

# **Unprecedented protection of the retina from glaucoma-induced nerve damage by topical administration of a novel prodrug**

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The preclinical development of a prodrug-based site-specific delivery strategy that allows for targeting a potent small-molecule neuroprotectant into the eye, and with preference to the retina, after topical administration as eye drops is being reported. The prodrug has improved physicochemical properties compared to those of the parent compound, which affords enhanced transport into the eye. The initial conversion rate in the retina has been the fastest among all ocular and non-ocular tissues. This observation has indicated that a rapid intraocular bioactivation in the retina results in sequestration and preferential release of the neuroprotective agent in this compartment of the eye. Treatment with the prodrug is not accompanied with toxicity and endocrine side-effects, unlike systemic treatment with the parent compound. In a model for glaucomatous retinopathy, prodrug treatment not only reduced cell death in the retina, but a trend was also observed that its topical application reduced cell death more than treatment with the parent compound and was less variable among sample points. In addition, prodrug treatment significantly preserved visual function and prevented loss of vision, measured as contrast sensitivity at a given spatial frequency. In conclusion, our pharmacological approach has great promise for the development of a novel alternative and complementary approach to glaucoma therapy.