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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

SHIRE LLC, SUPERNUS PHARMACEUTICALS, INC., AMY F.T. ARNSTEN, PH.D., PASKO RAKIC, M.D., and ROBERT D. HUNT, M.D.,

Plaintiffs,

v.

IMPAX LABORATORIES, INC., WATSON PHARMACEUTICALS, INC., WATSON LABORATORIES, INC.–FLORIDA, WATSON PHARMA, INC., and ANDA, INC.,

Defendants.

Case No. 10-CV-05467-RS

PLAINTIFFS' REPLY TO WATSON DEFENDANTS' OPPOSITION TO PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

Date: May 30, 2012
Time: 10:00 a.m.
Place: Courtroom 3 - 17th Floor
Judge: Hon. Richard Seeborg

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I. INTRODUCTION

Plaintiffs Shire LLC, Supernus Pharmaceuticals, Inc., Amy F.T. Arnsten, Ph.D., Pasko Rakic, M.D., and Robert D. Hunt, M.D. submit this reply to Defendant Watson Pharmaceuticals, Inc.'s, Watson Laboratories, Inc. – Florida's, Watson Pharma, Inc.'s, and ANDA, Inc.'s (collectively, "Watson") Opposition to Plaintiffs' Opening Claim Construction Brief.

Watson makes three incorrect arguments that pervade its opposition. First, Watson improperly urges the Court to apply collateral estoppel to rubberstamp an interlocutory memorandum opinion in an ongoing District of Delaware litigation involving different products and different defendants. Watson mistakenly believes that collateral estoppel should be applied because it claims that other courts are split as to whether claim construction in one case precludes a second court from independently examining a patent's claims itself. There is no split among the pertinent courts here. The Courts of Appeal for the Ninth Circuit and the Federal Circuit agree that collateral estoppel is not applicable when, as here, the earlier court's decision is not final, and that an interlocutory claim construction memorandum opinion, such as that of the Delaware district court, is not final. Accordingly, there is no inconsistency in Plaintiffs' positions, either.

Next, Watson argues, in the alternative, for the adoption of its proposed definitions of the five "most significant" patent terms in this case because Plaintiffs' constructions allegedly are not recited *ipsis verbis* in the patent specifications. However, *ipsis verbis* recitation from the specification is not essential to a claim. Rather, a claim term is interpreted based upon all of the intrinsic evidence as the term would be understood by those skilled in the art in the context of the field of the invention.

Finally, Watson argues that the claim terms should be construed in isolation apart from their context as component parts of the claimed pharmaceutical composition (*i.e.*, a formulation) that is designed to release the drug throughout the gastrointestinal tract. This argument ignores the maxim that a claim is interpreted based upon all of the intrinsic evidence as the term would be understood by those skilled in the art in the context of the field of the invention.

These pervasive errors, and the additional factual errors discussed below, render Watson's proposed claim construction poorly reasoned and incorrect and render its attacks on Plaintiffs'

construction baseless.

II. ARGUMENT

A. Collateral Estoppel Does not Apply to the Delaware *Markman* Memorandum Opinion

Watson argues that this Court should blindly adopt a memorandum opinion of a Delaware court, despite an alleged split among courts, because "the better-reasoned authority counsels that Plaintiffs should be precluded from re-litigating claim construction issues they already raised and lost in another court." Watson Opposition, Dkt. No. 154, Section II, p. 2. However, there is no split in the Ninth or Federal Circuits. It is clear that collateral estoppel does not apply here.

The Court of Appeals for the Federal Circuit applies the law of the circuit in which the district court sits when considering the application of collateral estoppel. *Vardon Golf Co., Inc. v. Karsten Mfg. Corp.*, 294 F.3d 1330, 1333 (Fed. Cir. 2002). The Ninth Circuit Court of Appeals has explained that:

> [i]ssue preclusion, or collateral estoppel, refers to 'the preclusive effect of a judgment in foreclosing relitigation of issues that have been actually and necessarily decided in earlier litigation.' [citation omitted]. Issue preclusion bars relitigation of issues adjudicated in an earlier proceeding if three requirements are met:
> (1) the issue necessarily decided at the previous proceeding is identical to the one which is sought to be relitigated;
> *(2) the first proceeding ended with a final judgment on the merits*; and
> (3) the party against whom [issue preclusion] is asserted was a party or in privity with a party at the first proceeding.

