IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

ZYMOGENETICS, INC., a Washington Corporation, Plaintiff, v. BRISTOL-MYERS SQUIBB CO., a Delaware Corporation, and DOES 1 through 100, Defendants.	C.A. No. 06-500-SLR **PUBLIC VERSION**

STATEMENT OF UNDISPUTED MATERIAL FACTS AND LEGAL ISSUES UPON WHICH JUDGMENT IS SOUGHT IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT OF INFRINGEMENT OF THE PATENTS-IN-SUIT

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In accordance with paragraph 2 of the Court's Scheduling Order, Plaintiff ZymoGenetics, Inc., ("ZymoGenetics"), by and through the undersigned counsel, submits this Statement Of Undisputed Material Facts And Legal Issues Upon Which Judgment Is Sought In Support Of Motion For Summary Judgment Of Infringement Of The Patents-In-Suit.

There is no genuine issue as to the following material facts:

1. ZymoGenetics is the assignee of United States Patent Nos. 5,843,725 (the "'725 Patent") and 6,018,026 (the "'026 Patent") (collectively, "the ZymoGenetics Patents") relating to fusion proteins. *See* Declaration of Paul J. Andre in Support of Zymogenetics, Inc.'s Motion for Summary Judgment of Infringement ("Andre Decl."), ¶¶2-3, Exs. 1-2.

2. Defendant Bristol-Myers Squibb Co. ("Bristol") sells a pharmaceutical product known as Orencia®, which is indicated for the treatment of rheumatoid arthritis. *See* Andre Decl., ¶5, Ex. 4 (package insert).

3. Orencia® is a fusion protein that consists of a portion of Cytotoxic T-Lymphocyte Antigen-4 ("CTLA-4") joined to a portion of an immunoglobulin heavy chain. *See* Andre Decl., ¶6, Ex. 5 at BMS001290162.

4. This immunoglobulin heavy chain in Orencia® contains the constant region domain, including the hinge region, the C_H2 domain, and the C_H3 domain. *See* Andre Decl., ¶6, Ex. 5 at BMS001290162.

5. The CTLA-4 portion and the immunoglobulin heavy chain in Orencia® are different molecules. *See* Andre Decl., ¶6, Ex. 5 at BMS001290162; ¶10, Ex. 9 (Ravetch I) at ¶¶65, 250); ¶9, Ex. 8 (Kuriyan) at ¶88; ¶8, Ex. 7 (Leister) at 13:5-15).

6. CTLA-4 is not an immunoglobulin. *See* Andre Decl., ¶8, Ex. 7 at 6 [Hood Immunology Textbook].

7. CTLA-4 exists in nature bound together in pairs, forming what is known as a dimer. *See* Andre Decl., ¶12, Ex. 11 (Nadler) at 85:17-20.

8. When CTLA-4 is not in a dimerized state (i.e., bonded in a pair), it does not exhibit biological activity. *See* Andre Decl., ¶12, Ex. 11 (Nadler) at 56:15-21.

9. The portion of the immunoglobulin heavy chain in Orencia® is a dimerizing protein. *See* Andre Decl., ¶12, Ex. 11 (Nadler I) at 63:16-19; ¶15, Ex. 14 (Ostrov) at 262:24-264:1; ¶15, Ex. 14 (Ostrov) at 272:2-273:7; ¶16, Ex. 15 [Deisenhofer Reference]; *see also* ¶17, Ex. 16 [Carter Paper, ZG054363-70] at ZG054363.

10. The portion of CTLA-4 in Orencia® binds ligands in nature. *See* Andre Decl., ¶5, Ex. 4 [Orencia® product insert].

11. Bristol produces Orencia® using a eukaryotic host cell system. *See* Andre Decl., ¶18, Ex. 17 at 35 (Bristol Response to Requests for Admission); ¶6, Ex. 5 (BLA) at BMS001290346.

12. The eukaryotic host cells used by Bristol are grown in an appropriate growth medium under physiological condition that allow the Orencia fusion protein the be produced. *See* Andre Decl., ¶18, Ex. 17 at 37 (Response to Request for Admission No. 48); ¶14, Ex. 13 (Smolin) at 61: 9-17.

13. To produce Orencia®, Bristol introduces a DNA construct into the host cells. *See* Andre Decl., ¶18, Ex. 17 at 35 (Bristol Response to Requests for Admission); ¶6, Ex. 5 (BLA) at BMS001290346.

14. The DNA construct includes DNA that encode for a transcriptional promoter, linked to a secretory signal sequence, followed by the DNA that encodes for the CTLA-4

portion. *See* Andre Decl., ¶18, Ex. 17 at 35 (Bristol Response to Requests for Admission); ¶6, Ex. 5 (BLA) at BMS001290346; ¶6, Ex. 5 (BLA) at BMS001290336.

15. In Orencia, two molecules of the CTLA-4-immunoglobulin fusion protein bind together to form a homodimer. *See* Andre Decl., ¶6, Ex. 5 (BLA) at BMS001290161.

ZymoGenetics seeks judgment on the following legal issues:

1. Whether Bristol's product, Orencia®, literally infringes the '725 Patent.

2. Whether Bristol's product, Orencia®, literally infringes the '026 Patent.

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CERTIFICATE OF SERVICE

I, Philip A. Rovner, hereby certify that on May 22, 2008, the within document was filed with the Clerk of the Court using CM/ECF which will send notification of such filing(s) to the following; that the document was served on the following counsel as indicated; and that the document is available for viewing and downloading from CM/ECF.

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