IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ELAN PHARMA INTERNATIONAL LIMITED,	)	
	)	C.A. No. 06-438-GMS
Plaintiff,	)	
v.	)	
ABRAXIS BIOSCIENCE, INC.,	)	
Defendant.	)	

MOTION FOR RECONSIDERATION

The Court's May 19 Order (D.I. 569) (the "Order"), which was intended to clarify the construction of the terms of plaintiff Elan Pharma International Ltd.'s ("Elan's") '363 Patent, has had the opposite effect and will lead to the introduction of clear legal error into the trial of Elan's infringement claims against defendant Abraxis Bioscience Inc. ("Abraxis"). Put more clearly, if the Order stands, Elan will be thwarted from presenting its literal and equivalents infringement case at all, a result tantamount to the granting of summary judgment in the absence of any motion therefor. Elan accordingly hereby respectfully moves under Fed. R. Civ. P. 59(a) and 59(b) for reconsideration of the decisions set forth in the Order, and respectfully requests that the Order be vacated and the claims remain construed as set forth in the original *Markman* Order (D.I. 271).

The Order creates, rather than obviates, confusion and complexity in the analysis of Abraxis's infringing conduct for at least six distinct reasons: (1) the Order suggests that it is the crystallinity of a "product" or a "medicament" that limits Elan's claims or their infringement by Abraxis, when the independent claim is drawn not to products, not to medicaments, but to

"***particles*** consisting essentially of 99.9%-10% by weight of a crystalline medicament useful in treating cancer" (emphasis supplied); (2) the Order introduces a new limitation ("entire") that is found nowhere in any claim, nowhere in the specification of the '363 Patent, and nowhere in the extrinsic evidence of record; (3) the Order, and the revised construction , are internally inconsistent and would render certain of the '363 Patent's claims internally redundant or redundant with each other; (4) the Order seemingly would cause the claims not to read on disclosed preferred embodiments of the '363 Patent, which is an illogical and legally-disfavored outcome; (5) the Order imposes an unsupported quantitative limitation on the crystallinity of the claimed invention, overlooking specific quantitative ranges already supplied in the claims; and (6) importantly, the Order suggests that infringement can be avoided by combining infringing particles otherwise meeting all claim limitations into a "product" with other particles that do not meet the claim limitations, excipients, or other "amorphous" substances.

Elan respectfully submits that each of these flaws in the Order rises to the level of legal error in the application of controlling Supreme Court and Federal Circuit precedent. If the Order stands, the clear outcome would be that claim construction would have to be re-conducted *de novo* consistent with the tenets of *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).

Elan does not question the Court's authority to revisit a claim construction, but rather respectfully argues that the significant revision to the claim interpretation two weeks before trial introduces legal error to adjudication of a claim whose construction was clear and which both Elan and Abraxis have been preparing for months to apply at trial. The confusing and unsupported aspects of the Order are precisely the type of "mistake . . . oversight . . . or inadvertence" that Rules 60(a) and 60(b) were intended to address.

Elan therefore also respectfully requests entry of the requested relief, namely, vacating of the May 19 Order, on an expedited basis, to avoid needless further expenditures by the parties.[1] As the Court is aware, under Rule 60(a), correction of an erroneous order is appropriate and timely to redress "a mistake resulting from oversight or omission ***whenever one is found*** in a[n] order . . . ," such that if the Court accepts Elan's submissions as to the Order, it need not entertain a customary briefing schedule, and need not hear from Abraxis, due to the plain nature of the errors in the Order and in view of the impending trial date. (emphasis supplied).

Elan respectfully submits the following bases for its argument that the Order introduced multiple grounds of error.