In re Reynoso, 477 F.3d 1117, 1122 (9th Cir. 2007) (Appeal No. 04-17190) (emphasis added).[1]

The Delaware district court memorandum opinion is not a final judgment on the merits; collateral estoppel cannot be applied. The Federal Circuit, using Ninth Circuit law, has only applied collateral estoppel to claim construction after a final judgment that has been appealed or where the time for appeal has expired. *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 252 F.3d 1306 (Fed. Cir. 2001). In *Mycogen*, the Southern District of California court concluded that collateral estoppel required it to adopt the Delaware claim construction because "[c]laim construction was

[1] Furthermore, "[a]ny reasonable doubt as to what was decided by a prior judgment should be resolved against giving it collateral estoppel effect." *Berr v. FDIC*, 172 B.R. 299, 306 (9th Cir. Cal. 1994).

litigated in *Delaware I* before both the district court and this court [*i.e.*, the Federal Circuit], and determination of that issue was necessary to the [summary] judgment in that case." *Id.* at 1311. The earlier proceeding ended with a final judgment on the merits, which is consistent with the more recent explanation of the application of collateral estoppel in *Reynoso*, as explained above.

This is also consistent with the Federal Circuit's application of collateral estoppel based upon the law of other circuits. *See Innovad, Inc. v. Microsoft Corp.*, 260 F.3d 1326, 1334 (Fed. Cir. 2001) ("No action before this court qualifies as fully resolved 'prior litigation'…Moreover, a 'resolution' and 'final judgment' envision a complete adjudicative process."); *RF Delaware, Inc. v. Pacific Keystone Tech., Inc.*, 326 F.3d 1255, 1260-61 (Fed. Cir. 2003) ("We conclude that collateral estoppel does not apply in the present case because no judgment, much less final judgment, was ever entered in the Virginia district court case."); *Pfaff v. Wells Elec., Inc.*, 5 F.3d 514, 518 (Fed. Cir. 1993) ("The prior claim interpretation has issue preclusive effect in the present case insofar as it was necessary to the judgment of non-infringement in the previous case."); *Vardon Golf*, 294 F.3d at 1331, ("We hold that the grant of partial summary judgment in *Vardon I* was not final for purposes of collateral estoppel …." "'Sufficient firmness, according to the Restatement, requires that the party against whom the estoppel is asserted have had the right, even if not exercised, to challenge on appeal the correctness of the earlier decision.'" [citation omitted]. *Id.* at 1334. "*Vardon I*'s partial summary judgment was not an appealable final judgment under 28 U.S.C. 1291 …." "[T]he possibility of interlocutory appeal does not render a decision final under the doctrine of collateral estoppel ….") *Id. See also Kollmorgen Corp. v. Yaskawa Elec. Corp.*, 147 F. Supp. 2d 464, 467 (W.D.Va. 2001) (*Markman v. Westview Instruments*, 517 U.S. 370 (1996) did not nullify pre-existing Federal Circuit analysis regarding collateral estoppel.)

Here, Watson urges this Court to apply collateral estoppel to a Delaware court interlocutory memorandum opinion. Furthermore, that opinion is the subject of a pending request for reconsideration in a case, and no judgment has been entered. *See* Watson Opposition, Dkt. No. 154, Section V.A.1.b, pp. 8-9, n.9. Clearly at least one of the requirements of the application of collateral estoppel – that the Delaware proceeding ended with a final judgment on the merits – is

not met. Collateral estoppel cannot be applied.[2]

B. Non-pH Dependent Sustained Release Agent

Watson's proposed construction ignores the art-recognized meaning of "sustained release", denies the reality that the same ingredient in a pharmaceutical composition can function differently under different conditions, and is completely blind to the essence of the claimed invention – a pharmaceutical composition (not individual components) that is administered orally and travels through the gastrointestinal tract. Claims should not be interpreted in a vacuum. They need context. That is why the words of the claim are given generally their ordinary meaning to one skilled in the art (*Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)), and particularly, a technical term is interpreted as having the meaning that it would be given by persons experienced in the field of the invention. *Markman v. Westview Instruments, Inc*., 52 F.3d 967, 1005 (Fed. Cir. 1995). That is also why claims are interpreted in light of the specification.

