NCX 470 (bimatoprost grenod)
Mont Blanc Data and Value Proposition

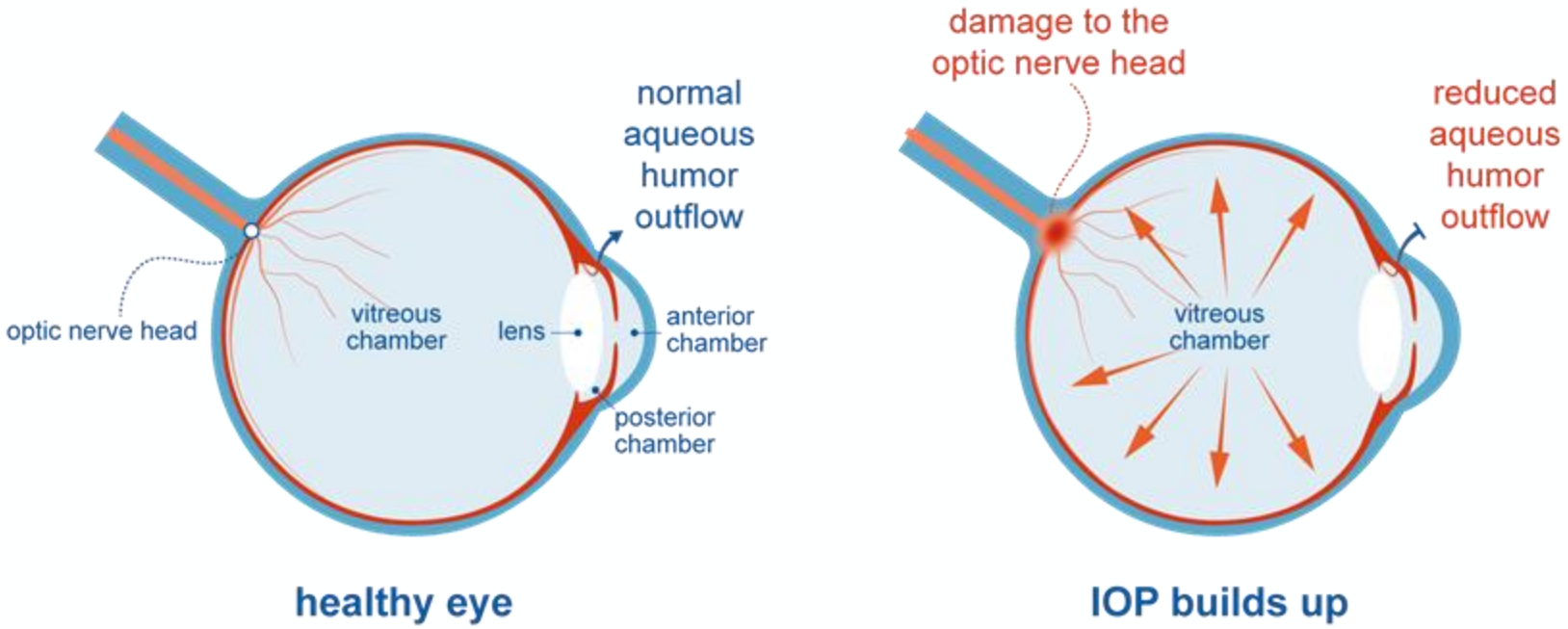
Value Proposition of NCX 470

- ✓ **Novel molecule with positive impact on lowering IOP, the leading cause of glaucoma**
- ✓ **Positive pivotal Phase 3 topline results from the Mont Blanc trial[1,2,3]**
- ✓ **First non-combination product to demonstrate statistical non-inferiority to a prostaglandin analog in a pivotal trial, thereby meeting the efficacy requirements for U.S. approval**
- ✓ **Large and established glaucoma drug market[4]: valued at ~$6 billion worldwide**
- ✓ **Over 3 million patients and over 36 million prescriptions[4] in the United States alone with additional safe and effective alternatives to first-line therapy required**
- ✓ **Over $300 million global peak net sales forecast[5] for NCX 470**
- ✓ **Only late-stage New Chemical Entity in glaucoma in the U.S.**

1. Nicox Press release October 31, 2022
2. Mansberg et al., 2023, World Glaucoma Congress, Abstract # P-339
3. Fechtner et al., 2023, World Glaucoma Congress, Abstract # P-288 b
4. IQVIA™ Analytics Link 2021
5. Nicox market research, partner and internal estimates – Press Release July 10, 2023

Glaucoma: a worldwide ophthalmic condition with unmet medical needs

Elevated IOP* contributes to irreversible optic nerve damage, leading to progressive vision loss



As published in the landmark EMGT study "…each mmHg of decreased IOP was related to an approximately 10% lowering [of risk of vision loss progression]"[1]

