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.	)	

PLAINTIFF'S OFFER OF PROOF
REGARDING TESTIMONY OF DR. ERIC J. MUNSON

WHEREAS, during a telephone conference with the parties on May 29, 2008, the Court granted defendant Abraxis Bioscience, Inc.'s ("Abraxis") oral motion to strike the Second Supplemental Expert Report of Dr. Eric J. Munson ("Munson Second Supplemental Expert Report"), submitted in response to the Court's May 19, 2008 Order (D.I. 569) clarifying its August 17, 2007 claim construction Order (D.I. 271);

NOW COMES plaintiff Elan Pharma International Ltd. ("Elan"), and submits the following offer of proof: If Dr. Eric J. Munson had been permitted to testify at trial concerning the facts underlying, and basis for the conclusions set forth in, the Munson Second Supplemental Expert Report (attached hereto as Exhibit 1), his testimony would have been as follows:

1. The Court's clarification Order contains a "Whereas" paragraph which noted that the term "'crystalline medicament' . . . forecloses the argument that a largely amorphous product can infringe the '363 patent."

2. A vial of Abraxane "contains 100 mg of paclitaxel and approximately 900 mg of human albumin." (ABRX0117420 at 477) The paclitaxel in Abraxane exists in the form of

nanoparticles. (ABRX0117420 at 477) Human albumin is adsorbed onto the surface of these nanoparticles. (ABRX0117420 at 480) The nanoparticles within Abraxane are 82% paclitaxel and 18% albumin. (ABRX0117420 at 529) Greater than 95% of the human albumin in Abraxane is not part of the particles. (ABRX0117420 at 529) Thus, the product Abraxane contains nanoparticles as well as free human albumin.

3. Elan's claims in its '363 patent are directed to particles. The particles claimed in the '363 patent have two components (1) "99.9 - 10% by weight of a crystalline medicament" and (2) "a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of 0.1-90% by weight."

4. Even if the Court's construction of "crystalline medicament" is directed only to the medicament portion within the claimed particles, I still hold the opinion that Abraxane contains particles that infringe the '363 patent because Abraxane contains particles consisting essentially of a crystalline medicament, as construed and now clarified by the Court. Although the Court's clarified construction would serve to reduce the *number* of infringing particles within Abraxane, because the clarified claim construction would not encompass particles that are only partially crystalline, my SSNMR data shows that there are still a large number of infringing particles within each vial of Abraxane that are entirely crystalline.

5. Assuming that under the Court's Clarification Order the term "crystalline medicament" means that the entire medicament within a particle has a regular arrangement of atoms or molecules in space lattice, as distinguished from amorphous, the Court's clarification has not changed my opinion that Abraxane contains many particles consisting essentially of 99.9 - 10% by weight of a crystalline medicament.

6. Because the particles within Abraxane are 82% paclitaxel by weight and 18% albumin by weight (ABRX0117420 at 529), by definition, the entirety of such a particle (medicament and surface modifier) could be no more than 82% crystalline. In my SSNMR testing data, crystalline paclitaxel was measured at levels between 3.5% and 12% of the total paclitaxel present in the samples prepared using the lyophylization method and the air-dried method. These samples consist of particles that contain a range of paclitaxel phases. Samples that are on average from 3.5 to 12% crystalline, such as those discussed above, include individual particles that are mostly crystalline.

7. Even a small percentage of particles containing medicament which is entirely crystalline constitutes a large number of infringing particles in each 100 mg vial of Abraxane. I have calculated that each vial of Abraxane contains approximately 60 trillion particles. Based on my data, there are approximately 2 trillion particles in Abraxane in which at least a portion of the paclitaxel is crystalline. Of these 2 trillion particles, most of them likely contain paclitaxel that is entirely crystalline. Applying the most conservative estimates, the minimum number of particles containing entirely crystalline paclitaxel is in the billions.

8. My data show that Abraxane contains a subset of particles wherein the paclitaxel medicament portion of the particles is entirely crystalline. This is required by general nucleation theory of crystallization, which is well known in crystallography. Stated briefly, this theory teaches that when one crystallizes a substance, it usually becomes completely or essentially completely crystalline. Thus, the crystalline paclitaxel I observed when analyzing Abraxane will be present for the most part in entirely crystalline particles. Other particles in Abraxane may be amorphous, or a mixture of crystalline and amorphous particles. As I am informed of the law, the presence of these other particles is irrelevant to either the construction of the '363 Patent, or

to its infringement, because the presence of essentially crystalline particles is not negated by their combination or admixture with other or different particles, nor would these particles affect the nature or chemical or biological properties of the essentially crystalline particles.