A. No Canon Of Claim Construction Provides A Justification For Adding In "Entire"

The Court construed the term "crystalline medicament useful in treating cancer," which is recited expressly in claim 1 of the '363 Patent, to mean "a medicament suitable for treating cancer that has a regular arrangement of atoms or molecules in a space lattice, as distinguished from amorphous." D.I. 271, Order Construing The Terms Of U.S. Patent Nos. 5,399,363 and 5,834,025. The Court has now revisited its construction and now newly defines the term "crystalline medicament' to require "that the *entire* medicament 'has a regular arrangement of atoms or molecules in space lattice, as distinguished from amorphous'." D.I. 569 at 2 (emphasis supplied). Elan respectfully believes there is no basis for importing the extraneous and

[1] By letter to Elan's counsel dated May 19, 2008, counsel for Abraxis requested that Elan confirm that it would not proceed with an infringement case at trial. Abraxis further noted in its Response (D.I. 573) filed today to Elan's Letter (D.I. 571), filed May 20, 2008, that Elan has not provided an answer to this request yet. This is so because Elan believes that the granting of this Motion For Reconsideration will make Abraxis's request moot. Should this Motion not be granted, Elan will evaluate Abraxis's request at that time. As Elan has shown by withdrawing its infringement claims under the '025 Patent , Elan is mindful of economic efficiencies and would not try a case on infringement that was effectively barred by a claim construction that Elan believes to be erroneous.

If the Court is unwilling to entertain and grant this Motion For Reconsideration, Elan would find itself in the position of requesting that the Court enter final judgment that Abraxis's accused product does not, on the current and disputed new claim construction of the Order, infringe Elan's claims.

unsupported limitation "entire" into the construction of the term "crystalline medicament useful in treating cancer." The specification and the prosecution history of the '363 Patent nowhere require or suggest that the *entire* medicament in the claimed particle have only crystalline character, i.e., a regular arrangement of atoms or molecules in a space lattice, as distinguished from amorphous. *Seachange Int'l., Inc. v. C-Cor, Inc.*, 413 F.3d 1361, 1376 (Fed. Cir. 2005) (citing *Ecolab, Inc. v. Envirochem, Inc.*, 264 F.3d 1358, 1366 (Fed. Cir. 2001)) ("conclud[ing] that district court erred" by "import[ing] a limitation into a claim [when the purported] limitation ha[d] no basis in the intrinsic record").

The '363 Patent teaches surface modified nanoparticles of cancer drugs, which have a better therapeutic index than other formulations of such drugs. '363 Patent, col. 1, lns. 19-26; col. 2, lns. 19-21. The better therapeutic index results from increased efficacy or decreased toxicity, or both. *Id; see also* Plaintiff Elan Pharma International Limited's Answering Claim Construction Brief, D.I. 148, at 7. The prosecution history supports and elaborates on these properties. *See id*. at 8. The claim terms must be considered in the context of this disclosure of what the patentee invented.

With respect to the term "crystalline medicament," the specification and prosecution history distinguish the nanoparticles of the '363 Patent claims, i.e., those containing a crystalline medicament useful in treating cancer, from solvent precipitated nanoparticles contaminated with solvent. '363 Patent, col. 2, lns. 30-34; *see also* Exh. 1 to the accompanying Declaration of Lisa A. Chiarini ("Chiarini Decl."), '363 Patent Prosecution History, Paper No. 6/a at 4, para. 5 ("Applicant's crystalline particles. . .are essentially free of solvent contamination."); Paper No. 7 ("The crystalline particles . . .are essentially free of solvent contamination."); Paper No. 2, at 3 (". . .solvent precipitation techniques such as described in U.S. Patent No. 4,826,689 for

preparing particles tend to provide solvent contaminated particles."); *id.* at 5 (". . .precipitation techniques for preparing particles tend to provide particles contaminated . Solvent contamination could lead to toxicity and destabilization of the particle."). Thus, the distinction made in prosecution, and crucial to understanding of the limitation in question, was made on the basis of having no solvent contamination and having crystalline character, i.e., some order, as distinguished from possibly-contaminated particles formed from solvent precipitation and lacking any order.

