United States District Court
Northern District of California

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

GILEAD SCIENCES, INC.,

Plaintiff,

v.

MERCK & CO, INC., et al.,

Defendants.

Case No. 13-cv-04057-BLF

ORDER CONSTRUING CLAIMS IN U.S. PATENT NOS. 7,105,499 AND 8,481,712

[Re: ECF 86, 91, 96, 99, 113]

Plaintiff Gilead Sciences, Inc. brings this declaratory relief action, asking the Court to declare that the manufacture, sale, and use of its drug sofosbuvir does not infringe two patents owned by Defendants, Merck & Co., Merck Sharp and Dohme Corp., and Isis Pharmaceuticals, Inc. (collectively "Merck"), U.S. Patent Nos. 7,105,499 ("the '499 Patent") and 8,481,712 ("the '712 Patent"). Presently before the Court is a dispute between the parties as to how to construe the term "administering" used in claim 1 of the '499 Patent.

I. BACKGROUND

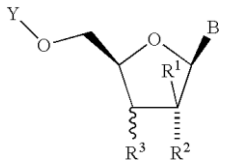
The parties provided the Court with a tutorial on the technology at issue on March 27, 2015, and appeared for a *Markman* hearing on April 3, 2015.

The two patents at issue in this case address treatment for Hepatitis C virus ("HCV") infections. The claims of the '712 Patent are directed to compounds having a specific structural formula, while the claims of the '499 Patent are directed to methods of treating HCV infections by administering therapeutically effective amounts of those compounds.

Claim 1 of the '499 Patent provides:

> 1. A method of treating hepatitis C virus (HCV) infection comprising *administering* to a mammal in need of such treatment a therapeutically effective amount of a compound of structural formula III, or a pharmaceutically acceptable salt or acyl derivatives thereof,

(III)



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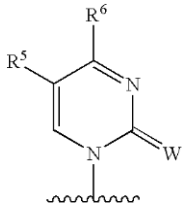

W is O or S;

Y is H, C_1-10 alkylcarbonyl, $P_3O_9H_4$, $P_2O_6H_3$, or $P(O)R^9R^{10}$;

R^1 is CF_3, or C_{1-4} alkyl and one of R^2 and R^3 is OH or C_{1-4} alkoxy and the other of R^2 and R^3 is fluoro;

R^6 is H, OH, SH, NH_2, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, or CF_3;

R^5 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} alkylamino, CF_3, or halogen; and

R^9 and R^{10} are each independently hydroxy, $OCH_2CH_2SC(=O)$t-butyl, or $OCH_2O(C=O)$iPr.

On December 6, 2013, Gilead received approval from the Food and Drug Administration to market and sell Solvaldi®, an orally-administered prescription drug containing the active ingredient sofosbuvir, to treat chronic HCV infection in patients. Sofosbuvir is a prodrug, and is inactive and has little to no therapeutic effect until transformed by enzymes in the body into an active form. Sofosbuvir has a specific chemical structure called a "phosphoramidate" that converts into an active form inside the body's liver cells. Once inside a liver cell, sofosbuvir is converted into three analogs, each with different structures: a monophosphate analog, a diphosphate analog, and a triphosphate analog (collectively the "sofosbuvir metabolites"). The triphosphate analog is the therapeutically effective form, and can target and effectively cure HCV infection in patients. *See* Gilead's Resp. Br., ECF 96 at 4.

The sofosbuvir phosphoramidate is not described by "compound[s] of structural formula III" in claim 1 of the '499 Patent, but all three sofosbuvir metabolites are so described. *See id.* at 7.

II. LEGAL STANDARD

Claim construction is a matter of law. *See, e.g., Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 387 (1996). It is a "bedrock principle of patent law" that the "claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). As such, the "appropriate starting point" for a court interpreting the patent "is always with the language of the asserted claim itself." *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998). In construing the claims of a patent, a disputed term is generally given "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips* at 1313. The Court reads claims in light of the specification, which is the "single best guide to the meaning of a disputed term." *Id.* at 1315.