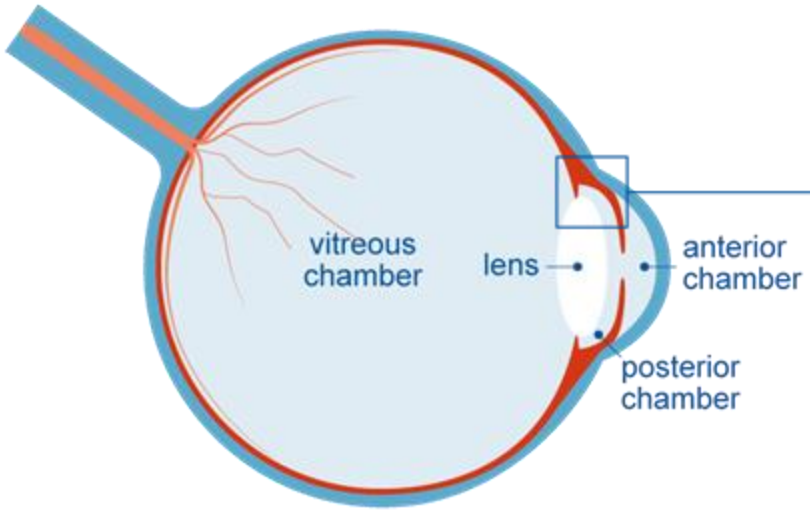
1. Heijl et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002; 120: 1268-1279

*Intraocular Pressure

NCX 470 lowers IOP through a validated[1] dual mechanism pathway

Clinically validated with the first NO-donating PGA, VYZULTA®

Two pathways for aqueous humor outflow



1 Primary or conventional outflow normally accounts for ~60% to 80% of outflow

Stimulated by nitric oxide (NO)

2 Secondary or uveoscleral outflow normally accounts for ~20% to 40% of outflow

Stimulated by prostaglandins (PGAs)

1. Same mechanism of action as Nicox's first commercialized NO-donating product, latanoprostene bunod

NCX 470 pivotal phase 3 program, Positive Mont Blanc topline results[1,2,3]

Phase 3 clinical program intended to support U.S. & China NDA submissions

Designed to demonstrate safety and efficacy of NCX 470 0.1% vs. latanoprost 0.005%, studies evaluate reduction of IOP from time-matched baseline at pre-established time points

MONT BLANC: Primary objective of non-inferiority achieved

N=691

56 clinical sites in the U.S. & one site in China

Adaptive design selected the 0.1% concentration

NCX 470 was statistically superior to latanoprost 0,005% in intraocular pressure reduction from baseline at 4 of the 6 timepoints, and numerically greater at all 6

Second efficacy objective, statistical superiority to latanoprost, was not achieved

DENALI: Fully enrolled

N=~670

~80 clinical sites in the U.S. & China

Includes a 12-month safety extension

Jointly conducted and equally financed with Chinese partner Ocumension Therapeutics

Topline results expected in Q3 2025

1. Nicox Press release October 31, 2022
2. Mansberg et al., 2023, World Glaucoma Congress, Abstract # P-339
3. Fechtner et al., 2023, World Glaucoma Congress, Abstract # P-288

Mont Blanc Phase 3 efficacy trial design[1]

Designed to evaluate NCX 470 vs. established therapy, latanoprost

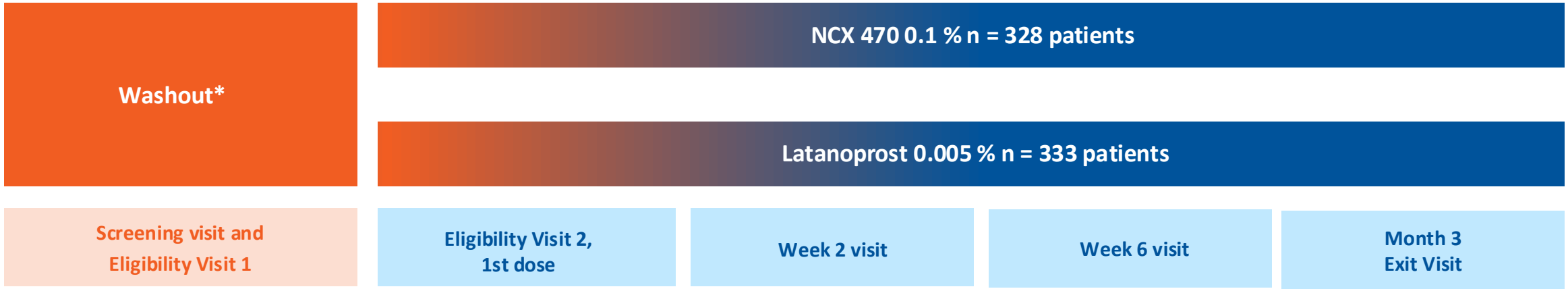
Randomized, controlled, double-masked, parallel design trial. Patients with open angle glaucoma or ocular hypertension were randomized 1:1 to once-daily treatment with NCX 470 0.1% or latanoprost 0.005%

Primary Endpoint:

Mean IOP reduction from time-matched baseline at 8 AM and 4 PM at the week 2, week 6 and month 3 visits

Enrollment:

The trial enrolled 691 patients across all arms (including ~30 patients on NCX 470 0.065% in the adaptive design part)



* Wash-out period according to the patient's previous IOP-lowering treatment

1. This schematic reflects the dosage arms which continued in the trial and do not include the NCX 470 0.065% dose which wasonly in the adaptive design portion of the trial

