laser treatment that accumulate preferentially in neovascular membranes [3]. Despite encouraging results these therapeutic options are much less used because they target only end-stage of the disease and do not act on its progression.

Anti-VEGF drugs are now the standard of care of the choroidal neovascularization pathogenesis. There are actually several VEGF inhibitors marketed for this indication: pegaptanib, ranibizumab, aflibercept, in addition to bevacizumab commonly used as an alternative off-label treatment. Use of these treatments is associated with significant visual stabilization and improvement. There are however two major issues: the need for a rigorous monthly administration, increasing the risk of complications such as endophthalmitis and the long-term safety issue of VEGF inhibitors that may potently enter the systemic circulation after ocular injection, especially bevacizumab and ranibizumab, leading to higher risk of vascular events. Much effort has focused on improvement of anti-VEGF treatments protocols in order to reduce the frequency of injections. As an example, the combination of anti-VEGF therapies together with photodynamic therapy and corticosteroids have been proposed, but recent results report insignificant improvements [4,5].

There is currently no treatment that stops or even slows down progression of the dry AMD. Many strategies are being tested in clinical trials. They aim at targeting either retinal toxins or complement or trophic factor supplementation or oxidative stress or inflammation.

There are obvious unmet medical needs concerning AMD treatments since non-fully satisfying treatments are available.

SUMMARY OF INVENTION

In one aspect of the present disclosure, there is provided a use of a composition comprising baclofen and acamprosate, or salt(s) or prodrug(s) or derivative(s) or sustained release formulation(s) thereof, in the manufacture of a medicament for treating or preventing a macular degeneration disorder in a subject in need thereof, or for inhibiting or stopping the progression of said disorder.

In another aspect, there is provided a use of baclofen, or a salt, prodrug, derivative or sustained release formulation thereof; in combination with at least acamprosate, or a salt, prodrug, derivative or sustained release formulation thereof, in the

manufacture of a medicament for treating or preventing a macular degeneration disorder in a subject in need thereof, or for inhibiting or stopping the progression of said disorder.

It is an object ~~of this invention~~ to provide a treatment for macular degeneration disorders. More precisely, this invention relates to compositions and methods for treating macular degeneration disorders based on the use of baclofen and acamprosate.

As shown in this application, the disclosed methods and compositions ~~of the invention~~ allow an unexpected and remarkable improvement in physiological ailments of the eyeball that are implicated in the etiology of several degenerative disorders of the macula. In

particular, the inventors have found that baclofen and acamprosate based compositions are efficient against angiogenic injuries of the retina and against retina degeneration.

Moreover baclofen and acamprosate are effective in lowering oxidative stress and improving mitochondrial dysfunction and retinal stress observed in AMD.

An object ~~of this invention~~ thus relates to a composition comprising baclofen and acamprosate for use in treating, preventing, inhibiting or stopping the progression of a macular degeneration disorder and, more particularly, of dry or wet Age-related Macular Degeneration (AMD), Stargardt disease, early or adult onset vitelliform macular dystrophies or diabetic retinopathy.

An object ~~of this invention~~ relates to baclofen for use in combination with acamprosate in treating, preventing, inhibiting or stopping the progression of a macular degeneration disorder and, more particularly, of dry or wet Age-related Macular Degeneration (AMD), Stargardt disease, early or adult onset vitelliform macular dystrophies or diabetic retinopathy.

Another object ~~of this invention~~ is the use of a composition comprising baclofen and acamprosate to prevent progression toward macular degeneration in a subject diagnosed as bearing drusen or retinal pigmentory changes or experiencing retinal degeneration or abnormal ocular angiogenesis.

The ~~invention~~ disclosure also relates to any pharmaceutical composition *per se* comprising a combination of baclofen and acamprosate as defined above.

The disclosed compositions ~~of the invention~~ typically further comprise one or several pharmaceutically acceptable excipients or carriers. Also, the compounds ~~as used in the present invention~~ disclosed herein may be in the form of salts, hydrates, esters, ethers, acids, amides, racemates, or isomers. They may also be in the form of sustained-release formulations. Prodrugs or derivatives of the compounds may be used as well. In a preferred embodiment, a calcium acamprosate is used.

As it will be disclosed in this application, compounds in the disclosed compositions ~~of the invention~~ may be formulated or administered together, separately or sequentially. Said combinations may also be formulated or administered together, separately or sequentially.

Another object ~~of this invention~~ relates to method for treating, preventing, inhibiting or stopping the progression of a macular degeneration disorder in a subject in need thereof, the method comprising administering to the subject an effective amount of baclofen and acamprosate.

Another object ~~of this invention~~ relates to the use of baclofen and acamprosate for the manufacture of a medicament for treating, preventing, inhibiting or stopping the progression of a macular degeneration disorder.

The invention may be used in any mammal, preferably human beings.

LEGEND TO FIGURES

Figure 1: Effect of baclofen and acamprosate combination therapy against 6OHDA induced oxidative stress. Baclofen and acamprosate therapy is efficient in protecting neuronal cells. The protection increases correlatively with concentration of mixes. A significant protective effect is observed with an increase in TH neurons survival by 34% with dose 1 (16 nM and 64 pM respectively), by 46 % with dose 2 (80 nM and 144 pM) and by 51% with dose 3 (400 nM and 1600 pM) (***$p<0.0001$; * $p<0.001$: significantly different from 6OHDA intoxicated cells (ANOVA + Dunnett test))

Figure 2: Effect of baclofen and acamprosate combination therapy against $A\beta_{1-42}$ induced oxidative stress. Baclofen and acamprosate therapy is efficient in protecting neuronal cells from oxidative stress as shown by the observed significant decrease in methionine sulfoxide levels in treated cells (grey bar, -61%) when compared to non-treated intoxicated cells (black bar). (***$p<0.0001$ significantly different from $A\beta_{1-42}$ intoxicated cells(ANOVA + Dunnett post hoc test))

Figure 3: Effect of baclofen and acamprosate combination therapy against $A\beta_{1-42}$ induced mitochondrial dysfunction. Baclofen and acamprosate therapy is efficient in protecting neuronal cells from mitochondrial impairment as shown by the observed significant