



**A Randomized Trial Comparing NCX 470
0.1%, a Nitric Oxide-Donating Bimatoprost,
and Latanoprost 0.005% for Open-Angle
Glaucoma or Ocular Hypertension:
The DENALI Trial**

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of the DENALI Investigators

Disclosures:

- ▶ **Advisory board: Nicox**
- ▶ **Consultant: Liquid medical, Polyactiva, Inc., Ripple Therapeutics.**

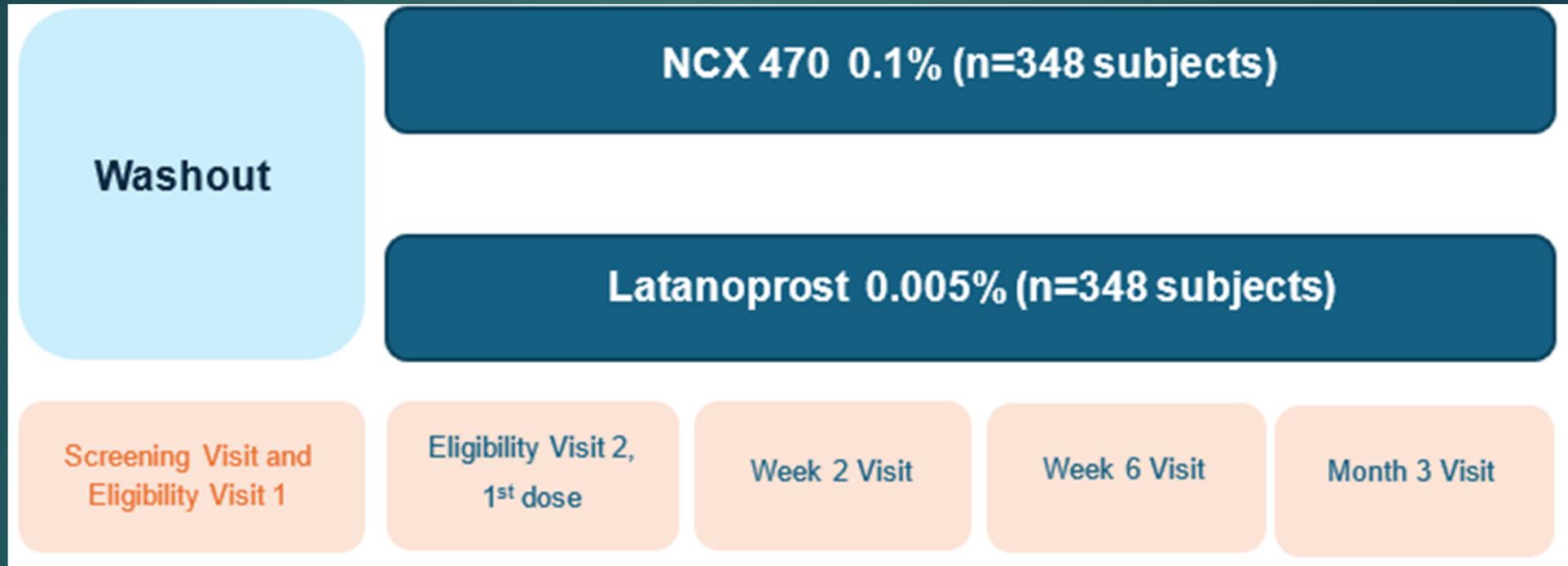
Introduction and Background

- Prostaglandin analogues (PGAs) are first-line therapy for OAG and OHTN, but additional IOP lowering through complementary outflow pathways is possible.
- NCX 470 is a nitric oxide-donating bimatoprost PGA designed to lower IOP through dual outflow pathways (trabecular meshwork and uveoscleral).
- In the first Phase 3 trial (MONT BLANC), NCX 470 demonstrated robust and consistent IOP lowering versus latanoprost.
- The Phase 3 DENALI trial was conducted as a second, independent evaluation of NCX 470 per the requirements for FDA NDA submission.
 - ▶ Commercial rights for the US granted to Kowa (Negoya, Japan)

Methods

- Randomized, double-masked, active-controlled, parallel-group Phase 3 trial.
- Conducted at 65 sites in the US and 25 sites in China.
- Adults with bilateral OAG or OHT and elevated untreated IOP
 - ≥ 26 mmHg at 8AM, ≥ 24 mmHg at 10AM, ≥ 22 mmHg at 4PM
- Randomized 1:1 to once-daily NCX 470 0.1% or latanoprost 0.005% for up to 12 months (primary endpoint at Month 3).
- Objective was to compare mean IOP reduction between treatments.