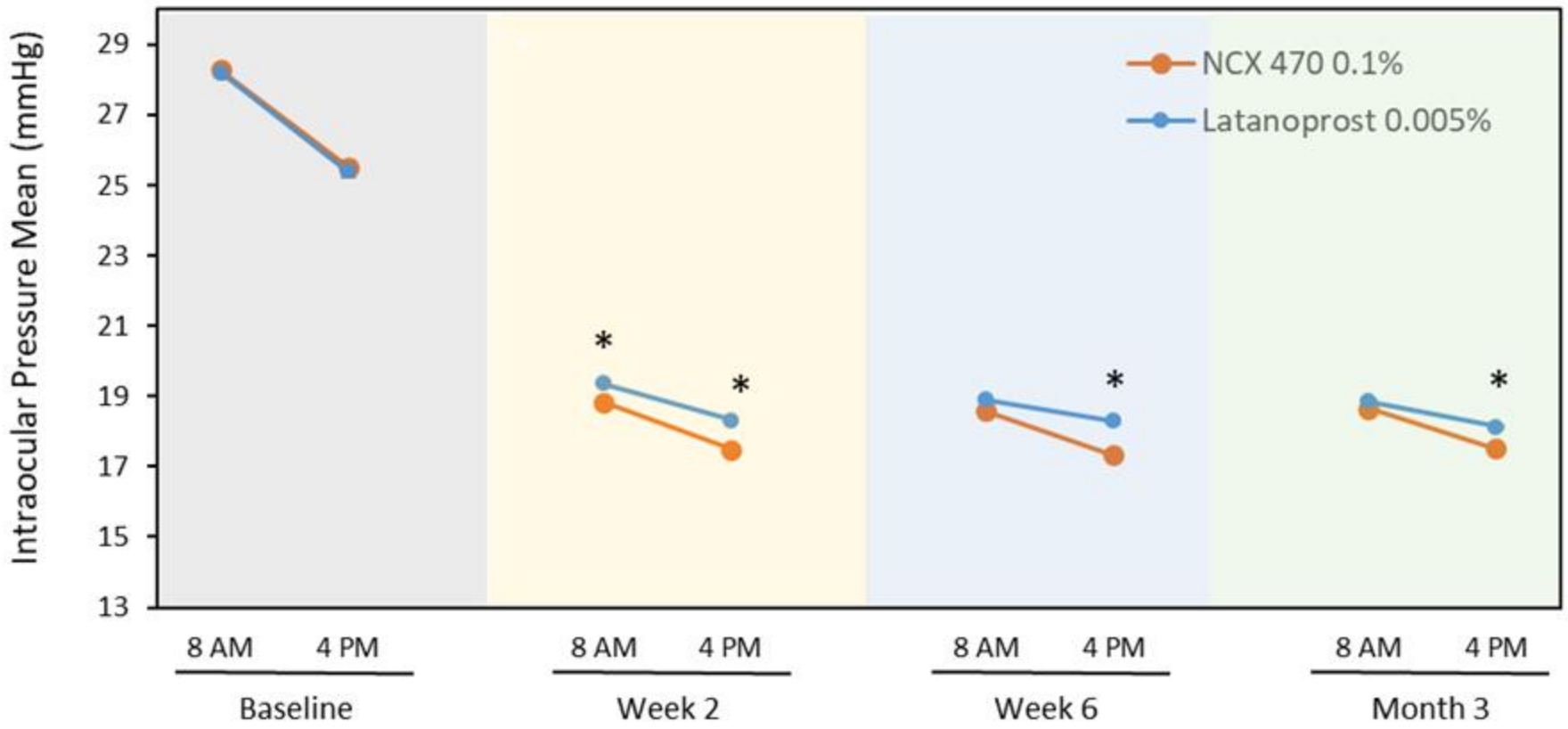
Mont Blanc Baseline characteristics, demographics and disposition[1]

	NCX 470 0.1% N = 328	Latanoprost 0.005% N = 333
Mean Diurnal Baseline (8am+4pm) IOP, mmHg, Study Eye (SD)	26.9 (2.04)	26.8 (2.02)
Gender, n (%) Female Male	 200 (61.0%) 128 (39.0%)	 188 (56.5%) 145 (43.5%)
Age, Years (SD)	63.6 (10.12)	62.7 (11.73)
Completed the Study	314 (95.7%)	316 (94.9%)
Discontinued Prior to Study Completion	14 (4.3%)	17 (5.1%)
Reasons for Discontinuation		
Adverse Event	8 (57.1%)	6 (35.3%)
Lost to Follow-up	1 (7.1%)	4 (23.5%)
Physician Decision	0	0
Sponsor or IRB Decision	1 (7.1%)	2 (11.8%)
Protocol Violation	0	1 (5.9%)
Withdrawal by Subject	3 (21.4%)	3 (17.6%)
IOP greater than 36 mmHg	0	0
Other	1 (7.1%)	1 (5.9%)

1. This data reflects the dosage arms which continued in the trial and do not include the NCX 470 0.065% dose which was only in the adaptive design portion of the trial.

