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Our Ref : 17283/P-1 **11th April 2014**

THE CONTROLLER OF PATENT
THE PATENT OFFICE
DELHI

Kind Attn.: Dr. Nilanjana Mukherjee
Controller of Patent and Design

Re: Pre-grant representation under Section 25(1)
in respect of Indian Patent Application No. 2899/DELNP/2005
Applicant: Abraxis BioScience, LLC
Opponent: NATCO Pharma Ltd.

Ma'am,

This is with reference to the hearing before the Learned Controller on 1st April and 2nd April 2014.

We are enclosing herewith the additional affidavit of Dr. Neil Desai which clearly provides that as to why the comparison of efficacy was done by the applicant between old formulation and new formulation with a ratio 19:1/20:1 versus 9:1.

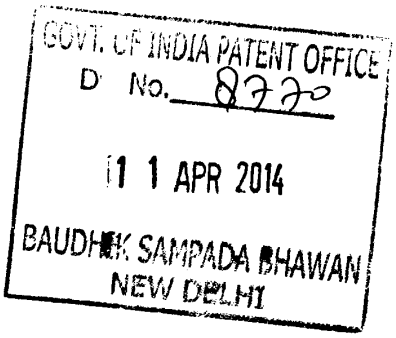
Additionally, the said affidavit also clarifies the nomenclature that has been used as being ABI-007 for nanoparticle albumin-bound paclitaxel products under different stages of development. There was no mention of these two issues in the pleadings of the opponent but in good faith in order to clarify any doubts the Learned Controller might have, we are filing the said affidavit.

Kindly take the said documents on record.

Yours faithfully

Archana Shanker

Encl: as stated above



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AFFIDAVIT OF DR. NEIL P. DESAI, C/o ABRAXIS BIOSCIENCE LLC OF LOS ANGELES, CALIFORNIA, USA

I, the above named Deponent do hereby solemnly affirm and declare as under:

1. I am the Vice President at Celgene, Inc., the parent company of Abraxis BioScience, LLC ("Abraxis"), the applicant/ assignee of Indian Patent Application No. 2899/DELNP/2005 (hereinafter referred to as "patent application"). Before Abraxis was acquired by Celgene, I was the Senior Vice President of Global Research and Development at Abraxis. A copy of my biography is attached hereto as Exhibit 1.

2. I have more than 20 years of experience in the research and development of drug delivery systems and biocompatible polymers. I was one of the individuals responsible for the development of Abraxis' nanoparticle-albumin bound (nab®) drug delivery platform and its product Abraxane®.

3. I am one of the named inventors of the above referenced patent application and am familiar with the technical features of the invention, the amended claims, and the specification.

4. In this declaration, I provide information about the nanoparticle albumin-bound paclitaxel products we developed and disclosed in the above referenced patent application and in WO00/71079.

5. Example 1 of WO00/71079 discloses a lab-scale preparation method of nanoparticle albumin bound paclitaxel composition by high pressure homogenization method. 30 mg paclitaxel was dissolved in 3 ml methylene chloride and added to 27 ml of 1% (w/v) albumin. The weight ratio of albumin to paclitaxel in the starting components was 9:1. Due to its poor water

solubility, paclitaxel is inherently lost during a preparation or manufacturing process which occurs in the aqueous state. In contrast, albumin, which is freely water soluble, remains in solution. Consequently more paclitaxel than albumin would be lost during the preparation process, which would alter the ratio of the components in the finished product. Taking into account loss of paclitaxel during the nanoparticle preparation process, the estimated albumin/paclitaxel ratio in the resulting nanoparticle albumin-bound paclitaxel composition was about 13.3:1. *See* Example 1 and page 36 of WO99/00113A1.

6. Because the experiment reported in Example 1 of WO00/70179 was on a very small lab scale using 30 mg paclitaxel (30 ml total volume), there was not sufficient nanoparticle composition made in Example 1 that could be used for further clinical studies.

7. The starting albumin/paclitaxel ratio was subsequently changed during the scaling-up process. Scaling-up of a pharmaceutical preparation manufacturing process from laboratory and bench scale to a manufacturing plant scale is usually done in a series of steps, each at a suitably larger scale than the previous scale, in order to determine the reproducibility of manufacturing and product quality in moving from the laboratory bench to the manufacturing plant. Changes in scale of equipment, processing time, process conditions, surface area of contact for the key components, and many other factors that change in going from small scale to larger scale, may affect the composition of the final product. Therefore, experimentation at different scales of manufacture were conducted and necessary adjustments were made during product development.

8. Examples 6 and 7 of WO00/71079 disclose a larger scale preparation method of albumin/paclitaxel nanoparticle composition by high pressure

homogenization using 225 mg paclitaxel (100 ml total volume). 225 mg paclitaxel was dissolved in 2.7 ml chloroform and 0.3 ml ethanol and then added to 97 ml 3% (w/v) albumin. The starting ratio of albumin to paclitaxel was about 13:1.

9. Example 16 of WO99/00113 provides a "Summary of the Presently Preferred Manufacturing Process: Starting with 1 gram Paclitaxel as the BDS." 51.7 ml of 25% albumin was added to 379.3 ml water to make a total of 431 ml of 3% albumin. The starting ratio of albumin to paclitaxel was about 13:1. While the scale in Example 16 of WO99/00113 was still relatively small (444 ml total volume) compared to the manufacturing scale, the 13:1 starting ratio was indeed what we had used when manufacturing the nanoparticle albumin bound paclitaxel formulation ("old formulation") before switching to a new formulation having a lower albumin/paclitaxel ratio ("new formulation").

10. Exhibit 2 provides the Master Formula for a manufacture lot of the old formulation (Product No. 101150, Lot No. C199-005). As shown in Exhibit 2, the initial concentration of paclitaxel per mL of the total solution was 2.25 mg. The initial concentration of albumin per mL of the total solution was 30 mg (20% x 0.15 ml). This makes a starting albumin/paclitaxel ratio of about 13:1. Exhibit 3 provides the Certificate of Analysis for the old formulation (Product No. 101150, Lot No. C199-005). As shown in Exhibit 3, the amount of paclitaxel in the finished product was 32.7 mg/vial. The amount of albumin in the finished product was 644 mg/vial. This makes the albumin/paclitaxel ratio in the finished product to be about 19:1. This old formulation having a final albumin/paclitaxel ratio of about 19:1 was used in the clinical study discussed in the affidavits submitted by me and separately by Dr. Anindiya during the pre-grant opposition proceedings.

11. To make a nanoparticle albumin bound paclitaxel formulation having a desired albumin/paclitaxel ratio, one can use routine methods and experimentation to determine the starting ratio of albumin and paclitaxel needed for the process, by taking into account the percentage of paclitaxel loss during the manufacturing process.

12. ABI007 is a code name we used at Abraxis to designate the nanoparticle albumin bound paclitaxel products under development. The code name ABI007 is not tied to any specific formulation having a specific albumin/paclitaxel ratio. While we altered the albumin/paclitaxel ratio from 19:1 (old formulation) to 9:1 (new formulation) during product development, we continued to refer to the product as ABI007. The way we distinguished the old formulation from the new formulation was by using a unique manufacturing product code. For example, Exhibit 4 (an excerpt from an amendment to the Technical Report for Abraxane®) provides a table summarizing various ABI-007 lots used in characterization studies. Product Code No. 101150 refers to the old formulation, while Product Code No. 103350 refers to the new formulation.

DEPONENT

Neil P. Desai, Ph.D.

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