Methods



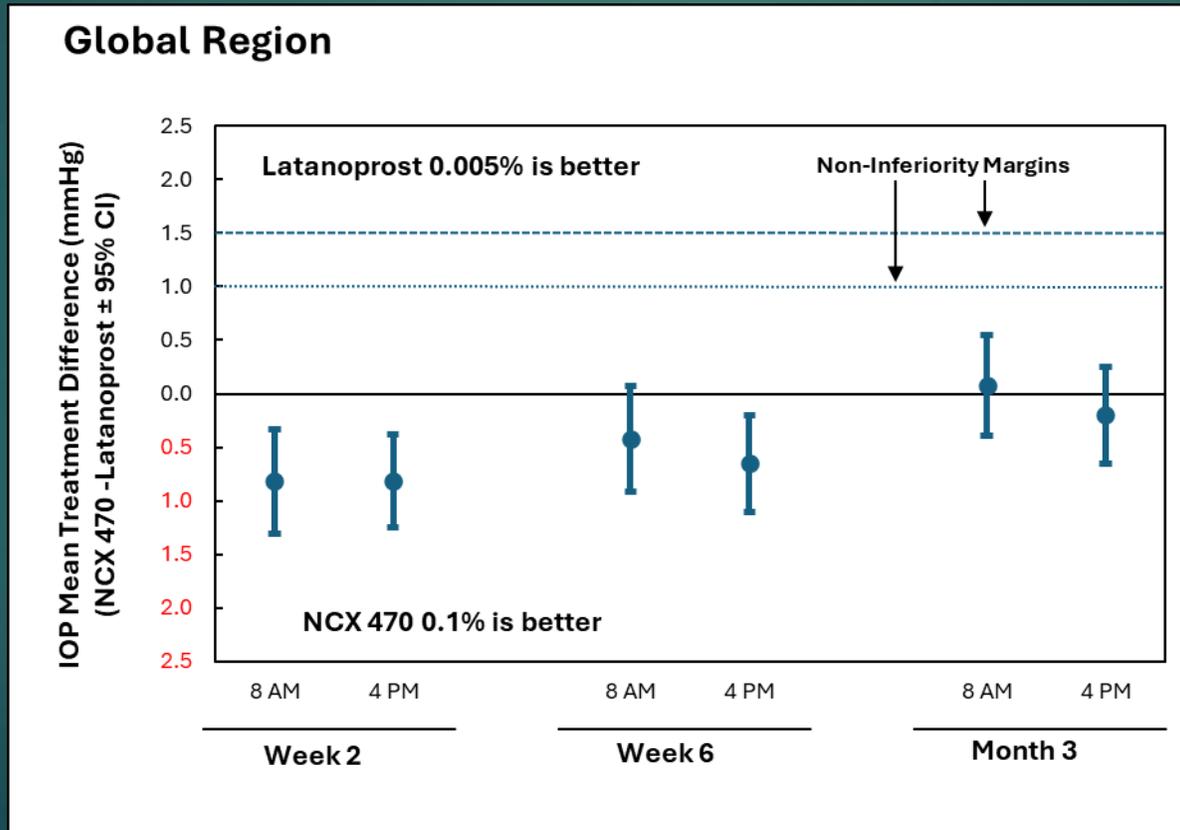
- ▶ **Primary endpoint:** noninferiority of mean IOP reduction from time-matched baseline at 8AM and 4PM at Weeks 2 and 6 and Month 3 (ITT population)

Results - Efficacy

- 696 subjects were randomized (348 per treatment group).
- Baseline demographics and IOP were balanced between treatment groups.
- IOP reduction was evident by Week 2 and maintained across all 6 timepoints, with mean reductions of **7.9-10.0 mmHg** for NCX 470 and **7.1-9.8 mmHg** for latanoprost.
- Noninferiority was demonstrated, with greater IOP reductions for NCX 470 versus latanoprost at **3 of 6 timepoints** (Week 2 [8AM, 4PM] and Week 6 [4PM]), with differences of up to 0.8 mmHg.

Results - Efficacy

NCX 470 0.1% met the primary endpoint of noninferiority and demonstrated greater IOP lowering than latanoprost at multiple timepoints (up to 0.8 mmHg)

