IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO
Honorable R. Brooke Jackson

Civil Action No. 11-cv-01110-RBJ-KMT

SHIRE LLC,
SUPERNUS PHARMACEUTICALS, INC.,
SHIRE DEVELOPMENT INC.,
SHIRE INTERNATIONAL LICENSING B.V.,
AMY F.T. ARNSTEN, PH.D.,
PASKO RAKIC, M.D., and
ROBERT D. HUNT, M.D.,

Plaintiffs,

v.

SANDOZ INC.

Defendant.

ORDER – CLAIM CONSTRUCTION

The case is before the Court on disputes concerning the meaning of five terms in a utility patent. The briefing was completed on March 23, 2012, and the Court heard argument on August 10, 2012.

Case History

This case involves a number of disputes arising from three utility patents involving pharmaceuticals. Shire LLC, along with plaintiffs Supernus Pharmaceuticals, Inc., Amy F.T. Arnsten, Ph.D., Pasko Rakic, M.D., and Robert D. Hunt, M.D., began this case on April 27, 2011, alleging that Sandoz, Inc. infringed United States Patent Nos. 5,854,290 ("the '290 patent"), 6,287,599 ("the '599 patent"), and 6,811,794 ("the '794 patent"). Sandoz, Inc.

answered and counterclaimed for a declaratory judgment of non-infringement and invalidity of the plaintiffs' patents [#19].

Drs. Arnsten, Rakic and Hunt are the owners of the '290 patent, entitled "Use of Guanfacine in the Treatment of Behavioral Disorders." Supernus Pharmaceuticals is the owner of the '599 and '794 patents, entitled "Sustained Release Pharmaceutical Dosage Forms with Minimized pH Dependent Dissolution Profiles." Shire holds an exclusive license under the '290, '599, and '794 patents with respect to drug products containing the active ingredient guanfacine. Shire is also the owner of New Drug Application ("NDA") No. 022037, which was approved by the Food and Drug Administration ("FDA") for the manufacture and sale of guanfacine hydrochloride extended release tablets, what are marketed under the name "Intuniv."

Sandoz sought approval from the FDA to engage in the commercial manufacture and sale of the generic guanfacine hydrochloride extended release tablets before plaintiffs' patents expired. On March 14, 2011, pursuant to §505(j)(2)(B)(ii) of the FDCA, Sandoz sent a notification to plaintiffs asserting the patents-in-suit are invalid, unenforceable, and/or will not be infringed by Sandoz's product. Following Sandoz's Notice Letter, Plaintiffs brought this infringement action. [#1].

On June 3, 2012 the Court granted the parties' Joint Motion for Consolidation [#112] and consolidated the present case with related case *Shire LLC et al. v. Sandoz, Inc.*, Case No. 1:12-cv-00040-MSK-MEH (D. Colo.) [#121]. On August 10, 2012 the Court held a Markman Hearing on the disputed claims in the '599 and '794 patents [#129]. Prior to the hearing, the parties jointly notified the Court that the '290 patent was dedicated to the public on March 22, 2012 and therefore would no longer be a subject of the current litigation.

Conclusions

Prior to and in the course of the Markman Hearing, the parties reached agreement on the construction of several claims identified as disputed in their claim construction briefing. The following terms remain before the Court for construction: (1) "pH dependent agent that increases the rate of release of said at least one pharmaceutically active agent from the tablet at a pH in excess of 5.5;" (2) "agent that increases the solubility of said at least one pharmaceutically active agent at a pH of greater than 5.5;" (3) "agent maintains an acidic microenvironment in the composition;" (4) "reducing the likelihood of side effects associated with the administration of guanfacine;" and (5) "about."

Claim construction is a matter of law for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384-91 (1996). The objective is to give disputed terms in a patent claim the meaning that a person of ordinary skill in the relevant art would have given them at the time of the invention unless the patent applicant has clearly and unambiguously defined the terms differently. *See, e.g., Honeywell Int'l Inc. v. Universal Avionics Sys. Corp.,* 493 F.3d 1358, 1361 (Fed. Cir. 2007).

The Court principally considers "intrinsic evidence," i.e., the words of the claim itself in the context of the entire patent including as relevant the specification and the prosecution history. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313-17 (Fed. Cir. 2005), *cert. denied*, 546 U.S. 1170 (2006). The specification is "the single best guide to the meaning of a disputed term." *Vitrionics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). The court may not, however, read limitations from the specification, particularly the disclosed embodiments, into the claim. *Phillips*, 415 F. 3d at 1323-24. "Extrinsic evidence" such as dictionaries, treatises and, in some

cases, expert testimony can also be considered, although such evidence generally should be given less weight than intrinsic evidence. *Phillips,* 415 F.3d at 1317-19.

The term "pH dependent agent that increases the rate of release of said at least one pharmaceutically active agent from the tablet at a pH in excess of 5.5." '599 Patent: Claims 1-30, '794 Patent: Claims 3-12

The parties set forth proposed definitions in a Joint Claim Construction and Prehearing Statement [#99]. Shire proposes the definition: "agent that increases the rate of release of the pharmaceutically active agent from a tablet in an environment that has a pH above 5.5 relative to an environment that has a pH of 5.5 or below." Sandoz proposes a definition of "a substance that increases the rate of release of a pharmaceutically active agent from a composition in surrounding media having a pH above 5.5."