The Court originally rejected Elan's proposed construction of "crystalline medicament useful in treating cancer" to mean "a medicament in which a portion of the atoms [or molecules] are regularly arranged in a space lattice." D.I. 271 at 2. Although the intrinsic and extrinsic evidence supported Elan's proposed construction, the Court found "no support in the claim language, the specification, or the prosecution history for reading this limitation into the claim, and therefore rejects it." D.I. 271, n. 4.[2] Given the Court's construction of this term without Elan's proposed use of "portion," Elan recognized that while not incorrect, its proposed term "portion" was arguably superfluous: the Court's construction provided that the "crystalline

[2] Elan respectfully disagrees with the Court's conclusion for several reasons. First, the '363 Patent specification discloses that "[t]he anticancer agent is present in *one or more* discrete crystalline *phases*." (emphasis supplied). If the anticancer agent, i.e., medicament, is present in more than one phase in the particle, then "a portion" of the medicament in that crystalline phase must by necessity exist. Indeed, the term "phase" is defined as ". . . [a] portion of matter. . . ." See Chiarini Decl. Exh. 2 (Webster's Ninth New Collegiate Dictionary, (1989)). Second, the disclosed preferred embodiment for preparing the particles, wet milling, fractures the medicament, creating at least surface discontinuity, cracks and fissures, and other non-crystalline characteristics in the medicament. *See*, *e.g.*, Plaintiff Elan Pharma International Limited's Opening Claim Construction Brief, D.I. 141, at 19. Third, the '363 Patent describes reducing particle size prior to milling by airjet fragmentation. Airjet fragmentation is known to cause polymorphic transitions, including formation of amorphous solid. See Chiarini Decl. Exh. 3 Broka-Pfeiffer, K. et al., "*Influence of mechanical activation on the physical stability of salbutamol sulphate*," Abstract ("A correlation between mechanical activation and the amount of the amorphous regions is shown clearly."); Larran et al., *Micronization of Pharmaceutical Powders for Use in Inhalation*" (". . .during a given micronisation process -either spiral jet milling or opposed jet milling -- it is possible that the forces required to produce material that is within the desired particle size range may also affect the amorphous content of the micronsized drug substance of the micronized rugs substance . . . ."Consequently, the '363 Patent discloses and clearly contemplates using partially amorphous drug as a starting material, and nowhere excludes nor implies the unsuitability of the presence in combination with crystalline particles of a cancer drug the co-existence of partly or wholly amorphous particles of that drug or any other substance.

medicament" limitation would be met as long as the drug component of a plurality of particles within an accused substance (i.e., two or more discrete particles of a crystalline medicament useful in treating cancer) had a regular arrangement of atoms or molecules in a space lattice, as distinguished from amorphous (no regular arrangement of atoms or molecules in a space lattice).

Elan understood that the Court had elected to apply a strict standard by not introducing an arguably superfluous word into the definition of the term "crystalline medicament." Now, however, the Court's clarification has introduced a term, "entire," that has no support in the claim language, the specification, or the prosecution history. Elan is unaware of extrinsic evidence supporting this construction, either. The clarification, then, amounts to a new and unsupported instruction of a significant claim term.

Elan also suggests that the new claim construction conflicts with other words of the claim. A claim construction should not lead to claim terms contradicting each other. *Z4 Techs., Inc. v. Microsoft Corp.*, 507 F.3d 1340, 1348 (Fed. Cir. 2007) ("Because a construction . . . conflicts with 'both the plain language of the claims and the teachings of the specification,'[] the district court's . . . claim construction cannot be sustained.") (quoting *NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1070 (Fed. Cir. 2002)). However, the Court's recent clarification Order seems to do just this.

