entity, having the capacity, when administered in a suitable amount, of slowing down or stopping the progression, aggravation, or deterioration of one or more symptoms of a disease or condition; alleviates the symptoms of a disease or condition; cures a disease or condition.

- "**Therapeutically effective amount**": the amount of a therapeutic agent necessary and sufficient for slowing down or stopping the progression, aggravation, or deterioration of one or more symptoms of the disease or condition; alleviating the symptoms of the disease or condition ; curing the disease or condition.

- "**Hydrophilic**": defines a molecule or a portion of a molecule that is typically charge-polarized and capable of hydrogen bonding, enabling it to dissolve more readily in water than in oil or other solvents.

- "**Lipophilic**": refers to a chemical compound capable to dissolve in fats, oils, lipids, and non-polar solvents.

- "**Non-miscible**": liquid which does not combine or blend with another liquid, or which does not combine or blend immediately with another liquid.

- **"implant"** is a solid dosage form which is implanted in a biological tissue usually composed of a polymer in which an active ingredient in incorporated to be slowly release.
- "**reservoir**" is a reserve of active ingredient which can be solid of liquid.

SUMMARY

This disclosure~~invention~~ relates to a composition for use in the treatment of a patient in need thereof by intraocular route, preferably by intraocular injection, of diseases or conditions of the eye, wherein the composition is a water-in-oil type emulsion comprising an oil phase, a lipophilic surfactant dissolved in the oil phase, an aqueous phase dispersed in the oil phase, a hydrophilic therapeutic agent dissolved in the aqueous dispersed phase, wherein the composition has a density lower than 1,

preferably ranging from 0.91 to 0.97 g/cm^3. The density was measured by filling a calibrated volumetric flask with the emulsion and weighed on a balance. Volume/mass ratio is then calculated.

In one aspect, there is provided a composition for use in the treatment by intraocular route of diseases or conditions of the eye, wherein the composition is a water-in-oil type emulsion comprising an oil phase, a lipophilic surfactant dissolved in the oil phase, an aqueous phase dispersed in the oil phase, a hydrophilic therapeutic agent dissolved in the aqueous dispersed phase, and wherein the composition has a density lower than 1, preferably ranging from 0.91 to 0.97 g/cm^3, wherein the composition has a viscosity ranging from 25 to 10 000 mPa.s at 20 °C, wherein the size of the droplets of water ranges from 20 nm to 600 nm, and wherein the use by intraocular route is intraocular injection.

In a preferred embodiment, the viscosity of the composition ranges from 25 to 10 000 mPa.s at 20 °C, as measured using a Kinexus Pro from Malvern U.K. at 20°C.

Preferably, the mean water droplet size ranges from 20 nm to 600 nm. In an embodiment, the mean water droplet size ranges from 25 nm to 500, preferably 30 to 200, more preferably 50-100 nm. In another embodiment, the mean water droplet size ranges from 20 nm to 100 nm. The mean particle size of the emulsions droplets was determined by quasi-elastic light scattering after dilution in water using a High Performance Particle Sizer (Malvern Instruments, UK).

The composition sustaineously releases the hydrophilic therapeutic agent within the eye.

In a preferred embodiment, the composition of the disclosure~~invention~~ is for use in the treatment, by intraocular route, of diseases or conditions of the eye of a patient, wherein the composition is a water-in-oil type emulsion comprising an oil phase, a lipophilic surfactant dissolved in the oil phase, an aqueous phase dispersed in the oil phase, a hydrophilic therapeutic agent dissolved in the aqueous dispersed phase, and wherein the composition has a density lower than 1, preferably ranging from 0.91 to 0.97 g/cm^3, and wherein the composition has a viscosity ranging from 25 to 10 000 mPa.s at 20 °C, and wherein the size of the droplets of water ranges from 20 nm to 600 nm, and wherein the use by intraocular route is intraocular injection.

According to an embodiment, the oil phase is selected from the group comprising triglycerides such as, for example, medium chain or long chain triglycerides, monoglycerides, diglycerides, vegetable oils or mineral oils.