The interpretation given to a term "can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop within the claim." *Id.*at 1316; *see also Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). The claim language, written description, and patent prosecution history form the intrinsic record that is most significant when determining the proper meaning of a disputed claim. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). In some cases, the ordinary meaning of claim language, as understood by a person of skill in the art, may be readily apparent. Claim construction in such cases involves little more than application of the widely accepted meaning of commonly understood words. *See, e.g., Phillips* at 1314. In *CCS Fitness, Inc. v. Brunswick Corp.*, the Federal Circuit stated that "[g]enerally speaking, we indulge a 'heavy presumption' that a claim term carries its ordinary and customary meaning." 288 F.3d 1359, 1366 (Fed. Cir. 2002). It continued, however, that "a claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in either the specification or prosecution history." *Id.* (citing *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 990 (Fed. Cir. 1999)).

To act as his own lexicographer, a "patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning." *Phillips* at 1316. When a patentee

"provide[s] a definition of [the disputed term] in the specification, the definition in the specification controls . . . regardless of any potential conflict with the term's ordinary meaning as reflected in technical dictionaries." *3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1374 (Fed. Cir. 2003). Absent a "clear disavowal in the specification or prosecution history, the patentee is entitled to the full scope of its claim language." *Home Diagnostics v. LifeScan*, 381 F.3d 1352, 1358 (Fed. Cir. 2004).

III. AGREED UPON CONSTRUCTIONS

In their initial joint claim construction statement, *see* ECF 86, the parties agreed on the construction of a single term, "in combination with," used in the '499 Patent. The Court accordingly adopts and approves the following construction:

Patent	Term	Construction
7,105,499: claim 2	in combination with	The term "in combination with" means "together with," whether given separately at different times during the course of therapy or concurrently in divided or single combination forms.

The parties' initial joint claim construction statement identified two disputed claim terms: "administering," used in claim 1 of the '499 Patent, and "compound," used in claims 1 and 2 of the '499 Patent and claims 1, 2, 3, 5, 7, 9, 10, and 11 in the '712 Patent. Following briefing, however, the parties agreed to the following construction of "compound," which the Court also adopts and approves:

Patent	Term	Construction
7,105,499: claims 1-2 8,481,712: claims 1-3, 5, 7, 9-11	compound	a substance that consists of two or more chemical elements in union.

IV. CONSTRUCTION OF THE DISPUTED TERM "ADMINISTERING"

Plaintiffs' Proposal	Defendants' Proposal	Court's Construction
providing a compound of the invention or a prodrug of a compound of the invention to the individual in need without reference to in vivo transformations of those compounds or prodrugs. The phrase 'prodrug of a compound' means those prodrugs that are expressly claimed.	providing a compound of the invention or a prodrug of a compound of the invention to the individual in need.	providing a compound of the invention or a prodrug of a compound of the invention to the individual in need.

This disputed term is found in claim 1 of the '499 Patent, which claims "[a] method of treating hepatitis C virus (HCV) infection comprising *administering* to a mammal in need of such treatment a therapeutically effective amount of a compound of structural formula III or a pharmaceutically acceptable salt or acyl derivatives thereof." '499 Patent, col. 137 ll. 1-6 (emphasis added).

As Merck explained at the *Markman* hearing:

> [O]ur theory of infringement is when sofosbuvir is provided, it is a prodrug that converts after it's swallowed into the monophosphate, the diphosphate, and the triphosphate. The monophosphate and the diphosphate are compounds of the invention also but are not themselves active drugs. They are, in fact, prodrugs that convert to the triphosphate which is active.
>
> And so we would view this as literally performing this claimed method by providing a prodrug, sofosbuvir, of a compound of the invention. It's, in fact, a prodrug of three compounds of the invention, the monophosphate, the diphosphate, and the triphosphate.

Hearing Tr., ECF 122 at 14:8-19.[1] Merck's infringement theory is based on the definition of "administering" found in the '499 Patent:

> The terms "administration of" and "administering a" compound

[1] Although the Court does not consider the accused products as extrinsic evidence when construing the claims, the court may refer to the accused products for context and to inform itself "of the specific issues presented by the infringement inquiry." *See Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1331 (Fed. Cir. 2006)

> should be understood to mean providing a compound of the invention or a prodrug of the compound of the invention to the individual in need.