Claim 1 of the '363 Patent recites "[p]articles consisting essentially of ***99.9%-10% by weight*** of a crystalline medicament useful in treating cancer." (emphasis supplied). Both plaintiffs and defendants have treated the "99.9%-10% by weight" limitation as a limitation with respect to the crystalline character of the drug component of the particles. *See* Proposed Pretrial Order, D.I. 508, Exh. 11 at 5 ("No Elan expert opined that the crystalline content of the *particles* was above 10% by weight. . . .") and Exh. 10 at 8 ("Because only two claim limitations

[crystalline and noncrosslinked] remain in dispute. . . ."). Thus, there is *already* a quantity limitation in the claims as construed modifying "crystalline medicament:" 99.9%-10% by weight. Under the construction required by the recent Order, the claim would recite "*99.9%-10% by weight* of an '*entire medicament* [that] has a regular arrangement of atoms or molecules in a space lattice, as distinguished from amorphous.'" In other words, the particle must contain both 99.9%-10% [crystalline] medicament and be entirely [crystalline] medicament. This is an irreconcilable conflict in claim terms. Alternatively, requiring the entire (100%) "crystalline medicament" to have a regular arrangement of atoms or molecules in a space lattice reads a limitation, i.e., "99.9%-10%" out of the claim, an outcome precluded by directly applicable case law. *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co*. 520 U.S. 17, 29 (1979) "[e]ach element contained in a patent claim is deemed material to defining the scope of the patented invention."

Elan also respectfully suggests that the Court's clarified claim construction excludes recited examples in the '363 Patent, including preferred embodiments, from falling within the scope of the claim. All of the examples of the '363 Patent describe particles prepared by wet milling crystalline medicament starting material. '363 Patent at 8:23-13:68. Wet milling of crystalline medicament starting material reduces particle size by fracturing the crystalline medicament into smaller particles. This fracturing process introduces imperfections into already imperfect crystals. A proper construction should not by law exclude preferred embodiments and examples absent some express reason in the prosecution history or specification for doing so. *Invitrogen Corp. v. Biocrest Mfg.*, L.P., 327 F.3d 1364, 1369 (Fed. Cir. 2003) (quoting *Vitronics Corp. v. Conceptronic, Inc*., 90 F.3d 1576, 1583 (Fed. Cir. 1996)) ("construing a claim to exclude a preferred embodiment 'is rarely, if ever, correct and would require highly persuasive

evidentiary support.'"). No such express reason to construe the claims so as to exclude preferred embodiments exists here.

The Court's construction "that the entire medicament 'has a regular arrangement of atoms or molecules in space lattice'" also precludes embodiments in which the particles contain more than one crystal polymorph. '363 Patent, col. 2, ll. 29-30 ("The anticancer agent is present in one or more discrete crystalline phases."). Discrete crystalline phases would require a discontinuity of the regular arrangement of atoms or molecules in a space lattice. Even Abraxis agrees that the specification discloses such an embodiment. *See* Abraxis's Answering Claim Construction Brief, D.I. 143, at 3-4 ("[A]n entirely crystalline medicament may have portions with differing crystalline lattice structures. [citations omitted].")

The evidence from learned treatises presented during the claim construction phase also preclude restricting the scope of the claim to particles that are "entirely" crystalline. "'[C]rystallinity was a variable property that ranged from 100% (a perfect crystal) to 0% (amorphous) depending on the state of order/disorder in the lattice.'" Elan Pharma International Limited Opening Claim Construction Brief, D.I. 141 at 19 (citing Exh. 9 of the Joint Appendix Of Intrinsic And Extrinsic Evidence, Suryanarayanan and Mitchell, *Evaluation of Two Concepts of Crystallinity Using Calcium Gluceptate as a Model Compound*, 24 Int'l J. of Pharmaceutics, at 1-2 (1985); Exh. 11 Saleki-Gerhardt et al., "*Assessment of disorder in crystalline solids*," Int'l. J. Pharmaceutics 101:237-47 at 237 (1994) ("In the processing of pharmaceutical solids [], as in milling . . . disruption or activation of the crystal structure often, leading to various degrees of disorder in the form of crystal defects and/or amorphous regions.")). Amorphousness is the absence of structure. See Exh. 4, Rebuttal Expert Report Of Abraxis's Expert Dr. Jerry Atwood, at para. 4 ("This complete lack of ordering of the molecules is the essential defining

character of an amorphous solid."); Elan Pharma International Limited Answering Claim Construction Brief D.I. 148 at 13-14 ("amorphous: without definite form or shape: formless; without real or apparent crystalline form; without structure; Exh. 42 at A 0781 (Webster's Third New Int'l Dictionary (1986)).").