9. Furthermore, I note that organic compounds can, and do, exist as partially crystalline and partially amorphous solids. My own research using SSNMR has shown this to be true.

10. Accordingly, based on Abraxis's statements to the FDA about its own product Abraxane, the particles within Abraxane are 82% by weight paclitaxel and 18% by weight human albumin. (ABRX0117420 at 529) Based upon my SSNMR data and the above-discussed calculations and analysis, a single vial of Abraxane contains at a minimum billions, and likely trillions, of particles in which paclitaxel is entirely crystalline.

11. Under the Court's August 17, 2007 claim construction order and May 19, 2008 clarification order, it remains my opinion that a vial of Abraxane contains particles (at least many billions of particles) consisting essentially of 99.9%-10% by weight of a crystalline medicament useful in treating cancer susceptible to treatment with a said medicament, said medicament having a solubility in water of less than 10 mg/ml. It accordingly remains my view that Abraxane meets the "crystalline medicament" limitation of the '363 patent claims.

ASHBY & GEDDES

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Dated: June 2, 2008

EXHIBIT 1

SECOND SUPPLEMENTAL EXPERT REPORT OF DR. ERIC J. MUNSON

Elan Pharma International Ltd. v. Abraxis Bioscience, Inc.,
No. 06-438-GMS, District of Delaware

1. I, Eric J. Munson, Ph.D., provide this report in the above-captioned case. The opinions expressed herein are my own and I have personal knowledge of the facts stated herein. If called as a witness, I could testify competently to the facts and opinions herein.

2. I am the same Eric Munson who served an Expert Report on September 28, 2007 in this matter and a Supplemental Expert Report on May 17, 2008

3. This Second Supplemental Expert Report is tendered in response to the Court's May 19, 2008 Order clarifying its previous claim construction order. The Court has clarified its construction of the term "crystalline medicament" to mean that "the entire medicament 'has a regular arrangement of atoms or molecules in space lattice, as distinguished from amorphous.'"

4. The Court's clarification Order contains a "Whereas" paragraph which noted that the term "'crystalline medicament' . . . forecloses the argument that a largely amorphous product can infringe the '363 patent."

5. A vial of Abraxane "contains 100 mg of paclitaxel and approximately 900 mg of human albumin." (ABRX0117420 at 477. A copy of this document is attached as Exhibit A.) The paclitaxel in Abraxane exists in the form of nanoparticles. (ABRX0117420 at 477.) Human albumin is adsorbed onto the surface of these nanoparticles. (ABRX0117420 at 480.) The nanoparticles within Abraxane are 82% paclitaxel and 18% albumin. (ABRX0117420 at 529.) Greater than 95% of the human albumin in Abraxane is not part of the particles. (ABRX0117420 at 529.) Thus, the product Abraxane contains nanoparticles as well as free human albumin.

6. Elan's claims in its '363 patent are directed to particles. The particles claimed in the '363 patent have two components: (1) "99.9 - 10% by weight of a crystalline medicament," and (2) "a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of 0.1-90% by weight."

7. If the Court's clarification of its earlier construction is taken to mean that a largely amorphous "product" (that is, a formulation composed of the claimed particles and other ingredients) cannot infringe the '363 patent, it is my opinion that the product Abraxane would not infringe the claims of the '363 patent. The product Abraxane contains nine parts amorphous

albumin, which is not a medicament useful for treating cancer, and 95% of this albumin is free albumin not associated with any particle.

8. If the Court's construction of "crystalline medicament" is directed only to the medicament portion within the claimed particles, I remain of the opinion expressed in my Expert Report, as explained more fully below. Specifically, I still hold the opinion that Abraxane contains particles that infringe the '363 patent because Abraxane contains particles consisting essentially of a crystalline medicament (i.e., crystalline paclitaxel), as construed and now clarified by the Court. Although the Court's clarified construction would serve to reduce the *number* of infringing particles within Abraxane, because the clarified claim construction would not encompass particles that are only partially crystalline, the SSNMR data of my Expert Report shows that there are still a large number of infringing particles within each vial of Abraxane that are entirely crystalline.

9. In my Expert Report I opined:

> Abraxane contains particles consisting essentially of 99.9%-10% by weight of a crystalline medicament useful in treating cancer susceptible to treatment with a said medicament, said medicament having a solubility in water of less than 10 mg/ml, where "particles consisting essentially of" is construed to mean "the particles, composed of crystalline medicament and surface modifier, may also include other ingredients that do not affect their basic and novel properties, and are essentially free of solvent and other contaminants," and where "crystalline medicament useful for treating cancer" is construed 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". The paclitaxel in Abraxane is present in one or more discrete crystalline phases.