NCX 470 demonstrated potent IOP-lowering from baseline and statistical superiority vs market leader latanoprost at 4 of 6 timepoints

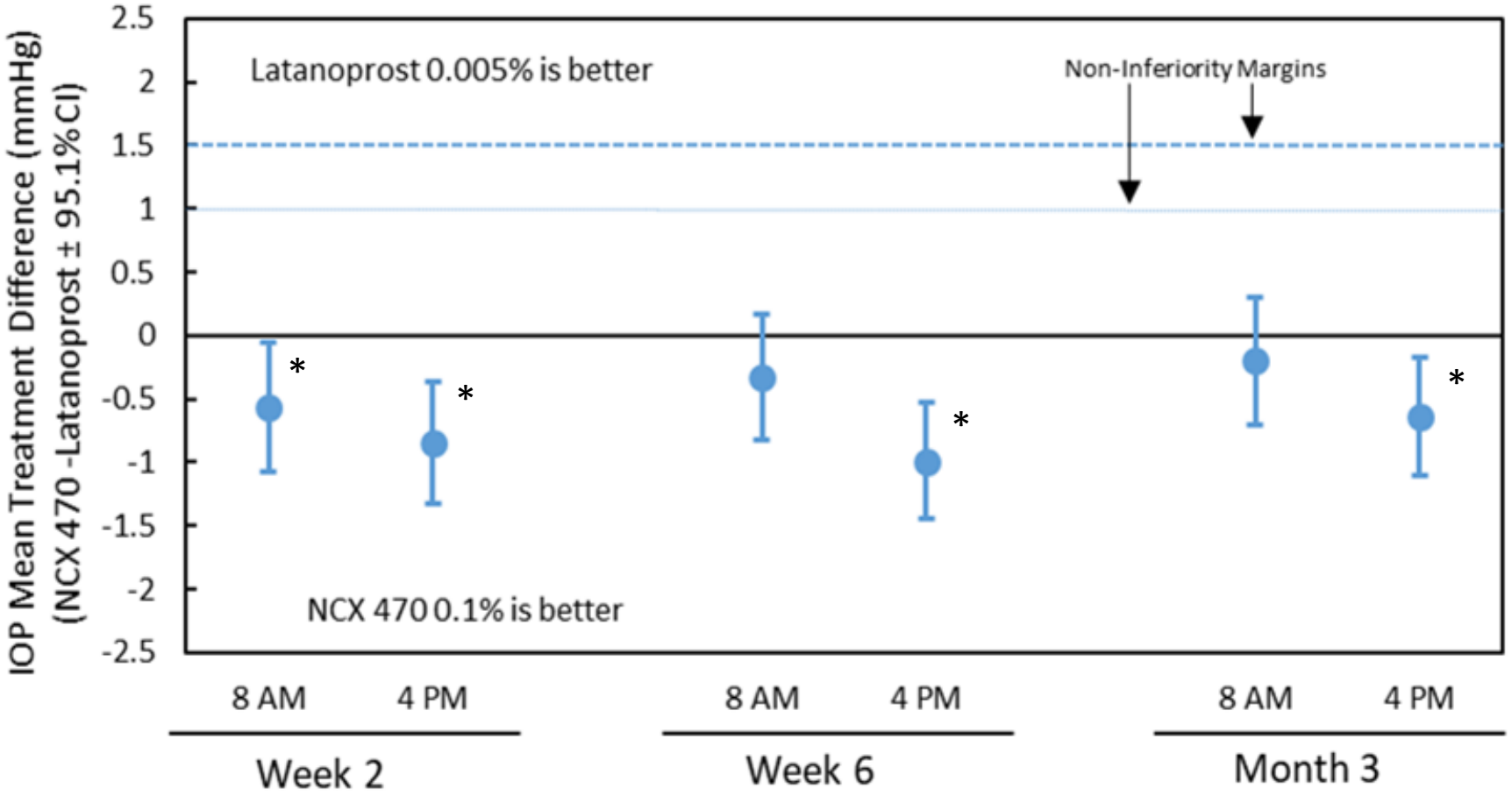
IOP-lowering from baseline was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for latanoprost



NCX 470 0.1%: N = 328
Latanoprost 0.005%: N = 333

- Denotes statistically significant differences vs latanoprost (p<0.049)
- Fechtner et al., AJO, 2024 Aug;264:66-74

NCX 470 achieved non-inferiority for IOP-lowering vs latanoprost, meeting the efficacy requirement in a pivotal study for FDA approval



To be non-inferior, the treatment difference between NCX 470 and latanoprost had to meet BOTH criteria:

- **For all 6 timepoints, the upper limit of all confidence intervals (95.1%) were required to be less than or equal to 1.5 mmHg and**
- **At least 4 of the 6 timepoints were required to be less than or equal to 1.0 mmHg**
- **NCX 470 0.1% demonstrated an IOP lowering effect greater than latanoprost 0.005% of up to 1.0 mmHg**

* Denotes statistically significant differences vs latanoprost ($p<0.049$)

NCX 470 topline results demonstrate robust efficacy and safety[1]

All comparisons are based on NCX 470 0.1% and latanoprost 0.005%

Topline results from this pivotal trial:

- **IOP-lowering effect from baseline was 8.0 to 9.7 mmHg for NCX 470 vs. 7.1 to 9.4 mmHg for latanoprost**
- **Statistical non-inferiority was met vs. latanoprost in the primary efficacy analysis. This trial therefore met the efficacy requirements for approval in the U.S.**
- **While NCX 470 failed to meet statistical superiority to latanoprost in a pre-specified secondary efficacy analysis of time-matched change from baseline IOP, NCX 470 was numerically superior to latanoprost at all time points and statistically significant ($p<0.049$) at 4 of 6 timepoints**

Data from the post hoc analysis:

- **Statistically significant percentage of patients achieve ≤ 18mmHg intraocular pressure (IOP) on NCX 470 compared to latanoprost**
- **Mean percentage reduction in IOP greater on NCX 470 than on latanoprost**
- **In eyes with an initial IOP of ≤ 28 mmHg the IOP-lowering effect from baseline was statistically significantly greater for NCX 470 compared to latanoprost at the majority of timepoints measured**
- **NCX 470 demonstrates a consistent lowering of IOP regardless of the baseline IOP, whereas the reduction in IOP with latanoprost is dependent on the baseline IOP**
- **A statistically significant greater proportion of patients who received NCX 470 showed an IOP reduction of greater than 10 mmHg from baseline, compared to those on latanoprost**

NCX 470 was well tolerated

- **The most common adverse event was ocular hyperemia in 11.9% of NCX 470 patients vs. 3.3% of latanoprost patients**
- **There were no ocular serious adverse events and no treatment-related non-ocular serious adverse events**
- **4.3% of patients on NCX 470 discontinued compared to 5.1% on latanoprost**

1. This data reflects the dosage arms which continued in the trial and do not include the NCX 470 0.065% dose which was only in the adaptive design portion of the trial.

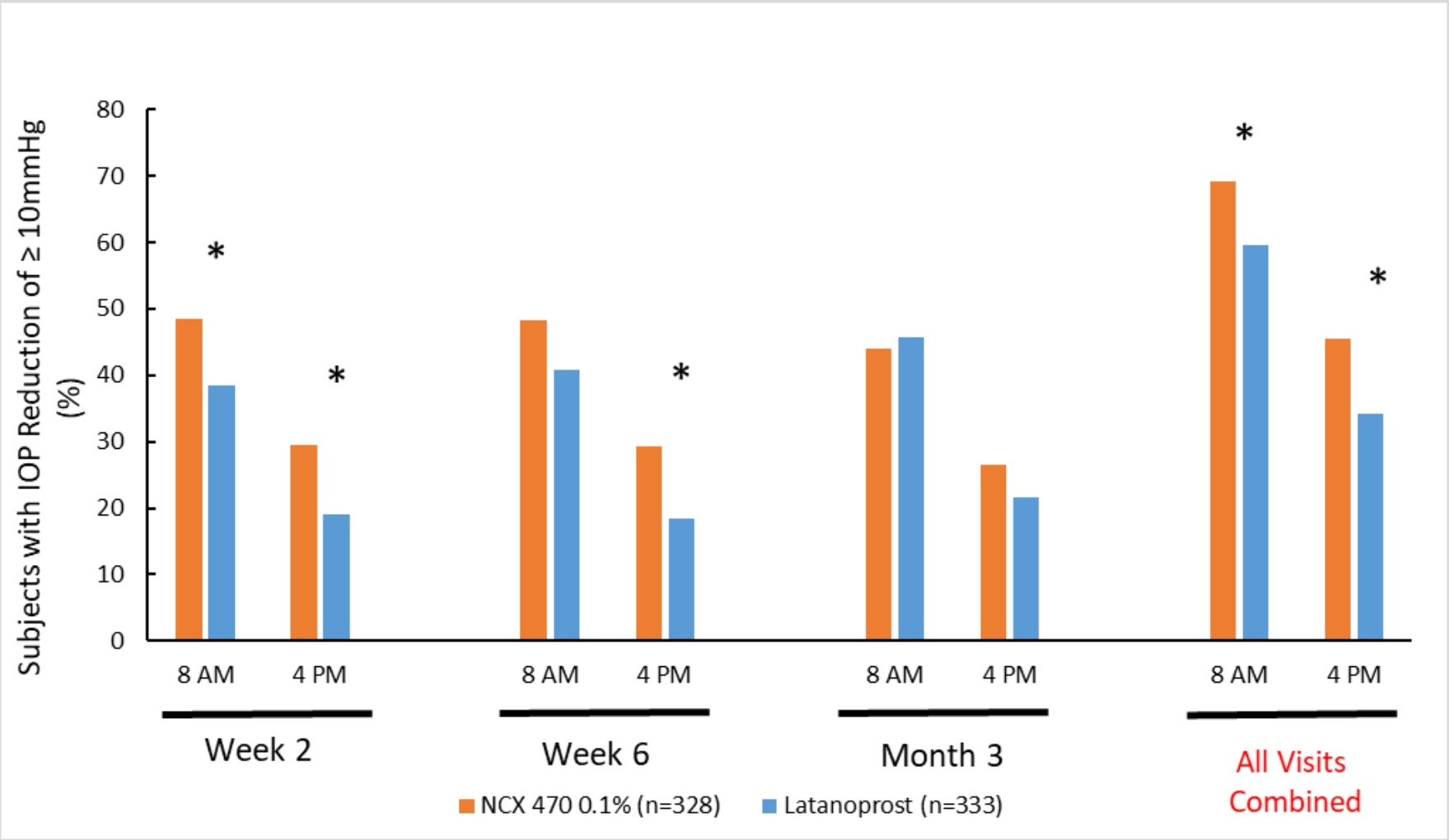
Mont Blanc post-hoc analysis supports robust differentiated NCX 470 efficacy