The Court's initial claim construction envisioned that crystallinity exists over a continuum, while amorphousness is an absolute. The new Order appears to reverse this.

The Court's clarification further requires a physical impossibility: few, if any materials, are found in which the "entire" material is crystalline. Abraxis's expert in crystalline materials, Dr. Atwood, states in his rebuttal expert report that "[a]lmost all real single crystals are, in a sense, imperfect, being composed of slightly misaligned minute regions (mosaic blocks, Fig. 4.4)." Chiarini Decl. Exh. 4 at para. 84.

Finally, the Court's requirement that the "crystalline medicament" refer to the entire medicament in the particle necessarily renders the construction of "consisting essentially of" as precluding any additional ingredients. Such construction is not consistent with the long standing patent law that "consisting essentially of" is a semi-open transitional phrase that does not preclude additional ingredients that do not affect the basic and novel properties of the invention as claimed. *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998).

In sum, the Court's clarified claim construction requires introducing a term that: (i) is not supported in the intrinsic evidence; (ii) is not supported in any extrinsic evidence; (iii) conflicts with other terms already in the claim; and (iv) excludes exemplary and preferred embodiments of the invention. This is the first reason that Elan submits the Order should be vacated.

B. <u>The Court's Construction Appears To Confuse "Particles" And "Product"</u>

The Court's Order (D.I. 569) suggests that the word "medicament" refers to more than the drug component of each particle. The Court states that the term "crystalline medicament . . . requires a medicament that is not amorphous, foreclos[ing] the argument that a largely amorphous *product* can infringe the '363 patent or, more specifically, the term 'particles consisting essentially of' as construed by the court." *Id.* (emphasis supplied).

Claim 1 of the '363 Patent claims "particles," and nothing except particles. These particles can be used to form a product or composition (*see* '363 Patent claim 9), *e.g.*, a powder, suspension, or dispersion; they can also be administered to a subject (see '363 Patent claims 9, 10, and 11), *e.g.*, intravenously or orally in any of these forms of products. Thus, a product may include as part of its composition one or more of the claimed particles, but the "product" is not what is claimed. A product containing more than one, or a process using more than one, particle that meets the limitations of the claim would necessarily, and always, infringe the '363 Patent's claim 1, and possibly other of its claims. *Suntiger, Inc. v. Scientific Research Funding Group*, 189 F.3d 1327, 1336 (Fed. Cir. 1999) ("[W]e have never required that a claim read on the entirety of an accused device in order to infringe. If a claim reads merely on a part of an accused device, that is enough for infringement."). Accordingly, Elan respectfully reasserts its position that a product containing both infringing and non-infringing particles infringes the '363 Patent. However, the Court's Order suggests that such a product would *not* infringe the claim. The last preamble clause and footnote 1 appear now to require every particle of an accused product to be entirely "crystalline." Elan respectfully suggests that this is simply not the law.

Such a position would, among other things, violate the doctrine of claim differentiation. The doctrine of claim differentiation, while not conclusive, does and should inform claim construction. *Tandon Corp. v. U. S. Int'l Trade Comm'n*, 831 F.2d 1017, 1023 (Fed. Cir. 1987)

("There is presumed to be a difference in meaning and scope when different words or phrases are used in separate claims. To the extent that the absence of such difference in meaning and scope would make a claim superfluous, the doctrine of claim differentiation states the presumption that the difference between claims is significant."); *Autogiro Co. of Am. v. U.S.* 384 F.2d 391, 404 (Ct. Cl. 1967) ("[T]he concept of claim differentiation [ ] states that claims should be presumed to cover different inventions. This means that an interpretation of a claim should be avoided if it would make the claim read like another one.").. In the '363 Patent, dependent claim 8 is directed to a *composition* (that is, something much like a "product") comprising the prior-claimed particles of claim 1. Thus, under the doctrine of claim differentiation, claim 1 is broader than claim 8, and therefore broader than a *composition* comprising the particles. Claim 1 is directed to *particles*, which may be a part of a composition, but are a claimed invention on their own. *See also* Elan Opening Claim Construction Brief, D.I. 141 at 18-19.

