Repeated dosing of NCX 667, a new nitric oxide (NO) donor, retains IOP-lowering activity in animal models of glaucoma

E. Bastia¹, F. Impagnatiello¹, E. Ongini¹, J.B. Serle² and M.V.W. Bergamini³
¹Nicox Research Institute, Milan, Italy; ²Icahn School of Medicine at Mount Sinai, New York, NY, USA; ³Nicos Ophthalmics, Inc., Forth Worth, TX, USA

INTRODUCTION
A wealth of experimental and clinical data support the role of nitric oxide (NO) in lowering intraocular pressure (IOP) by increasing aqueous humor outflow via relaxation of the trabecular meshwork and Schlemm’s canal (conventional route). NCX 667 is a novel NO-donor, proven to effectively lower IOP in rabbit and non-human primate models of glaucoma after single administration.

METHODS
Treatment paradigm A - repeated topical ocular dosing over 1 day
Ocular normotensive New Zealand white rabbits were treated every hour for 4 consecutive hours with NCX 667 (1%, 30 μL) or vehicle (PBS with cremophor EL 5%, DMSO 0.3%, BAC 0.02%). Intraocular pressure (IOP) was monitored hourly for 4 hours (in rabbits) and 9 hours (in non-human primates) on days 1, 3 and 5. A pneumotonometer (Model 30™ Reichert, Depew, NY, USA) was used to measure IOP. One topical drop of the local anesthetic, Novesina® 0.4% (Novartis) was applied to the eye prior to each IOP measurement.

Treatment paradigm B - repeated topical ocular dosing over 1 week
NCX 667 (1%, 30 μL) or vehicle (PBS with cremophor EL 5%, DMSO 0.3%, BAC 0.02%) were administered twice a day (9AM and 4PM) for 5 consecutive days to ocular normotensive NZW rabbits or laser-induced ocular hypertensive non-human primates. IOP was measured hourly through 4 hours (in rabbits) and 9 hours (in non-human primates) on days 1, 3 and 5. A pneumotonometer (Model 30™ Reichert, Depew, NY, USA) was used to measure IOP. One topical drop of Novesina® 0.4% (Novartis) was applied to the rabbit eye prior to each IOP measurement. Non-human primates were treated topically with one drop of 0.5% proparacaine hydrochloride, five minutes before tonometry, and ketamine hydrochloride 2-5 mg/kg of body weight administered intramuscularly for adequate sedation.

Safety assessment
Safety assessment by slit lamp of the anterior segment of the non-human primate hypertensive eyes was conducted at baseline, day 1, 3 and 5 following the first daily administration using the Hackett-McDonald ocular scoring system.

Statistical analysis
Data are expressed as mean ± SEM of IOP change. Data were analyzed using GraphPad Prism 6. The significance level was set at p < 0.05. Treatment effect was evaluated using two-way ANOVA followed by Bonferroni’s multiple comparison test.}

REFERENCES

CONTACT INFORMATION
E. Bastia
Head of Research Projects, Nicox Research Institute
Via Ariosto 21, 20091 Bresso (Milano), Italy
bastia@nicox.it