IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application of: DIX, Daniel, *et alia*	Confirmation No.: 9604
Application No.: 12/835,065	Art Unit: 1647
Filed: 13 July 2010	Examiner: STOICA, Elly Gerald
For: VEGF Antagonist Formulations	

RESPONSE TO OFFICE ACTION UNDER 37 C.F.R. § 1.111

INTRODUCTORY COMMENTS

In response to the Office action dated July 13, 2011 and due for response on October 13, 2011, Applicants submit the following remarks and papers. Since this response is filed within the two-month period of extension, Applicants hereby petition the Office for a two-month extension of time under 37 C.F.R § 1.136(a)(3) and authorize the Commissioner to deduct the requisite fee of $560 under § 1.17(a)(2) from deposit account number 18-0650.

Submitted herewith is a declaration by the inventors under § 1.131 and exhibits A – G, which demonstrate the making of the claimed invention prior to the publication date of the U.S.C. § 102(a) reference.

Remarks/Arguments begin on page 2 of this paper.

CELLTRION EXHIBIT - 1023
Celltrion, Inc. v. Regeneron Pharmaceuticals, Inc.

REMARKS

STATUS OF THE CLAIMS

Claims 1, 3, 4, 6, 8 and 25 were examined and currently stand rejected.

REJECTION UNDER 35 U.S.C. § 102(a)

Claims 1, 3, 4 and 6 stand rejected under § 102(a) for allegedly being anticipated by Fraser *et al.,* (J. Clin. Endocrin. Metab., 90, 1114-1122, 2005) ("Fraser"). Fraser is cited for teaching 24.3 mg/mL VEGF Trap comprising immunoglobulin domain 2 of Flt-1, immunoglobulin domain 3 of Flk-1, and Fc in 5 mm phosphate and 5 mm citrate at pH 6.0, 100 mM NaCl, 0.1% Tween 20 (a.k.a. polysorbate 20), and 20% sucrose.

Applicants have submitted with this paper a declaration of all the inventors (*i.e.,* Daniel Dix, Kelly Frye, and Susan Kautz) and exhibits under 37 C.F.R. § 1.131 demonstrating the claimed invention was made before the Fraser publication date of November 23, 2004. The enclosed exhibits, which are signed and dated, clearly demonstrate:

1. the completion of a 25 mg/mL VEGF Trap formulation containing 5 mM phosphate, 5 mM citrate, 5% sucrose, 50 mM NaCl, and 0.1% polysorbate-20, by November 21, 2000; and the completion of initial stability studies of that formulation by December 5, 2000;
2. the completion of two formulations: (a) 35.4 mg/mL VEGF Trap protein, 5 mM phosphate, 5 mM citrate, 100 mM NaCl, and 0.04% polysorbate-20, pH 6.17; and (b) 24.3 mg/mL VEGF Trap protein, 5 mM phosphate, 5 mM citrate, 100 mM NaCl, 20% sucrose, and 0.1% polysorbate-20, pH 6.05, which is the actual lot and formulation used in Fraser;

3. the completion of the 37°C stability analysis data for 25 mg/mL VEGF Trap protein, 5 mM phosphate, 5 mM citrate, 100 mM NaCl, 20% sucrose, and 0.1% polysorbate-20, pH 6.0 by February 28, 2001; and
4. the completion *inter alia* of a 5°C six-month stability study for 50 mg/mL VEGF Trap protein, 5 mM phosphate, 5 mM citrate, 100 mM NaCl, 20% sucrose, and 0.1% polysorbate-20, pH 6 by May 24, 2004,

which places the date of the invention prior to the date of the Fraser publication.

In view of the Rule 131 declaration, Applicants submit that the invention was made before Fraser, thereby obviating the rejection under 35 U.S.C. § 102(a). Applicants therefore respectfully request that the rejection of claims 1, 3, 4 and 6 under § 102(a) over Fraser be withdrawn.

REJECTION UNDER 35 U.S.C. § 103(a)

The Office has rejected claims 8 and 25 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Fraser in consideration of the alleged routine optimization of workable ranges of VEGF Trap protein to arrive at the 50 mg/mL formulation (*In re Aller,* 220 F.2d 454, 456 accord).

The Rule 131 declaration provides that the 50 mg/ml VEGF Trap, 5 mM phosphate buffer, 5 mM citrate buffer, 100 mM NaCl, 20% sucrose, 0.1% polysorbate 20 stable formulation was completed by the inventors by May 24, 2004, which is prior to the publication of Fraser. In view of the Rule 131 declaration, Applicants submit that the invention was made before Fraser, thereby obviating the rejection under 35 U.S.C. § 103(a). Applicants therefore respectfully request that the rejection of claims 8 and 25 under § 103(a) over Fraser be withdrawn.

CONCLUSION

In view of the remarks, the Rule 131 declaration of the inventors, and exhibits A – G submitted in response to the Office action of July 13, 2011, Applicants believe that claims 1, 3, 4, 6, 8, and 25 are patentable over the disclosure of Fraser. Applicants therefore respectfully ask the Office to withdraw its rejection of the claims and allow the patent to grant.

If any outstanding matters still remain in this case, the Examiner is invited to call the undersigned Agent for Applicants.

Respectfully submitted,

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