STATEMENT OF GROUNDS

ANNEX A

Conditional amendments to EP (UK) No. 2 364 691 ("EP 691"):

1. An ophthalmic formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising:

(a) 40-50~~1-100~~ mg/ml of a VEGF antagonist consisting of amino acids 27-457 of SEQ ID No: 4, which is glycosylated at Asn residues 62, 94, 149, 222 and 308;

(b) 0.01-5% of one or more organic co-solvent(s) which is one or more of polysorbate, polyethylene glycol (PEG), and propylene glycol;

(c) 30-150 mM of a tonicity agent selected from sodium chloride or potassium chloride;

(d) 5-40 mM of sodium phosphate buffer; and

(e) 1.0-7.5% of a stabilizing agent selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol, pH between about 5.8-7.0, wherein the formulation is suitable for intravitreal administration.

2. An ophthalmic formulation according to claim 1, comprising 40-50~~about 1-100~~ mg/ml~~, preferably 10-80 mg/ml,~~ of the VEGF antagonist, 10 mM sodium phosphate buffer, 40 mM NaCl, 0.03% polysorbate, and 5% sucrose, pH about 6.2-6.3.

3. An ophthalmic formulation according to claim 2, comprising VEGF antagonist at a concentration ~~selected from the group consisting~~ of ~~10 mg/ml, 20 mg/ml,~~ 40 mg/ml~~, and 80 mg/ml~~.

4. An ophthalmic formulation according to ~~any one of the above~~ claim~~s~~ 1, comprising 40-50~~10-80~~ mg/ml VEGF antagonist, 10 mM sodium phosphate, 0.03% polysorbate, and 135 mM sodium chloride, pH about 6.2-6.3.

5. An ophthalmic formulation according to claim 1 comprising:

(a) ~~10 mg/ml or~~ 40 mg/ml of a VEGF antagonist consisting of amino acids 27-457 of SEQ ID No: 4, which is glycosylated at Asn residues 62, 94, 149, 222 and 308;

(b) 0.03% of polysorbate 20;

(c) about 40 mM of sodium chloride;

(d) 10 mM of sodium phosphate buffer; and

(e) 5% sucrose,

wherein the pH of the formulation is pH 6.2-6.3.

6. A lyophilizable formulation of a vascular endothelial growth factor (VEGF) antagonist, comprising

(a) 5-50 mg/ml of the VEGF antagonist, preferably 5 mg/ml, 10 mg/ml, 20 mg/ml or 40 mg/ml, consisting of amino acids 27-457 of SEQ ID No: 4, which is glycosylated at Asn residues 62, 94, 149, 222 and 308;

(b) 5-25 mM of sodium phosphate buffer, pH about 5.8-7.0;

(c) 0.01-0.15% of an organic co-solvent, selected from the group consisting of polysorbate, polyethylene glycol (PEG), propylene glycol, and a combination thereof; and

(d) 1-10% of a stabilizing agent selected from the group consisting of sucrose, sorbitol, glycerol, trehalose, and mannitol; or 20-150 mM of a tonicity agent, preferably sodium chloride; or 1-10% of the stabilizing agent and 20-150 mM of the tonicity agent,

wherein the formulation can be reconstituted so it is suitable for intravitreal administration.

7. A lyophilizable formulation according to claim 6, comprising about 20 mg/ml of the VEGF antagonist, about 10 mM sodium phosphate buffer, about 0.03% polysorbate, about 0.1 % PEG, and about 2.5% sucrose, pH about 6.2-6.3.

8. A lyophilizable formulation according to claim 6, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, about 2.5% sucrose, and further comprising sodium chloride at about 20 mM, pH about 6.2-6.3.

9. A lyophilizable formulation according to claim 7, comprising about 20 mg/ml of the VEGF antagonist, about 5 mM sodium phosphate buffer, about 0.015% polysorbate, and further comprising sodium chloride at about 67.5 mM, pH about 6.2-6.3.

10. A method of producing a lyophilized formulation of a VEGF antagonist, comprising subjecting the pre-lyophilized formulation according to claim 6 to 9 to lyophilization to generate a lyophilized formulation.

11. A pre-filled syringe suitable for intravitreal administration comprising the formulation of any one of claims 1 to 5.