1. Watson's Interpretation of "Sustained Release" Confuses the Non-pH Dependent Agent with the pH Dependent Agent and Ignores the Art-Known Meaning of the Term

Watson says that "sustained release", which modifies the non-pH dependent agent in the patent claims, should mean "to slow the rate of release" rather than to "slow release" because the patent explains that the pH-dependent agent increases the rate of release. Watson Opposition, p. 7. However, the pH-dependent agent claim limitation is not accompanied by the term "sustained release". The patent specification gives no reason why the art-accepted meaning of the term "sustained release", as shown by the technical publication cited by Plaintiffs (REMINGTON'S PHARMACEUTICAL SCIENCES (Gennaro Ed., Mark Publishing Co., 1990)) should be ignored or modified. *See* Plaintiffs' Brief, Dkt. No. 148, Section IV, A.3, p. 10; Ettinger Decl., Dkt. No.

[2] It should also be noted that there is a good chance that the Delaware court memorandum opinion is incorrect. "[A]lthough the Federal Circuit generally declines interlocutory appeals, when the court dismisses the claim or when the parties battle the patent dispute to trial and then appeal the court's claim interpretation, 'nearly 40 percent of the claims [sic] constructions are changed or overturned by the Federal Circuit.'" *Kollmorgen*, 147 F. Supp. 2d at 467. Given this high error rate, this Court should evaluate the evidence itself and should make its own learned analysis, rather than abrogate to another court this most significant issue in this litigation.

148-8, Exh. 6, p. 1677.

Watson also says that the art-recognized meaning of "sustained release" should be ignored because the patent incorrectly states that its comparative examples were controls (*i.e.*, PD-0052-22A and PD-0052-25B (incorrectly identified as -22B in Watson's Brief, Dkt. No. 154, Section V.A.1.a, p. 8)). Watson claims that these are not controls because Table 2, column 5 of U.S. Patent No. 6,287,599 (the "'599 patent") is headed "Guanfacine Sustained Release Tablets." However, Watson missed that '599 patent Table 1 (where the components of the formulations tested in Table 2 were identified) under the preface "Note:" reads that "PD0052-22A and PD0052-25B contain no ionic materials in the formulations. These two formulations serve as a control." Ettinger Decl., Dkt. No. 148-3, p.5. Watson forgot to "Note" PD-0052-22A and -25B were controls, as they did not include all of the claimed components. Watson's dispute with the data in Table 2 also disappears in light of this fact. These controls did not include all of the components required by the claimed invention, and that is why they are legitimate controls. Plaintiffs' representation of the Table 2 data in the patent is correct. Plaintiffs' Brief, Dkt. No. 148, Section IV, pp. 10-12.

2. Watson Is Incorrect - The Same Chemical Entity Can Have Non-pH Dependent Sustained Release Properties and pH-Dependent Properties in a Formulation

Watson claims that the non-pH dependent sustained release agent cannot also function as a pH-dependent agent in the same formulation because that is what the Delaware court said. Watson Opposition, Dkt. No. 154, Section V.A.1.b, pp. 8-9. Watson does concede that the Delaware court's construction is the subject of a pending request for reconsideration, however. *Id.* at 8-9, n. 9. Further, as explained above, the Delaware court memorandum opinion has no binding effect on this Court. Rather, the Court should make its own interpretation here.

Furthermore, nothing in the patent specifications precludes a chemical entity from having both non-pH dependent and pH dependent properties in a single formulation. The claims do not say that the chemical entity that acts as non-pH dependent must be a unique chemical entity when compared to the pH dependent agent. All that is required is that there are two different properties

in the formulations. Baseless restrictions ungrounded in the claim language, like the one that Watson proposes, should not be read into the claims.

