NCX 1741, a novel NO-donating derivative of the phosphodiesterase-5 inhibitor avanafil, reduces IOP in models of ocular hypertension and glaucoma

**INTRODUCTION**

The nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) signaling pathway plays a major role in aqueous humour drainage and intraocular pressure (IOP) homeostasis. The effects of this signaling pathway are silenced when cGMP is degraded by the phosphodiesterase type-5 enzyme (PDE5).

**OBJECTIVE**

Address the IOP-lowering effects of NCX 1741, a novel NO-donating derivative of the PDE5 inhibitor avanafil in rabbit and non-human primate models of ocular hypertension and glaucoma.

**RESULTS**

NO-donating derivative of avanafil (avanafil is a US- and EU-approved second-generation PDE5 inhibitor for the treatment of erectile dysfunction), is a new molecular entity holding two modes of actions (MoAs), namely PDE5 enzyme inhibition and NO/soluble guanylyl cyclase (sGC) signaling activation that could co-operate to effectively lower IOP in patients with ocular hypertension and glaucoma. Specifically, here we report on the initial pharmacological characterization of NCX 1741 in animal models of glaucoma and ocular hypertension.

**CONCLUSIONS**

- Avanafil is found in AH of ONT-rabbits following NCX 1741 ocular dosing
- NCX 1741 safely and effectively lowers IOP in ONT-rabbits and OHT-monkeys
- In OHT-monkeys, the IOP-lowering effects of NCX 1741 appear to last up to 24 hours
- NCX 1741 may represent a new and effective IOP-lowering agent to treat ocular hypertension and glaucoma

**REFERENCES**