'499 Patent, col. 32 ll. 5-9. The parties' claim construction arguments thus focus on whether the term "administering" could encompass the administration of prodrugs that are not themselves "compounds of the invention." The parties agree that "compound of the invention" means the compounds claimed, i.e., any "compound of structural formula III, or a pharmaceutically acceptable salt or acyl derivatives thereof." *See* Hearing Tr. at 25:19-24 (Merck); *see also id.* at 58:11-15 (Gilead).

The parties also agree that the '499 Patent includes a definition of the term administering. *See* '499 Patent, col. 32 ll. 5-9; *see also id.* at col. 30 ll. 4-5 ("Throughout the instant application, the following terms have the indicated meanings . . ."). Where a patent includes a definition, "the inventor's lexicography governs" and "the inventor's intention, as expressed in the specification, is regarded as dispositive." *Phillips*, 415 F.3d at 1316. That is the case even where the inventor's definition differs from the term's plain and ordinary meaning to a person of ordinary skill. *Id.*; *see also CCS Fitness*, 288 F.3d at 1366. Nonetheless, the court should read the definition in light of the specification as a whole. *Allergan, Inc. v. Apotex, Inc.*, 754 F.3d 952, 957-58 (Fed. Cir. 2014) (approving district court's construction that "read[] the patentee's own lexicography in light of the whole specification"); *Trading Techs. Int'l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1353 (Fed. Cir. 2010) ("The district court's definition may seem narrower than the inventors' express definition at first glance. However, the claims, the rest of the specification, and the prosecution history support the district court's definition.").

Gilead's proposed construction begins with the definition and seeks to add two further limitations, which Gilead contends both reflect the plain and ordinary meaning of "administering" and are supported by the specification of the '499 Patent. Gilead argues that the first limitation, "without reference to in vivo transformations of those drugs or compounds," is necessary because "[n]othing in the intrinsic record suggests that the patentees altered the ordinary meaning of 'administering' to refer to in vivo compound transformations," and because "Defendants' infringement theory for the '499 patent relies on the fact that the body transforms sofosbuvir—

which is not expressly covered by the claims—into other compounds that are expressly claimed." Gilead's Br. at 14. Gilead further argues that the second sentence, "The phrase 'prodrug of a compound' means those prodrugs that are expressly claimed," is necessary because the intrinsic record shows that the patentee claimed only a limited set of prodrugs – those explicitly recited in the claim – and not all prodrugs. *See id.* at 21-22.[2]

The Court considers both of these disputes below.

A. Whether "administering" encompasses in vivo transformation

Merck argues that the Court should adopt its construction of "administering" because its proposed construction is identical to the definition of administering included in the '499 Patent. It argues that because the patent itself includes no pre-ingestion limitation, the Court should not limit the claim in the manner suggested by Gilead. In response, Gilead argues that the Court should alter the definition provided in the '499 Patent to conform the definition to the plain and ordinary meaning of "administering." Gilead contends that "administration is complete at the point when the patient swallows a tablet . . . [and] does not extend beyond [] to encompass whether and how the body transforms a drug." Gilead's Br. at 15. It also argues that a review of the entire intrinsic record shows that Merck intended "administering" to mean only providing a compound to an individual in need, and not what happens to that compound after it is ingested. *See id.* at 18. The Court finds neither of Gilead's arguments persuasive.

The Court begins with the definition included in the specification of the '499 Patent. "Administering" is specifically defined in the '499 Patent to mean "providing a compound of the invention or a prodrug of a compound of the invention to the individual in need." A "prodrug of a compound" is, the parties agree, a precursor drug that must be transformed in the body before it becomes an active therapeutic compound. *See, e.g.*, V.J. Stella *et al.*, *Prodrugs: Do They Have*

[2] Though the phrase "prodrug of a compound" does not itself appear in the claim, the Court may nonetheless construe the term if it is necessary to elucidate the claim's meaning. *See Adv. Fiber Techs. (AFT) Trust v. J&L Fiber*, 674 F.3d 1365, 1373 (Fed. Cir. 2012) ("We note, as an initial matter, that 'we do not ordinarily construe words that are not in claims.' However, in those cases in which the correct construction of a claim term necessitates a derivative construction of a non-claim term, a court may perform the derivative construction in order to elucidate the claim's meaning.") (internal citations omitted).

