextrorotatory enantiomer"). This is particularly clear when contrasting the disputed terms with broader claims which reference the compound without regard to the stereochemical configuration. See U.S. Patent No. '230, at col. 27:30-55, 28:23-47. In such instances, a POSA would understand these claims to cover racemic mixtures, which is

within the scope of the invention, per the specification. See id. at col. 8:1-8 (stating "[t]he compounds of the present invention possess a center of chirality and can exist as optical isomers. Both the racemates of these isomers and the individual isomers themselves, as well as diastereomers when there are two chiral centers, are within the scope of the present invention").

Additionally, courts interpreting claims directed to single enantiomers have consistently excluded the racemic mixture. See Teva Neuroscience, Inc. v. Watson Labs., Inc., 10-5078, 2013 WL 1595585, at *7 (D.N.J. Apr. 12, 2013) (construing "R(+)-N-propargyl-l aminoindan" to mean, in relevant part, "at least substantially pure and may include small amounts of the other enantiomer"); Ortho-McNeil Pharm., Inc., 348 F. Supp. 2d at 724 (noting that "each type of compound has its own unique nomenclature. 'S(-)' clearly designates the levorotatory enantiomer in this case. Had the inventor meant to designate the racemic compound, he would have used the designation '(±)' or "RS"). Consistent with this approach, this Court construes "said compound has the R-configuration" as "the stereochemical configuration of the compound is all or substantially all the R-isomer, thus excluding a compound that is a racemic mixture" and "said compound has the S-configuration" as "the stereochemical configuration of the compound is all or substantially all the S-isomer, thus excluding a compound that is a racemic mixture."

2. "Hemihydrate"

The parties disagree on the construction of "hemihydrate" as used in claims 1 through 14 of the '800 Patent. Plaintiff defines "hemihydrate" as "a hydrate containing approximately half a mole of water to one mole of the compound forming the hydrate." Defendants contend that "hemihydrate" means "a solid crystalline form of lenalidomide containing one water molecule for every two molecules of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione, formally associated with one another within the unit cell in the solid crystalline structure, and

which crystal form is specifically identified in the '800 patent as the Form B polymorphic form, and demonstrated TGA, Karl Fischer analysis, powder X-ray diffraction patterns, IR spectra, and/or DSC analysis, as distinguishable from other polymorphs, such as the anhydrous form."

This Court finds that "hemihydrate" means "a hydrate containing approximately half a mole of water to one mole of the compound forming the hydrate." This construction is supported by the intrinsic evidence. The claim language does not limit the molar ratio to be an exact 1:2 ratio of water to lenalidomide. See e.g., U.S. Patent No. '800, at col. 22:40-43 (stating in claim 10 that "[t]he hemihydrate of claim 1 having between approximately 0.46 and approximately 0.59 moles of water per mole of 3-(4-amino-1-oxo-1,3 dihydro-isoindol-2-yl)-piperidine-2,6-dione"); see also id. at col. 6:67-7:5, Figs 9, 37, 38, 39. Moreover, a hemihydrate cannot mean an exact 1:2 ratio while simultaneously limiting the claims to Form B because the specification explicitly describes an example of a Form B polymorph as a hemihydrate that contains a ratio of water to lenalidomide that is not an exact 1:2 ratio. U.S. Patent No. 800, at col. 6:64-7:6, 22:40-43, figs 9, 37-39 (describing hemihydrates containing anywhere from 0.46 to 0.59 molecules of water per molecule of lenalidomide). As the Federal Circuit has articulated, "although the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments." Phillips, 415 F.3d at 1323. Reading in the specific embodiments of an exact 1:2 ratio would thus be improper here. Accordingly, this Court finds that "hemihydrate" means "a hydrate containing approximately half a mole of water to one mole of the compound forming the hydrate."

3. "Form A"

The parties dispute the construction of "Form A" as used in the following instances: (1) the '357 Patent in claims 1 through 14; and (2) the '598 Patent in claims 1 through 4. Plaintiff

defines "Form A" as "a polymorphic form of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione that can be distinguished from other forms." Defendants contend that "Form A" means "the lenalidomide crystal form described in the specification as Form A, having all of the characteristics assigned to Form A in the specification."