Watson's argument about "controls" discussed above proves Plaintiffs' present point and the point discussed in the immediately following section. Watson complains that the control formulations included chemicals that could act as non-pH dependent sustained release agents but that "any variation in dissolution data set forth in Table 2 cannot be attributed to the presence of a sustained release excipient, because each formulation disclosed contains a sustained release agent." Watson Opposition, Dkt. No. 154, Section V.A.1.a, p. 8. The properties of a chemical must be evaluated *in the formulation*. The patents claim compositions, not individual components. The properties of the claimed composition depend upon the component parts of the formulation.

The composition may be formulated in many manners where different amounts of one chemical entity may be distributed in different ways in the tablet. That means, for example, that the chemical may be present in different parts of the tablet. For example, the chemical, when near the surface of the tablet, may act one way and when present deeper in the tablet may act another way. A component, for example, does not typically act to sustain release of guanfacine at any point in time unless the guanfacine is solubilized so that it can leave the tablet. Guanfacine has poor solubility at basic pH. '559 patent at col. 1, ll. 14-16. The invention provides for this. The differences in "environment" in a single tablet are evident, for example, from '599 patent dependent claim 13, which notes a microenvironment in the composition.

The bottom line is that a chemical in the composition must be evaluated in its context as formulated. One chemical can have two functions in a single formulation. All that is required by the claims is that both functions, *i.e.*, non-pH dependent sustained release and pH-dependency, are imparted to the composition. The specification says just that by including the same chemical entities as non-pH dependent and pH dependent agents. Watson actually agrees when it says that all that matters is the "impact on the rate of release of the pharmaceutically active agent." Watson Opposition, Dkt. No. 154, Section V.A.1.c, p. 10. That is precisely why one chemical can act as both in a single formulation.

3. A Component's Properties Must Be in the Context of a Formulation

Watson complains that the patent specification does not support the phrase "when the composition is formulated" because "[n]othing in the specification suggests that an excipient's function only can be determined when the entire composition is formulated." Watson Opposition, Dkt. 154, Section V.A.1.c, p. 10. Watson's argument fails to consider what is being claimed – a composition or formulation. The patents do not claim individual components that are unassociated. They are all combined to form the claimed composition. The non-pH dependent and pH dependent properties function to affect the release of the pharmaceutically active component. Absent the pharmaceutically active agent, the other parts of the composition have no function at all. In other words, everything is essentially useless, for the purpose of the claimed invention, until combined or formulated. It is disingenuous to insist that the effects of the components of the claimed composition should be evaluated in the absence of the entire composition, as that would ignore what this entire invention is all about.

That the same components are identified in the specifications as both "pH-dependent agents" and non-pH dependent sustained release agents" is only one indication of why the components are evaluated when formulated. Watson Opposition, Dkt. No. 154, Section V.A.1.c, p. 11. *See also* Section II.B.2, above. Ordinary logic is the most persuasive evidence that this phrase must be in the definition.

4. Non-pH Dependency Must Be in the Context of Gastrointestinal pH

The purpose of claim construction is to define the claim with greater precision than had the patentee. *Pall Corp. v. Hemasure, Inc.*, 181 F.3d 1305, 1308 (Fed. Cir. 1999). Watson appears to believe that this means that the only correct claim construction must recite, *ipsis verbis*, the words of the patent specification. *See, e.g.*, Watson Opposition, Dkt. No. 154, Section V.A.1.d, p. 11 ("The term 'gastrointestinal' does not appear anywhere in the '599 patent specification."). Again, the claim construction must be made in the context of the invention, its purpose, and the patent specification. The patents claim a pharmaceutical composition for administering guanfacine to a patient. Guanfacine is administered orally, such as by tablet. A tablet, when swallowed, travels through the gastrointestinal tract. The whole purpose of the

presently claimed invention is to deliver guanfacine over a large portion of the time that the tablet travels through the system. Whether the tablet releases guanfacine at pHs outside of those to be encountered in the gastrointestinal tract is too far removed from the context of the present invention. Consequently. Plaintiffs' construction is correct. *See also* the logic applied in Sections II.B.2 and II.B.3, above.

