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-MPT **REDACTED PUBLIC VERSION**

BRISTOL-MYERS SQUIBB COMPANY'S STATEMENT OF UNDISPUTED FACTS IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT OF NONINFRINGEMENT

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Dated: May 16, 2008

In accordance with the Court's March 13, 2008 Order (D.I. 148 at 1), Bristol-Myers Squibb Company ("Bristol") submits this Statement of Undisputed Facts Regarding Noninfringement in support of its Motion for Summary Judgment of Noninfringement providing a short and concise statement of the material facts as to which there is no genuine issue to be tried, along with citations to the record supporting each contention.

INTRODUCTION

ZymoGenetics, Inc. alleges that Bristol's Orencia® -- which contains CTLA4-Ig -- and the method for producing CTLA4-Ig infringe the asserted claims of U.S. Patent Nos. 6,018,026 and 5,843,725 (collectively the "patents-in-suit"). This Statement of Undisputed Facts Regarding Noninfringement is filed in support of Bristol's Motion for Summary Judgment of Noninfringement that was filed concurrently.

Bristol's Motion for Summary Judgment of Noninfringement generally concerns the fact that Bristol's CTLA4-Ig and the method for producing Bristol's CTLA4-Ig lack the following claim terms as required by the asserted claims: (1) "dimerizing protein"; (2) "requiring dimerization for biological activity"; and (3) "non-immunoglobulin polypeptide". For convenience of the Court, Bristol has separately addressed the undisputed facts for each of the three claim terms.

The citations below are citations to the Exhibits filed along with the Declaration of John W. Kirkland In Support of Bristol's Motion for Summary Judgment of Noninfringement.

STATEMENT OF UNDISPUTED FACTS

I. "dimerizing protein"

1. ZymoGenetics construes the claim term "dimerizing protein" to be "a polypeptide chain having affinity for a second polypeptide chain, such that the two chains associate under physiological conditions to form a dimer. The second polypeptide chain may be the same or a different chain." (D.I. 153, Exh. A at 3, 4).

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13. The asserted claims of the patents-in-suit require the "dimerizing protein" be "selected from the group consisting of yeast invertase; at least a portion of an immunoglobulin light chain comprising at least an immunoglobulin light chain constant region domain; and at

least a portion of an immunoglobulin heavy chain comprising at least an immunoglobulin heavy chain constant region domain." (Exh. 1 at ZG000003; Exh. 2 at ZG000844).

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II. "requiring dimerization for biological activity"

21. All claims of the asserted patents either require a "non-immunoglobulin requiring dimerization for biological activity" or a "ligand-binding domain of a receptor requiring dimerization for biological activity". (D.I. 153, Exh. A at 2, 3, 5, 6).

22. ZymoGenetics did not provide a proposed construction for the term requiring dimerization for biological activity in the Joint Claim Construction Chart. (D.I. 153, Exh. A at 2).

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30. An article authored by Bristol scientists entitled "Binding Stoichiometry of the Cytotoxic T Lymphocyte-associated Molecule-4 (CTLA-4)" in 1995 reports:

> Each monomeric polypeptide chain of CTLA4 contains a high affinity binding site for B7 molecules.
>
> * * *
>
> To determine if monomeric CTLA-4 contained an intact binding site for B7 molecules, we compared B7 binding properties of monomeric and dimeric forms of CTLA-4. . . . . Fractionization of CTLA4X preparations by gel permeation separated monomeric and dimeric forms of CTLA-4. Both forms were immunoprecipitated with CD80Ig and CD86Ig [two forms of B7]. Identical results were obtained when purified CTLA4X was used for analysis. Thus, monomeric and dimeric forms of CTLA-4 bound CD80 and CD86 [both forms of B7].

(Exh. 10 at 15417, 15421).

31. An article authored by Bristol scientists entitled "CD28/CTLA4 Receptor Structure, Binding Stoichiometry and Aggregation During T-Cell Activation" in 1995 reports:

> CTLA4 was stably expressed as a monomer when cysteine 120 was mutated to serine, and monomeric CTLA4 contained a high affinity binding site for B7 molecules.

(Linsley *et al.*, *CD28/CTLA-4 receptor structure, binding stoichiometry and aggregation during T-cell activation*, RESEARCH IN IMMUNOL., 146:130 at 133)(Exh. 30).

32. An article authored by Bristol scientists entitled "Binding Stoichiometry of the Ctyotoxic T Lymphocyte-associated Molecule-4 (CTLA-4)" in 1995 reports:

> The relative avidities of monomeric and dimeric CTLA-4 were compared by competitive binding assay in the experiment . . . . Monomeric CTLA-4 was a more effective competitor than multimeric CD28 . . . .

(Exh. 10 at 15421-22) (internal citation omitted).

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35. A naturally occurring form of CTLA4 exists in the human body as a monomer. (Exh. 6 at 3596-3602).

36. The naturally occurring monomeric form of CTLA4 shows a significant inhibitory effect in an *in vitro* MLR experiment. (Exh. 7 at 150-151); (Exh. 8 at 193-94).

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42. High affinity binding of CTLA4 to B7 is a natural cell interaction. (Exh. 10 at BMS 3700199).

REDACTED

REDACTED

III. "non-immunoglobulin polypeptide"

REDACTED

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UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on May 16, 2008, I electronically filed the foregoing document with the Clerk of Court using CM/ECF and caused the same to be served on the plaintiff at the address and in the manner indicated below:

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UNITED STATES DISTRICT COURT
DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on May 23, 2008, I electronically filed the foregoing document with the Clerk of Court using CM/ECF and caused the same to be served on the plaintiff at the address and in the manner indicated below:

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