Advantages in Clinic Practice?, 29 Drugs 455, 455 (1985). The Court is persuaded by Merck's argument that the use of the term "prodrug of a compound" within the definition of "administering" in the '499 Patent necessarily includes what happens once a prodrug enters the patient's body and transforms through metabolism from the inactive prodrug form into the active therapeutic form. *See* Merck's Reply Br. at 10 ("The ability to undergo metabolism in the body is the very hallmark of a prodrug, and distinguishes prodrugs from mere drugs."); *see also Adv. Fiber*, 674 F.3d at 1373. Gilead's construction would read out the words "prodrug of a compound" from the definition of "administering" in the patent, which is inappropriate. *See Phillips*, 415 F.3d at 1316; *CCS Fitness*, 288 F.3d at 1366.

Gilead nonetheless argues that the definition should be read in conjunction with other language in the '499 Patent that it contends supports an ex vivo limitation. But the language Gilead points to does not support such a reading. Gilead argues that the '499 Patent states that "[t]he compounds of the present invention *may* be administered in the form of a pharmaceutically acceptable salt," and since pharmaceutically acceptable salts are "prepared by man," the word "administering" only includes "a timeframe before the body transforms the compounds." Gilead's Br. at 17. This reading, however, ignores the word "may"; this disclosure identifies one way in which the invention can be practiced, not the only way in which the invention can be practiced.

Additionally, the two District of New Jersey cases Gilead cites in support of its argument, *Hoffman-La Roche Inc. v. Apotex* and *Schering Corp. v. Glenmark Farms*, are inapposite. In *Apotex*, the patent at issue did not include a definition of the term "administering," *see* 2010 WL 1875569, at *8 (D.N.J. May 10, 2010) ("[E]xamination of the intrinsic evidence does not indicate that the patentee acted as his own lexicographer."), and the claim language itself suggested that administering ended at the point at which the compound entered the patient's body. A careful reading of *Apotex*, in fact, supports Merck's argument here: the court noted that because the specification stated that the compound could be "administered in solid form," the claim "suggest[ed] that administering a solid would end when the solid itself ended." *Id.* at *9. The *Apotex* court thus explicitly looked to the manner in which the compound was being provided to the patient in order to determine how to construe "administering." This Court does the same.

Because Merck expressly states that the treatment can be administered through a "prodrug of the compound," which requires metabolism into a therapeutically effective form in the body, the claim should not be limited to only what occurs ex vivo. Similarly, in *Schering*, the district court also looked to extrinsic evidence and ordinary meaning of the term "administering" because the patent at issue did not include a definition of the term. 2008 WL 4307189, at *8 (D.N.J. Sept. 16, 2008).[3]

Gilead is correct that the Court must read the definition included in the specification in light of the entire intrinsic record. *See Allergan,* 754 F.3d at 957-58; *see also Trading Techs.*, 595 F.3d at 1353. Such a review supports Merck's construction. Per the definition of administering, the treatment claimed by the '499 Patent can be given to the patient in the form of a compound of the invention or a prodrug of a compound of the invention. Gilead's proposal of limiting the '499 Patent's definition of administering by adding "without reference to in vivo transformations of those compounds of prodrugs" cannot be squared with the use of the phrase "prodrug of a compound" in the definition of administering. Gilead does not persuasively point to any language in the written description that supports limiting administration to include only what happens up to the point of ingestion.