C. 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

1. A Claim Term Is not Construed by Merely Parroting Its Language

Watson complains that the patents provide only that the pH dependent agent increases the rate of release of the pharmaceutically active agent at pHs above 5.5, but "provides no additional information regarding this claim term." Watson Opposition, Dkt. No. 154, Section V.A.2.a, p. 13. Therefore, Watson urges the Court to interpret this claim term merely by parroting the claim language itself. However, in claim construction, "the court establishes the scope and limits of the claim, interprets any technical or other terms whose meaning is at issue, and thereby defines the claim with greater precision than had the patentee." *Pall Corp.*, 181 F.3d at 1308. Watson's proposed construction does not do this. Watson finds nothing more in the specification than the exact claim language itself because Watson refuses to think about the claim limitation. It is reading the claims in a vacuum.

On the other hand, Plaintiffs' construction is correct because it considers the field of the invention, the patent specifications, and the language of the claims. It provides that the property of being pH dependent is evaluated when the claimed composition is formulated and the only feasible comparators for "increases".

2. Neither a Patent nor Its Claims Are required to Give the Scientific Reason Why the Invention Works

Watson faults the patents construed by the parties and Plaintiffs' claim construction because "[t]he patent is silent as to how [the pH dependent] agents behave at pHs at or below 5.5 and what impact these agents have on the rate of release of the pharmaceutically active agents at pHs at or below 5.5. Thus, the specification does not explain how these agents depend on pH."

Watson Opposition, Dkt. No. 154, Section V.A.2.a, p. 13. However, a patentee is not required to explain how her invention works. *S3, Inc. v. nVIDIA Corp.*, 259 F.3d 1364, 1369 (Fed. Cir. 2001).

3. Watson Is Incorrect - The Same Chemical Entity Can Have pH Dependent Properties and Non-pH Dependent Sustained Release Properties in a Formulation

For the reasons discussed in Section II.B.2, above, the same chemical entity can have pH dependent properties and non-pH dependent sustained release properties in a formulation. *See* Watson Opposition, Dkt. No. 154, Section V.A.2.b, p. 13.

4. A Component's Properties Must Be in the Context of a Formulation

For the reasons discussed in Section II.B.3, above, a component's properties must be in the context of a formulation. *See* Watson Opposition, Dkt. No. 154, Section V.A.2.c, p. 13.

5. Comparing the Release Rate Above and Below pH 5.5 Is Correct

Watson argues that the first comparator for the pH dependent agent proposed by Plaintiffs (*i.e.*, in an environment having a pH of 5.5 or less) is wrong because it "contradicts the patent's stated goal" of providing pharmaceutical compositions with pH-independent or minimized pH-dependent active agent dissolution profiles. Watson Opposition, Dkt. No. 154, Section V.A.2.d, p. 14. Watson's proposition is absurd. Following Watson's path, one would not be able to include a pH dependent component in the claimed composition at all, since that component is, by definition, contrary to the alleged goal of pH independence.

Watson can only come to its erroneous conclusion by ignoring that the stated goal is that of the entire composition, not just one component. The claimed composition is the sum of its parts and acts in a pH-independent manner because of its parts.

6. Plaintiffs' Construction Does not Make the pH-Dependent Agent's Function Optional

Watson argues that Plaintiffs' construction makes it optional for the pH-dependent agent to be responsible for increasing the release rate. Watson Opposition, Dkt. No. 154, Section V.A.2.d, p. 14. It is impossible to understand how that is so, particularly since Watson does not explain its point. All that Plaintiffs' propose is that there are two comparators for the term

"increases" and that meeting either is encompassed by the claims. When something is increased, it must be increased over something else. That is simply logical. There are two things over which the increase can occur in this claim term, as exemplified in the specification. *See* Ettinger Decl., Dkt. No. 148-3, Exh. 1, Tables 1 and 2. Plaintiffs' proposed construction articulates these two possibilities, and either will meet the claim limitation of increasing release at a pH greater than 5.5.

7. Watson's Agreement with Impax that this Term Is indefinite Is Inconsistent with the Fact that Watson Offers a Construction of the Term

Watson drops a footnote in which it agrees with Impax that this claim limitation is indefinite under 35 U.S.C. 112. Watson Opposition, Dkt. No. 154, Section V.A.2, p. 12, n. 12. Watson's claim of indefiniteness cannot be reconciled with its leading point concerning this claim term that "Watson's proposed construction most closely mirrors the claim language, clarifies the claim language, and stays true to the patentee's teachings in the specification." *Id*. at p. 12. If this term were indeed indefinite, Watson could not allege the foregoing.