The parties' definitions are nearly identical aside from Shire's proposed comparative language. During oral argument, the parties made it clear that the crux of their disagreement is the inclusion of the phrase "relative to an environment that has a pH of 5.5 or below." Shire insists that the comparison is implicit in the disputed term: i.e., the agent must be pH-dependent and therefore behave differently at different pH levels.

Shire contends that both the plain language of the claim and the specification illustrate that their proposed comparative language is implied. In support, Shire points to the representation of the dissolution data represented in Table 2 of the '599 and '794 patents. That an agent is "pH-dependent" means that the agent increases the release of the pharmaceutically active agent more in higher pH environments than in lower pH environments. Shire argues that a person of ordinary skill in the art would interpret the term as having to do with different things at different pH levels. If Sandoz's definition is adopted, Shire contends that the construction would

allow for an increase of the rate of release at pH levels below 5.5 which would be in contravention of the invention.

Although not binding on this Court, Shire's proposed construction is further supported by the claim constructions of other district courts who have construed these same patents. The United States District Court for the District of Delaware construed an identical term to mean "agent that is neither the non-pH dependent sustained release agent nor the pharmaceutically active agent, and that increases the rate of release of the pharmaceutically active agent from a tablet *more in an environment that has a pH above 5.5 than in an environment that has a pH of 5.5 or below.*" *Shire LLC, et al v. Teva Pharmaceuticals USA Inc., et al*, No. 10-329-RGA, 2012 WL 975694, at *5-6 (D. Del. March 22, 2012) (emphasis added). The United States District Court for the Northern District of California, San Francisco Division also adopted plaintiffs' proposed definition for the identical term. In that case the court found that "[t]he ordinary, supported, and sufficiently definite meaning of the term is that the agent increases the rate of release of the drug in an environment having a pH in excess of 5.5, as compared to an environment of pH 5.5 or below." *Shire LLC, et. Al v. Impax Laboratories, Inc., et al.*, No. 10-5467 RS, 2012 WL 1980803, at *5-7 (N.D. Cal. June 1, 2012).

Sandoz, in contrast, argues that Shire's definition improperly narrows the term. Sandoz argues that Shire's proposed language is unsupported by the claim language and the specification. The proper comparison, in Sandoz's view, is between a tablet with and without a pH-dependent agent. Sandoz argues that their definition is supported by the intention behind the alleged invention. The "problem" that the alleged invention is trying to solve is how to increase the rate of release in the intestine, where there is a higher pH level. A high rate of release in the stomach, where the pH is 1 or 2, is not an issue the invention seeks to solve.

Although Sandoz's definition appears at first blush to be simpler, the Court finds that it is Shire's definition that most closely reflects the specification and the purpose of the patent. Table 2 of the '599 patent compares the controls against the compositions covered by the patent above pH 5.5 and below pH 5.5. *See* PD0052-22A and PD0052-25B. The Court also finds the specification language cited by both parties supports Shire's definition. The specification states that "[i]t is an object of the present invention to provide a pharmaceutical composition with a minimized pH dependent or a pH-independent dissolution profile." '599 col. 1: 28-30. This goal is achieved only by improving the rate of release in pH levels above 5.5 more than in areas below pH 5.5. Although Sandoz would have the Court focus only on the invention's behavior while in the small intestine, there is intrinsic evidence that the invention is intended and designed to be active throughout the entire gastrointestinal tract. The Court finds that the intrinsic evidence more strongly supports that additional comparator language that Shire proposes.

Therefore, The Court adopts for the meaning of the term "pH dependent agent that increases the rate of release of said at least one pharmaceutically active agent from the tablet at a pH in excess of 5.5," Shire's proposed definition of: "agent that increases the rate of release of the pharmaceutically active agent from a tablet in an environment that has a pH above 5.5 relative to an environment that has a pH of 5.5 or below."

The term: "agent that increases the solubility of said at least on pharmaceutically active agent at a pH of greater than 5.5." Patent '599: Claims 4, 11, 12, 14.

For this term Shire proposes the construction "agent that increases the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance in an environment which was a pH above 5.5 relative to an environment which has a pH of 5.5 or below." Sandoz's proposed construction is as follows: "a substance that increases the amount of

a pharmaceutically active agent that will dissolve when the surrounding media has a pH above 5.5."

Both parties agree that their dispute here is in effect the same as for the previous disputed term. That is, the dispute is over Shire's proposed comparator. As the Court resolved the previous term in favor of Shire's proposed definition, Shire's definition will be adopted here as well for the reasons articulated above.

Therefore, the Court adopts the meaning for the term "agent that increases solubility of said at least one pharmaceutically active agent at a pH of greater than 5.5" Shire's proposed definition of "agent that increases the amount of the pharmaceutically active agent that will dissolve in a given amount of another substance in an environment which has a pH above 5.5 relative to an environment which has a pH of 5.5 or below."