B. Whether "administering" encompasses only those prodrugs referenced in the '499 Patent

The second limitation Gilead's proposed construction adds to the definition of "administering" is the sentence: "The phrase 'prodrug of a compound' means those prodrugs that are expressly claimed." Gilead contends that the '499 Patent claims "a limited group of prodrug moieties," specifically acyl derivatives and SATE prodrugs. *See* Gilead's Br. at 21 (citing '499 Patent at col. 137 ll. 2-6, col. 138 ll. 14-15). Acyl derivatives and SATE prodrugs are both "compound[s] of structural formula III, or a pharmaceutically acceptable salt or acyl derivatives thereof." Gilead argues that by including these limited categories of prodrugs in claim 1 and the

[3] Gilead's further argument that the Court should interpret "administering" based on evidence contained in the *Merck Manual* is not persuasive. Gilead's Br. at 18-19. As Merck correctly points out, the *Merck Manual* does not address the specific definition of administering set forth in the '499 Patent. This extrinsic evidence, even to Merck's own technical manual, cannot overcome the definition included in the specification. *See, e.g., Vitronics*, 90 F.3d at 1585.

written description of the '499 Patent, Merck has claimed only these specific prodrug forms. *Id.* at 21-22. As Merck's counsel put it, "[Gilead is] trying to turn 'prodrug of a compound of the invention' to 'prodrug *that is* a compound of the invention.'" Hearing Tr. at 30:20-22 (emphasis added). Gilead's proposed construction thus invites the Court to commit "one of the cardinal sins of patent law—reading a limitation from the written description into the claims." *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001).

The ultimate problem with Gilead's position is that the phrase "prodrug of a compound of the invention" is not limited to those prodrugs that are also compounds of the invention. A "prodrug of a compound" is *any* derivative of the compound which converts into the compound after it is ingested into the body. *See, e.g.*, Stella, 29 Drugs 455, 455-73. The '499 Patent claims a method of "administering" "a compound of structural formula III, or a pharmaceutically acceptable salt or acyl derivatives thereof." The definition of "administering" explains that administration is accomplished by providing the actual compound claimed or a prodrug of that compound. There is no indication from the definition of administering that Merck intended to limit itself to only administering certain prodrugs—those prodrugs that are also "compound[s] of the invention."[4]

Finally, Gilead argues that the file history supports its proposed construction because the patentee "disclaim[ed] prodrugs that [we]re not expressly covered by the claims." Gilead's Br. at 22. It points to the amendment to pending claim 53 (which issued as claim 1) during prosecution to replace the phrase "ester prodrug" with "acyl derivative," and argues that this replacement "shows a clear disclaimer of any kind of prodrug in favor of just those that were both described and expressly claimed." *Id.* at 23 (citing *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314 (Fed. Cir. 2003)). This argument is unpersuasive for two reasons. First, in *Omega Engineering*, the Federal Circuit held that prosecution disclaimer is inappropriate where the "alleged disavowal of

[4] The Court notes that Merck's preferred construction could pose invalidity problems for Merck down the road. It rejects, however, Gilead's argument that it should adopt Gilead's proposed construction in order to preserve the claims' validity. *See* Gilead's Br. at 24; *see also Phillips* at 1327 ("[W]e have certainly not endorsed a regime in which validity analysis is a regular component of claim construction.").

claim scope is ambiguous." *Id.* at 1325. The history Gilead points to is too spare to support a finding of unambiguous disavowal of all non-recited prodrugs. Second, because the definition of "administering" included the phrase "prodrug of a compound", the phrase "ester prodrug" in the claim was redundant. *Cf.* Merck's Reply Br. at 12.

In sum, Gilead fails to show prosecution disclaimer, and the intrinsic record shows that Merck did not intend to limit claim 1 to include only those prodrugs expressly referenced. The Court rejects Gilead's attempt to read the additional limitation "the phrase 'prodrug of a compound' means those prodrugs that are expressly claimed" into the definition of "administering" found in the '499 Patent.

Accordingly, the Court adopts Merck's construction of "administering" and construes the term to mean "providing a compound of the invention or a prodrug of a compound of the invention to the individual in need." As is clear from the Court's analysis, this construction does not include the two limitations that Gilead sought in its proposed construction.

V. ORDER

For the reasons set forth above, the Court construes the following terms:

Claim Term	Court's Construction
in combination with	The term "in combination with" means "together with," whether given separately at different times during the course of therapy or concurrently in divided or single combination forms.
compound	a substance that consists of two or more chemical elements in union.
administering	providing a compound of the invention or a prodrug of a compound of the invention to the individual in need.

IT IS SO ORDERED

Dated: May 1, 2015

BETH LABSON FREEMAN
United States District Judge