Of comparable concern, the Court seems to treat the entire nanoparticle, and not just the medicament within the particle, as crystalline: "In other words, because the *particles* composed of crystalline medicament claimed in the '363 Patent *cannot be amorphous* under the court's clarified claim construction Order, the term 'particles consisting essentially of' *cannot encompass amorphous, as opposed to crystalline, particles*." D.I. 569, n. 1 (emphasis supplied).

No party has ever disputed that 90% of Abraxis's commercial "product" Abraxane® is human albumin, a protein that both parties agree is amorphous. *See* Chiarini Decl. Exh. 6, Selvaraj Dep. Tr. at 96:8-9 ("Albumin is amorphous").[3] Thus, even a particle in Abraxane® that

[3] Elan's purpose in noting these facts is to point out that either the Court or Abraxis would err in advancing a characterization of or claim construction influenced by the alleged degree of crystallinity or amorphousness of respective particles within Abraxane® until Abraxis's proofs on this subject have been aired in open court, and not in one-sided allegations by Abraxis. Indeed, just today, Elan elicited remarkable testimony from Katherine Melody, the Abraxis-retained technician who performed key steps of Abraxis's XRPD testing and whose deposition the Court authorized at the pretrial conference following Abraxis's late and selective disclosure of certain pages of her laboratory notebooks. Ms. Melody testified that even as the person who conducted Abraxis tests of

contains a perfect paclitaxel crystal would still also contain amorphous human albumin adsorbed on its surface. It cannot be the case that by combining infringing crystalline paclitaxel particles with amorphous albumin (or, for that matter, with an admixture of amorphous paclitaxel products) Abraxis can avoid liability for infringement of claim 1, which is drawn solely to a plurality of crystalline particles. Yet the Court's new construction invites such a contention by Abraxis.

While it is proper to construe a claim with regard to the accused product, it is not appropriate to construe a claim with a view towards an ultimate decision on infringement or a conclusion as to whether the accused product, or some other hypothetical product, can infringe. *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326-1327 (Fed. Cir. 2006) *citing Multiform Desiccants, Inc.. v. Medzam*, Ltd., 133 F.3d 1473, 1476-78 (Fed. Cir. 1998) ("While a trial court should certainly not prejudge the ultimate infringement analysis by construing claims with an aim to include or exclude an accused product or process, knowledge of that product or process provide meaningful context for the first step of the infringement analysis, claim construction.") . Elan requests that the Court avoid this error and vacate its Order.

Conclusion

The Order, if taken to "foreclose the argument that a largely amorphous product can infringe the '363 Patent", effectively would require Elan to request the entry of judgment of non-

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Abraxane®, she was "still not sure" whether the particles of paclitaxel in Abraxane were crystalline or amorphous. Melody Tr. at 104:13-105:1

> Q: Is the x-ray powder diffraction work that you did for Abraxis sufficient enough to make a conclusion about the nanoparticles in Abraxane, whether they're crystalline or amorphus?
>
> . . .
>
> A: I'm still not sure I understand whether they are crystalline or amorphus.

The fact that at this late date Abraxis's own key vendor technicians cannot vouch for XRPD as a conclusive distinguishing assay method between crystalline and amorphous materials cautions strongly against any claim construction influenced by Abraxis's characterizations of the supposedly-amorphous nature of the Abraxane® "product," quite apart from the other reasons why such a claim construction would be legally unfounded.

infringement. For the reasons set forth above, .such an outcome -- which is functionally equivalent to entry of a directed verdict on the merits of Elan's infringement claim, based on the current claim construction -- is not justified by the content of the claims and specification of the '363 Patent as interpreted under governing law, and is premature given that the parties have not had an opportunity to present their substantive claims to the jury...

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