Preferably, the lipophilic surfactant is selected from the group comprising sorbitan ester such as, for example, sorbitan stearate, sorbitan laurate and sorbitan monopalmitate; bentonite; glycerol monostearate; propylene glycol monolaurate and mixtures thereof.

In a preferred embodiment, the aqueous phase is present in the composition of the disclosure~~invention~~ in an amount ranging from 0.1 to 70% in weight to the total weight of the composition, preferably from 2 to 50% w/w, more preferably from 10 to 30% w/w.

Preferably, the hydrophilic therapeutic agent is selected from the group comprising monoclonal antibodies (full or Fab fragment), such as for example ranibizumab, bevacizumab, trastuzumab, cituximab or rituximab;

anti-angiogenic molecules, such as for example pegaptanib;

ROCK (Rho-kinases) inhibitors, such as for example fasudil;

proteins such as anti-CD160 S-HLA-G or WNT3A protein which activates WNT (Wingless - Integration site) for survival of photoreceptor cells;

growth factors such as epithelium growth factors (EGF), anti-EGF or TGF (Transforming growth factor);

siRNA such as siRNA anti-arginase;

miRNA;

oligonucleotides such as antisens DNA or antisens RNA;

iron chelating molecules such as deferiprone and salicylaldehyde isonicotinoyl hydrazone;

anti-inflammatory molecules such as epigallocatechin gallate;

antibiotics for back of the eye infection such as linezolide, clavulamic acid, macrolides;

anti-inflammatory molecules preferably selected from the group comprising cortico-steroids such as dexamethasone and its hydrophilic derivatives; and mixtures thereof.

In one embodiment of the disclosure~~invention~~, the composition further comprises a lipophilic therapeutic agent in the oil phase, said lipophilic therapeutic agent being selected from the group comprising cyclosporine A, lutein, alpha-tocopherol and dexamethasone palmitate.

According to the disclosure~~invention~~, the composition may further comprise viscosity modifying agents, such as, for example an hydrogel of sodium hyaluronate, carbopol gels, hydroxyethyl cellulose, dextran, carboxymethyl cellulose, polyethylene glycol, polyvinyl alcohol, collagen, and/or pH buffering agents, such as, for example, phosphate, citrate, tris, histidine or acetate buffer, and/or osmolality modifying agents,

such as, for example NaCl, KCl, $CaCl_2$, glycerol, mannitol, alpha-trehalose or propylene glycol.

In a preferred embodiment, the composition of the disclosure~~invention~~ is intravitreally injectable.

The diseases or conditions of the eye that may be treated with the composition of the invention are preferably selected from the group comprising glaucoma, anterior uveitis, retinal oxidation, age related macular degeneration, posterior uveitis, diabetic macular edema and central vein occlusion.

This disclosure~~invention~~ also relates to a pharmaceutical composition comprising the composition of the disclosure~~invention~~, and further comprising one or more pharmaceutically acceptable excipients.

In another aspect, there is provided a pharmaceutical composition comprising the composition as defined above, in association with one or more pharmaceutically acceptable excipients.

In another aspect, there is provided a medicament comprising the composition as defined above.

This disclosure~~invention~~ also relates to a medicament comprising a water-in-oil type emulsion as described above.

This disclosure~~invention~~ also relates to a method for treating a condition or disease of the eye, which comprises administering to a patient in need thereof by intraocular route, a composition of the disclosure~~invention~~, wherein a therapeutic amount of a hydrophilic therapeutic agent is dissolved in the aqueous dispersed phase. In the method of the disclosure~~invention~~, said therapeutic agent is sustaineously released within the eye of the patient.

In an embodiment, the volume of the injected composition ranges from 5 to 250 microliters.

In an embodiment, the composition or the medicament is injected in the vitreous chamber or in the anterior chamber of the eye of the patient.

In another aspect, t~~T~~his disclosure~~invention~~ also relates to a device comprising the composition or the medicament as defined above~~according to the invention~~. According to an embodiment, the device comprises a volume of 20 to 350 microliters of the composition of the disclosure~~invention~~.

According to a preferred embodiment, the composition, the pharmaceutical composition, the medicament or the device are not implants.