Consistent IOP lowering after 3 months' treatment regardless of baseline unlike latanoprost

- **In subjects with baseline pressures < 28 mmHg, NCX 470 lowered IOP from baseline more than latanoprost and, that difference was greater at lower baselines.**
- **A greater proportion of subjects on NCX 470 achieved IOP lowering from baseline by ≥ 10 mmHg compared to those on latanoprost.**
- **Statistically significantly more subjects on NCX 470 were able to achieve target IOP of ≤ 18 mmHg compared to those on latanoprost.**
- **After 3 months' treatment, NCX 470 lowered IOP by ~ 8.2 mmHg regardless of the starting IOP. This predictable IOP lowering was not seen with latanoprost**

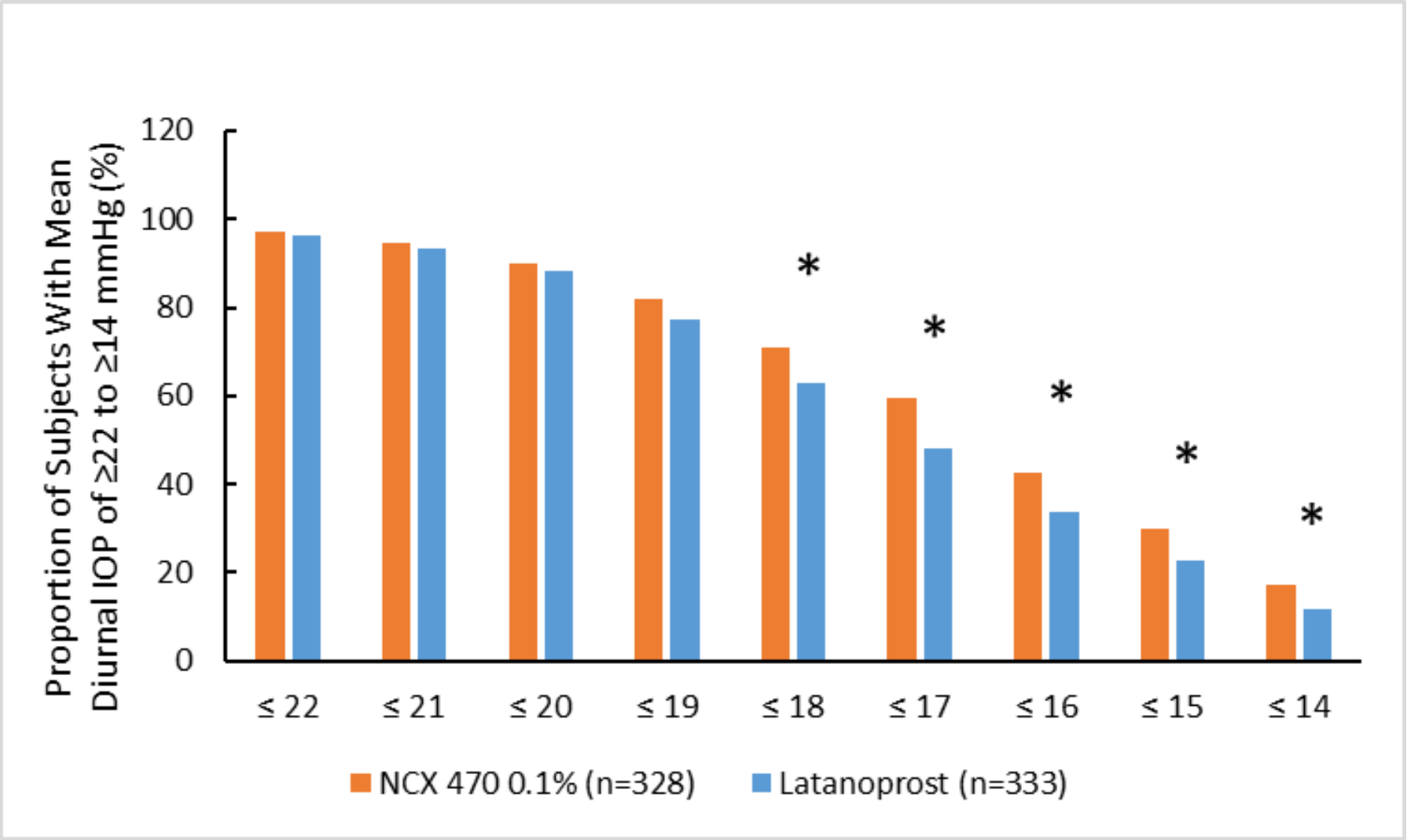
Significantly more patients achieved ≥ 10 mmHg Time-Matched IOP Reduction from Baseline on NCX 470 vs latanoprost for all study visits combined and for 3 individual timepoints