10. Assuming that under the Court's Clarification Order the term "crystalline medicament" means that the entire medicament within a particle has a regular arrangement of atoms or molecules in space lattice, as distinguished from amorphous, the Court's clarification has not changed my opinion that Abraxane contains many particles consisting essentially of 99.9 - 10% by weight of a crystalline medicament.

11. Because the particles within Abraxane are 82% paclitaxel by weight and 18% albumin by weight (ABRX0117420 at 529), by definition, the entirety of such a particle (medicament and surface modifier) could be no more than 82% crystalline. As stated in my

Expert Report, "crystalline paclitaxel was measured at levels between 3.5% and 12% of the total paclitaxel present in the samples prepared using the lyophylization method and the air-dried method. These samples consist of particles that contain a range of paclitaxel phases. Samples that are on average from 3.5 to 12% crystalline, such as those discussed above, include ***individual particles that are mostly crystalline***." (My emphasis.)

12. Even a small percentage of particles containing medicament which is entirely crystalline constitutes a large number of infringing particles in each 100 mg vial of Abraxane. I have calculated that each vial of Abraxane contains approximately 60 trillion particles. Based on my data, there are approximately 2 trillion particles in Abraxane in which at least a portion of the paclitaxel is crystalline. Of these 2 trillion particles, it is my opinion that most of them contain paclitaxel that is entirely crystalline. Applying the most conservative estimates, however, the minimum number of particles containing entirely crystalline paclitaxel is still in the billions.

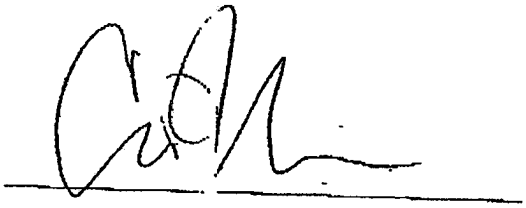
13. My data show that Abraxane contains a subset of particles wherein the paclitaxel medicament portion of the particles must be entirely crystalline. This is required by general nucleation theory of crystallization. Stated briefly, this theory teaches that when one crystallizes a substance, it usually becomes completely or essentially completely crystalline. (See, for example, D.J. Grant, "Theory and Origin of Polymorphism" in Polymorphism in Pharmaceutical Solids, Chp. 1, pp. 23-26, Harry G. Brittain Ed. 1999; J.T. Carstensen, Advanced Pharmaceutical Solids, pp.91-93, 2001. A copy of this reference is attached as Exhibit B). Thus, most of the crystalline paclitaxel I observed when analyzing Abraxane was present in particles in which the paclitaxel was entirely crystalline. Paclitaxel in other particles within Abraxane may be entirely amorphous, or a mixture of crystalline and amorphous. I am informed that the presence of these other particles is irrelevant to either the construction of the '363 Patent, or to its infringement. The presence of particles having entirely crystalline medicament is not negated by their combination with other or different particles, nor would these other or different particles affect the nature, chemical, or biological properties of the particles having entirely crystalline medicament.

14. Furthermore, I note that organic compounds can, and do, exist as partially crystalline and partially amorphous solids. (See, for example, USP (941) X-Ray Diffraction 1995 ("A solid substance can be classified as being crystalline, noncrystalline, or a mixture of the two forms.") A copy of this reference is attached hereto as Exhibit C). My own research using

SSNMR has shown this to be true. (See, for example, Padden, B. E.; Zell, M. T.; Dong, Z.; Schroeder, S. A.; Grant, D. J. W.; Munson, E. J "Comparison of Solid-State NMR Spectroscopy and Powder X-Ray Diffraction for Analyzing Mixtures of Polymorphs: 1. Neotame", *Anal. Chem.*, **1999**, 71, 3325-3331.)

15. Accordingly, based on Abraxis's statements to the FDA about its own product Abraxane, the particles within Abraxane are 82% by weight paclitaxel and 18% by weight human albumin. (ABRX0117420 at 529.) Based upon my SSNMR data and the above-discussed calculations and analysis, a single vial of Abraxane contains at least billions, and likely trillions, of particles in which the paclitaxel is entirely crystalline.

16. Under the Court's August 17, 2007 claim construction order and May 19, 2008 clarification order, it remains my opinion that a vial of Abraxane contains particles consisting essentially of 99.9%-10% by weight of a crystalline medicament useful in treating cancer susceptible to treatment with a said medicament, said medicament having a solubility in water of less than 10 mg/ml.



Eric J. Murason, Ph.D.

May 27, 2008