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Title:

Safety, tolerability, and ocular hypotensive efficacy of QLS-111, a novel topical ATP-sensitive potassium channel opener

Purpose/Relevance:

QLS-111 is a novel ATP-sensitive potassium channel opener that uniquely lowers IOP by reducing episcleral venous pressure (EVP) through vasodilation. We evaluated the safety, tolerability, and efficacy of multiple concentrations and dosing regimens of QLS-111 alone or added to latanoprost in patients with primary open-angle glaucoma (POAG) and ocular hypertension (OHT) in two double masked phase 2 studies (Osprey and Apteryx). Chronic tox, pharmacokinetics (PK), and embryo fetal development (EFD) were evaluated in animal models.

Methods:

In Osprey (NCT06016972), POAG/OHT patients (n=62) washed out of IOP meds were randomized to QLS-111 or vehicle for 21 days. In Apteryx (NCT06249152), 32 patients stable on latanoprost, received QLS-111 or vehicle. Safety and tolerability were evaluated by adverse events (AEs), vitals, and comprehensive ophthalmic exams. IOP was measured by GAT. PK profile and chronic toxicity of QLS-111 were evaluated in rabbits and dogs after 6 and 9 months of daily topical treatment and in EFD studies in rats and rabbits.

Results:

Mean patient age was 67.2 years, consisting of White (63%), Black (34%), Asian (2%), and unspecified (1%) races. In Osprey, mean diurnal IOP lowering from baseline (~24 mmHg) was

significant for all doses, with 0.015% showing the best efficacy with IOP reductions of 2.8 mmHg (QAM, p=0.0018), 3.7 mmHg (QPM, p=0.0001), and 2.8 mmHg (BID, p=0.0018). In Apteryx, QLS-111 offered an additional 3.2 mmHg (QPM, p=0.0005) and 3.6 mmHg (BID, p=0.0002) of IOP lowering from baseline (19.8 mmHg). No ocular or systemic AEs were reported except for transient mild hyperemia. No changes were noted on slit lamp exams. PK analysis showed no quantifiable plasma concentrations > 6 hours post dose. QLS-111 caused no embryo fetal lethality, fetotoxicity, or teratogenicity.

Discussion:

QLS-111 provides meaningful and clinically significant IOP lowering with an excellent safety profile and no notable tolerability nor toxicity issues. Because IOP lowering with current therapies is often limited due to the floor that EVP establishes, QLS-111, with its novel mechanism of lowering EVP, represents a promising adjunctive to current topical IOP lowering agents as well as fixed-dose combination (FDC) therapy with PGAs and MIGs.

Conclusion:

This is a novel compound that could add value to our glaucoma armamentarium. Phase 2 clinical trials are underway in normal tension glaucoma patients and Phase 3 studies are planned with QLS-111 and prostaglandin analog FDC to start in 2026.

Osprey					Apteryx				
Regimen	QLS-111 treatment conc.	Baseline (mm Hg)	LS Mean Change (mm Hg)	P-value (vs. baseline)	Regimen	QLS-111 treatment conc.	Baseline (mm hg)	LS Mean Change (mm Hg)	P-value (vs. baseline)
QAM	0.15%	23	-2.8	0.0018	QPM	0.15%	19.8	-3.2	0.0005
	0.30%	23.7	-2.5	<0.0001		0.30%	19.5	-2.9	0.0011
	0.75%	24.1	-1	0.128		0.75%	19.7	-1	0.0385
	Vehicle	24.2	-1.4	0.2086		Vehicle	19.7	-1.5	0.0159

QPM	0.15%	23	-3.7	0.0001	BID	0.15%	19.8	-3.6	0.0002
	0.30%	23.7	-2.5	<0.0001		0.30%	19.5	-2.5	0.0036
	0.75%	24.1	-1.6	0.0151		0.75%	19.7	-1.4	0.0096
	Vehicle	24.2	-1.7	0.1516		Vehicle	19.7	-0.9	0.1176
BID	0.15%	23	-2.8	0.0018					
	0.30%	23.7	-2.4	0.0001					
	0.75%	24.1	-0.7	0.2405					
	Vehicle	24.2	-1.5	0.1968					

References:

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