Proportion of Subjects Achieving Time-Matched IOP Reduction from Baseline of ≥ 10 mmHg
(Observed Data from 8AM and 4PM) Intent-to-Treat Population



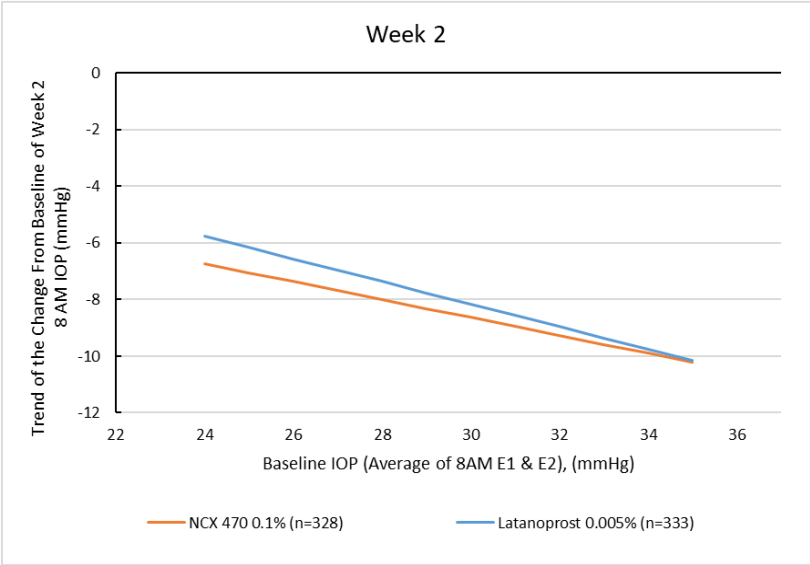
Proportion of Subjects Achieving a Mean Diurnal IOP of ≤ 22 to ≤ 14 mmHg in 1 mmHg Increments for All Visits Combined

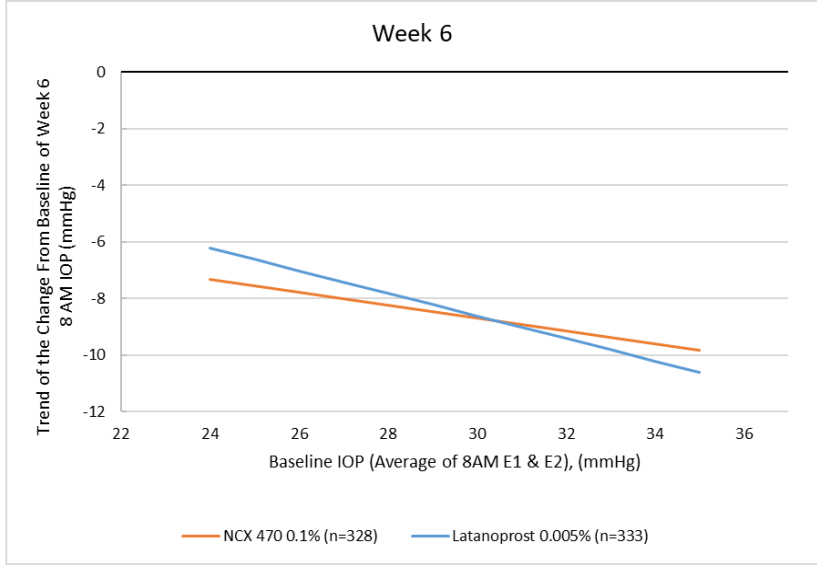
(Observed Data from 8AM and 4PM) Intent-to-Treat Population

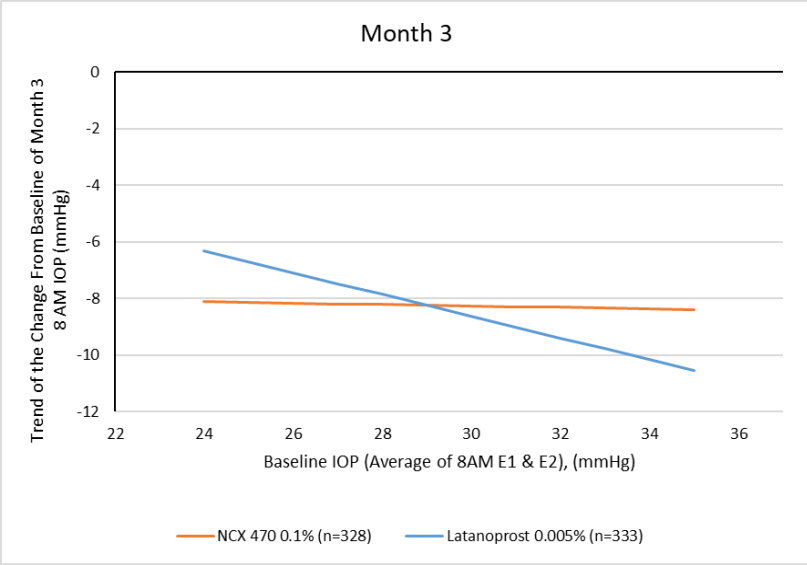


After 3 months' treatment NCX 470 was able to lower IOP by ~ 8.2 mmHg irrespective of starting IOP. This predictable IOP lowering was not seen with latanoprost