This Court finds that "Form A" means "the lenalidomide crystal form described in the specification as Form A, having all of the characteristics assigned to Form A in the specification." This construction is supported by the intrinsic evidence. The '357 Patent specification expressly defines Form A based on observed attributes that are distinguishable from the other disclosed forms—B, C, D, E, F, G, and H. U.S. Patent No. '357, at col 6:13-10:30. Examples of such characteristics unique to Form A include a specific X-ray powder diffraction pattern, specific IR and Raman spectra, specific thermal characteristics, and representative moisture sorption and desorption data. Id. at col. 6:13-54, Figs. 1-5. Notably, the other "Forms" are also defined in the specification based on their observed attributes. Id. at col. 6:55-10:30 (defining Forms B through H). Based on the specification, a POSA would understand Form A to mean a particular polymorph with these distinguishing characteristics.

Moreover, construing "Form A" to have all of these characteristics clarifies the scope of the term as read in context of the claim language. See Smith v. Snow, 294 U.S. 1, 14 (1935) (noting that "if the claim were fairly susceptible to two constructions, that should be adopted which will secure to the patentee his actual invention"); Modine Mfg. Co. v. United States Int'l Trade Comm'n, 75 F.3d 1545, 1556 (Fed. Cir. 1996) ("When claims are amenable to more than one construction, they should when reasonably possible be interpreted so as to preserve their validity."). To ignore the specific attributes of Form A as defined in the specification would render such language meaningless and give no meaning to the term "Form A." Accordingly, this

Court finds that "Form A" means "the lenalidomide crystal form describe in the specification as Form A, having all of the characteristics assigned to Form A in the specification."

4. Phrases Including "Form A" Terms

The parties dispute the construction of "Form A" as it appears in the following instances: (1) "unsolvated crystalline Form A of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione, which has a differential scanning calorimetry thermogram having an endotherm at approximately 270°C" as it appears in claim 1 of the '357 Patent; and (2) "unsolvated crystalline Form A of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione having a differential scanning calorimetry thermogram having an endotherm at approximately 270°C" as it appears in claim 1 of the '598 Patent. Defendants propose that the disputed term means "the lenalidomide crystal form described in the specification as Form A, having all of the characteristics assigned to Form A in the specification." Plaintiff contends that no construction is necessary for these terms.

For all of the reasons articulated above, this Court finds that "Form A" as it appears in the disputed terms means "the lenalidomide crystal form described in the specification as Form A, having all of the characteristics assigned to Form A in the specification."

5. "Unsolvated Crystalline [lenalidomide]" Terms

The parties dispute the construction of the following terms: (1) "unsolvated crystalline 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione having an X-ray powder diffraction pattern comprising peaks at approximately 8, 14.5, 16, 17.5, 20.5, 24, and 26 degrees 2θ" as it appears in claim 1 of the '219 Patent; (2) "an unsolvated crystalline form of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione having a differential scanning calorimetry thermogram endotherm at approximately 270°C and an X-Ray powder diffraction

pattern comprising peaks at approximately 8, 14.5, and 16 degrees 2θ and a thermogravimetric analysis curve of indicative of an unsolvated material" as it appears in claim 5 of the '598 Patent; (3) "an unsolvated crystalline form of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione having an X-Ray powder diffraction pattern comprising peaks at approximately 8, 14.5, 16, 17.5, 20.5, 24, and 26 degrees 2θ" as it appears in claim 10 of the '598 Patent; and (4) "an unsolvated crystalline form of 3-(4-amino-1-oxo-1,3 dihydro-insoindol-2-yl)-piperidine-2,6-dione having a differential scanning calorimetry thermogram endotherm at approximately 270°C" as it appears in claims 1 and 17 of the '598 Patent. Defendants propose the following construction for all the disputed terms: "the lenalidomide crystal form described in the specification as Form A, having all of the characteristics assigned to Form A in the specification." Plaintiff contends that the disputed terms do not require construction.

This Court finds that the disputed terms do not require construction. Unlike the instances that specifically reference "Form A," the disputed terms here do not. Phrases that do not use the term "Form A" should not be construed to have the same meaning as those including the term "Form A." No viable or cogent arguments have been presented to the contrary. Accordingly, this Court finds that the disputed terms do not require construction.

CONCLUSION

For the reasons stated above, this Court orders that the disputed claims in the '230 Patent, the '554 Patent, the '800 Patent, the '357 Patent, the '598 Patent and the '219 Patent be construed as set forth in this Opinion. A summary of this Court's construction of the disputed claims is provided in the corresponding Order.

s/ Susan D. Wigenton
Susan D. Wigenton, U.S.D.J.

cc: Madeline Cox Arleo, U.S.M.J.