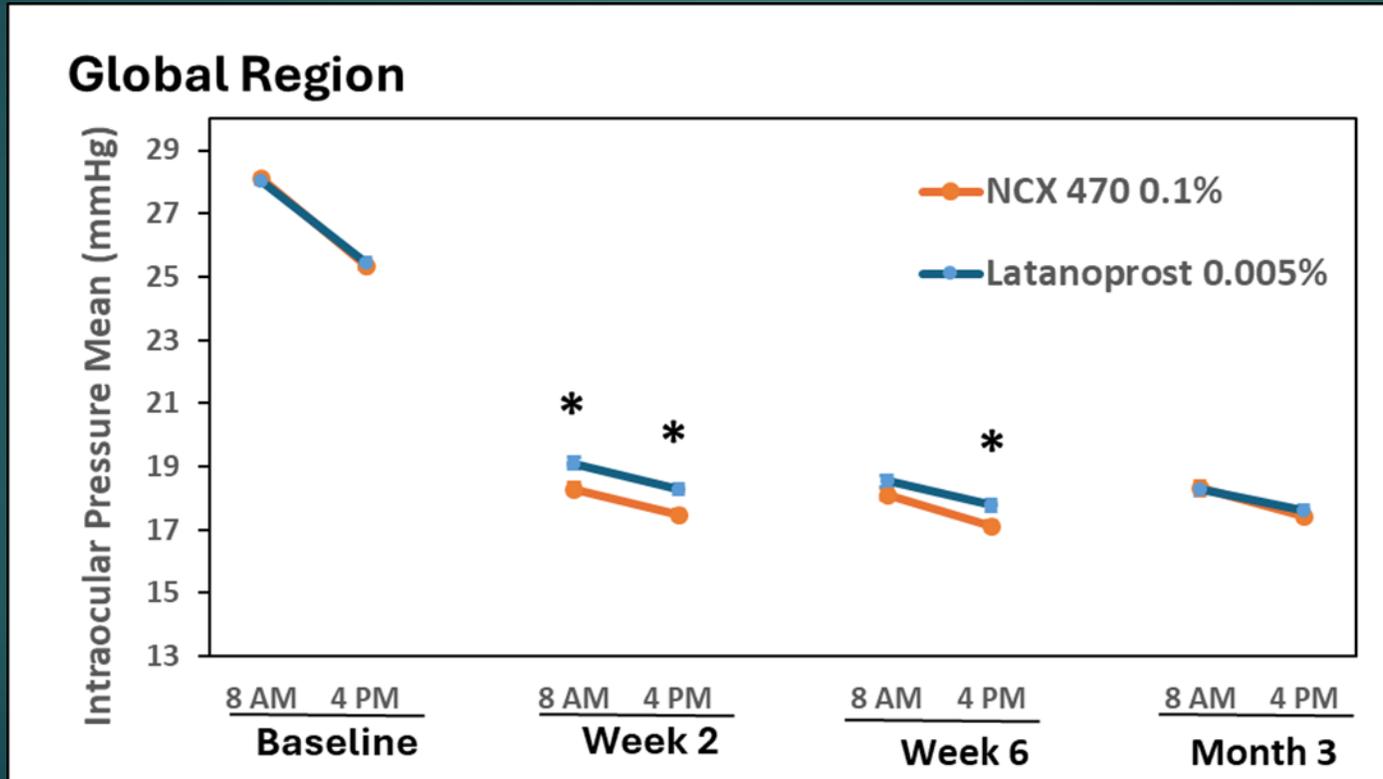


NCX 470 0.1% (n=348)
Latanoprost (n=348)

Noninferiority criteria:
Upper bound of the 95% confidence interval ≤ 1.5 mmHg at all 6 timepoints and ≤ 1.0 mmHg at 4 or more timepoints

Results - Efficacy

NCX 470 0.1% demonstrated statistically greater IOP reduction than latanoprost at Week 2 and at the Week 6 afternoon assessment, with sustained efficacy at the primary Month 3 endpoint



NCX 470 0.1% (n=348)
Latanoprost (n=348)

**Statistically significance difference between treatments ($p < 0.05$)*

Results - Safety

- NCX 470 was safe and well tolerated over 12 months.
- Common adverse events included:
 - Conjunctival hyperemia (22.0% with NCX 470; 9.2% with latanoprost)
 - Eyelash growth (8.1% vs 1.7%)
- No treatment-related serious adverse events occurred.
- Discontinuation due to adverse events (0.9% vs 0.3%) or lack of efficacy (1.7% vs 1.1%) were uncommon and similar between treatment groups.

Discussion

- The DENALI Phase 3 trial met its primary endpoint, demonstrating noninferiority of NCX 470 0.1% to latanoprost 0.005% across all evaluated timepoints.
- NCX 470 provided rapid, robust, and consistent IOP lowering over 3 months, with statistically greater reductions at 3 of 6 timepoints.
- NCX 470 was safe and well tolerated, with low and comparable discontinuation rates between treatment groups.
- Results are consistent with the previously published, first phase 3 trial, Mont Blanc.

Conclusion

- ▶ NCX 470 is a novel nitric oxide-donating bimatoprost in development for intraocular pressure lowering in patients with OAG or OHT.
- ▶ In the Phase 3 DENALI trial, NCX 470 met the primary endpoint of noninferiority to latanoprost and was safe and well tolerated.



Thank You

Reference: 1. Fechtner, R. and S. Mansberger, J. Branch, J. Mulaney, S. Ziebell. K. Lopez and D. Hubatsch A Randomized, Controlled Comparison of NCX 470, a Nitric Oxide-Donating Bimatoprost, and Latanoprost in Subjects with Open-Angle Glaucoma or Ocular Hypertension: **The MONT BLANC Study** *Am J Ophthalmol* 2024;264: 66–74