The term: "agent that maintains an acidic microenvironment in the composition." Patent '599: Claim 13

At the hearing held on August 10, 2012 Sandoz represented to the Court that there was no longer a dispute over this term and stipulated to Shire's proposed definition. Therefore, the Court adopts the following proposed construction: "agent that imparts an acidic character to the regions immediately around or in close proximity to the pharmaceutically active agent in the composition."

The term: "reducing the likelihood of side effects associated with the administration of guanfacine." Patent '794: Claims 8-12.

Shire proposes the following definition: "reducing the probability of side effects resulting from guanfacine administration." Sandoz proposes a definition of "decreasing the incidence or

severity of side effects compared to administering the same amount of guanfacine as an immediate-release."

Shire's proposed definition is nearly identical to the language of the disputed claim. During the Markman hearing Shire clarified that it would also accept the use of the word "likelihood" instead of "probability," which would make their proposed definition the same as the disputed term. Shire, in effect, is arguing that this term is unambiguous and does not require construction. Shire argues that the specification in the '794 patent lays out three possibilities for the reduction of side effects: (1) the reduction in the number of side effects, (2) the reduction in the likelihood of side effects, and (3) the reduction of the severity of possible side effects. Col. 3, line 48-61. Shire argues that the disputed term is simply restating the second of those three options, and thus Sandoz's proposed construction adds limitations that are not present in the claim language.

Whereas Shire argued for a comparator in earlier disputed terms, Sandoz does so now. Sandoz argues that Shire's proposed definition provides no context. Sandoz maintains that Shire's definition fails to describe what the claimed reduction in side effects is compared to. The proper comparator, as found in the specification, is "immediate release composition." '794 patent: col. 11, line 61-67; Table 10. According to Sandoz, the term can only be understood by looking to the comparison suggested in the specification.

The Court finds that the claim term is clear on its face and requires no construction or substitution of the word "probability" for "likelihood." Those words are not appreciably different, and at the Markman hearing Shire stated that it could not articulate why such a substitution was made. The example given in the specification does indeed show the claimed invention's reduction of side-effect with respect to an available immediate release composition.

However, adding that limitation to a clear claim term is unnecessary and will not aid a person of ordinary skill in the art to understand the term. The Court declines to limit the claim term because of an example given in the specification: "claims will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words of expression of manifest exclusion or restriction." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1381 (Fed. Cir. 2009).

Therefore, the Court finds that the term is clear on its face and adopts the following definition: "reducing the likelihood of side effects associated with the administration of guanfacine."

The term "about." Patent '599: Claims 18-23

Several claims in the '599 patent state that a component is "present in the composition in an amount of from about __ wt. % to about ___ wt. %." The parties disagree on the meaning of the term "about." Shire proposes that "about" should be construed to mean "approximately." Sandoz proposes that "about" should be construed to refer to proposed numeric ranges that account for uncertainty based on the number of significant figures used in the numeric ranges cited in the claims.

Shire argues that under the case law it is improper to ascribe a numerical value to the word "about." Shire cites to the case *Modine Mfg. Co. v. U.S. Int'tl Trade Comm'n*, 75 F.3d 1545, 1551 (Fed. Cir. 1995) for the proposition that "[o]rdinarily a claim element that is claimed in general descriptive words, when a numerical range appears in the specification and in other claims, is not limited to the numbers in the specification or other claims."

Sandoz argues that the meaning of the term "about" is subject to interpretation, because it does not have a universal meaning in patent claims. Sandoz correctly points out that neither the

specification nor the prosecution history of the '599 patent provides a definition of the scope of the ranges described by the "about" term. Sandoz argues that a person having ordinary skill in the art would understand "about" to "allow for standard measuring errors by applying basic rounding concepts based on the number of significant figures in the measurements." [#90] at 29. Sandoz suggests a unique range for Claims 18-23. The proposed ranges were agreed to, and accepted by the court, in the prior case in the Northern District of California. *See* [#95]-1 at 13-15.

Although Shire agreed to Sandoz's proposed ranges in another action, neither party argues that they are now bound by the prior agreement. Importantly, no other court has been asked to construe this claim term. Sandoz is correct that nothing in the specification indicates what numerical range is meant by "about." It is for that reason that the Court is disinclined to impose such a range in this instance. Neither party has pointed to any supporting reference in the specification that supports their construction. Therefore, the Court must turn to extrinsic evidence. *See Philips*, 415 F.3d at 1317. As stated above, "claims will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words of expression of manifest exclusion or restriction." *Martek* 579 F.3d at 1381 (Fed. Cir. 2009). Without some indication in the specification that the patentee intended a reference to a definite numerical limitation, the Court will not impose one here. Further, the Court finds that a person having ordinary skill in the art would understand "about" to mean an approximate, but non-specific, numerical range.

Therefore, the Court adopts the construction "approximately" for the term "about."

DATED this 13th day of November, 2012.

BY THE COURT:

R. Brooke Jackson
United States District Judge