D. Polymer that Swells at a pH in Excess of 5.5

1. Watson's Reading into the Claim Limitation that the Relevant pH Is of the Surrounding Media Is Confusing and Unwarranted

Watson contends that "for the polymer to swell in response to a changing pH, the variable pH must be that of the surrounding media." Watson Opposition, Dkt. No. 154, Section V.3.a, p. 15. However, the plain language of the claim indicates that when the polymer is at a pH greater than 5.5, it expands. No further explanation is necessary; swelling at a pH in excess of 5.5 is a property of the polymer as formulated. The claimed invention is a formulation, not isolated components. It does not matter whether the tablet is in a medium having a pH greater than 5.5, if the polymer itself is not in contact with that media. For example, it is possible that the tablet is in a surrounding medium having a pH greater than 5.5 but that none of that medium is in contact with the polymer. It is also possible that only a portion of the polymer is at the tablet surface and is contacting the surrounding medium having a pH greater than 5.5 while the polymer distributed inside the tablet is not. In the former instance, none of the polymer would be at a pH greater than

5.5, and in the latter instance, only that polymer on the surface of the tablet would be at a pH greater than 5.5, despite the medium surrounding the tablet having a pH greater than 5.5. These differences in a single tablet are evident, for example, from '599 patent dependent claim 13, which notes a microenvironment in the composition.

Watson's additional language about the surrounding media only confuses the construction of a simple claim term.

2. A Component's Properties Must Be in the Context of a Formulation

For the reasons discussed in Section II.B.3, above, a component's properties must be in the context of a formulation. *See* Watson Opposition, Dkt. No. 154, Section V.A.3.b, p. 15.

E. Agent that Increases the Solubility of Said at Least One Pharmaceutically Active Agent at a pH greater than 5.5

Watson's arguments b.-d. (Watson Opposition, Dkt. No. 154, Section V.A.4, p. 16) concerning this claim term are a rehash of its arguments that are exposed as incorrect in Sections II.B.3 (A Component's Properties Must Be in the Context of a Formulation), II.C.5. (Comparing the Release Rate Above and Below 5.5 Is Correct), and II.C.6 (Plaintiffs' Construction Does not Make the pH-Dependent Agent's Function Optional), above.

F. Reducing the Likelihood of Side Effects

1. Watson's Construction of "Likelihood" as Incidence Rate Is Inconsistent with the Patent Specification

Watson wants "likelihood" to mean "incidence rate" or how many times a side effect was experienced because Tables 9 and 10 of U.S. Patent No. 6,811,794 (the "'794 patent") summarize data consisting of "count" information, or the number of instances when a patient experienced side effects." Watson Opposition, Dkt. No. 154, Section V.A.5.a, pp. 17-18. Watson supports its novel number-specific construction of the plain and ordinary term "likelihood" by arguing that "number of side effects" as used in the patent means "the number of distinct side effects the formulation caused in a study whereas incidence rate refers to the number of times any side effect was reported." Watson Opposition, Dkt. No. 154, Section V.A.5.b, p. 18. Either way Watson argues, its definition is a number of side effects, and that is the wrong construction of this claim

term.

Plaintiffs' correctly pointed out in their opening brief that the patent expressly distinguishes between number of side effects and likelihood of side effects. Plaintiffs' concluded from this that the patentee intended likelihood to have its ordinary meaning, *i.e.*, "probability". Plaintiffs' Brief, Dkt. No. 148, Section IV.E.1, p. 18-19. There is no need to torture the term "number" in Plaintiffs' proposed construction, to split hairs, or to explain how one concept of "number" differs from another. The patent distinguishes between number and likelihood, so any construction that uses a number of side effects, whether the number means type or incidence, must be incorrect.

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III. CONCLUSION

The Court is requested, for the foregoing reasons and reasons in Plaintiffs' Opening Claim Construction Brief, to interpret the claims of the patents-at-issue as proposed by Plaintiffs.

Dated: May 4, 2012

/s/ *Matthew D. Murphey*

Matthew D. Murphey
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