Trends of the Change from Baseline in Response to Treatment by IOP at 8 am on Randomization Visit (Baseline IOP)NCX 470 0.1% (n=328), Latanoprost 0.005% (n=333)







Retinal benefits: A potential differentiator for NCX 470

Elevated IOP is the main risk factor in glaucoma, however a variety of IOP-independent risk factors, including ischemia, contribute to damage of the optic nerve head and the retina, ultimately causing vision loss.

Initial exploratory studies generated encouraging results

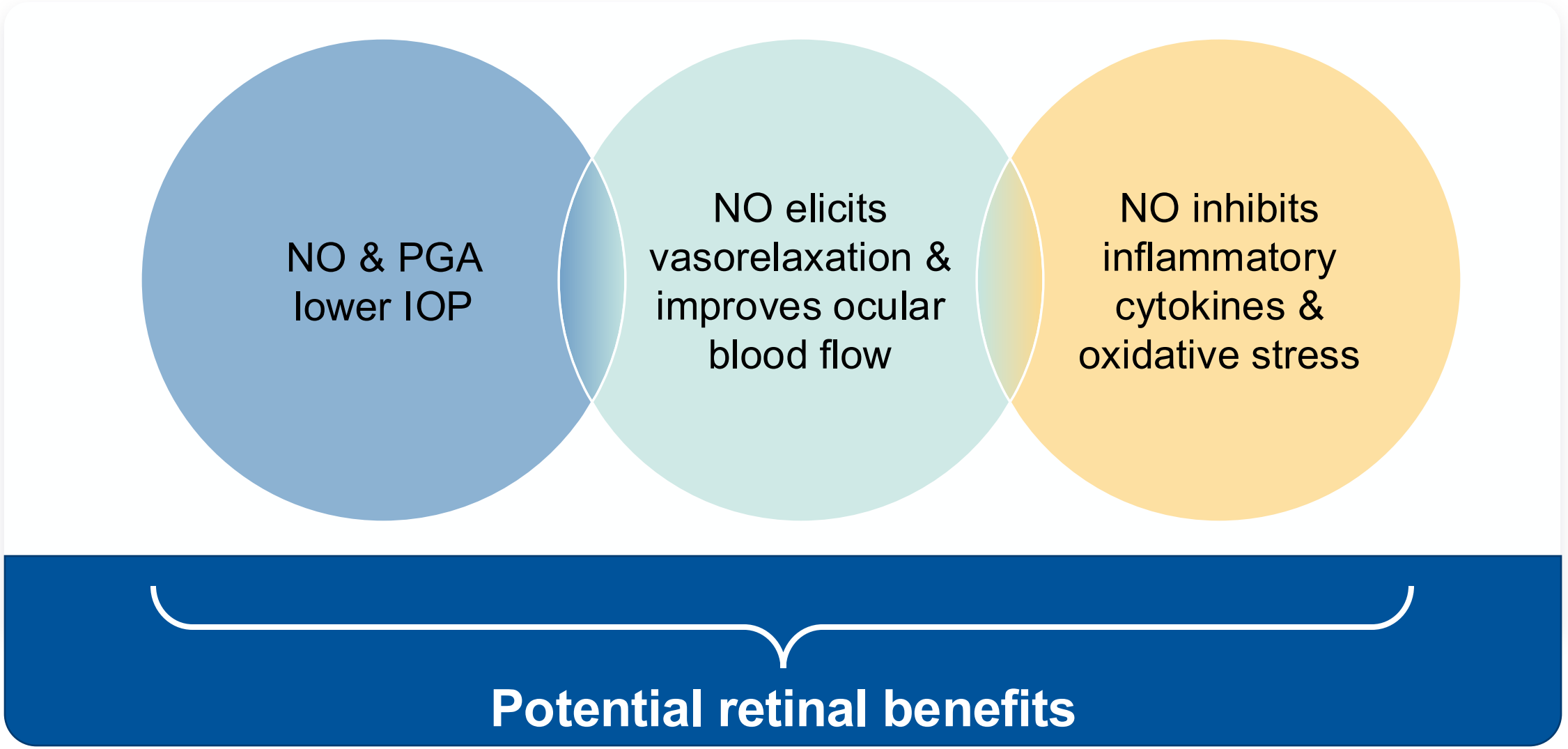
Exploratory nonclinical studies in a well-defined model with optic nerve head and retina damage (ET-1-induced ischemia/reperfusion) investigated the NCX 470 effects beyond IOP lowering.
The results suggest that NCX 470 improves ocular perfusion and retinal function in damaged eyes compared to vehicle[1,2] and to Lumigan®[2] and may therefore have protective properties for the retina.

Next Steps

Potential Phase 3b clinical trials to further explore NCX 470's potential benefits on the retina beyond its IOP lowering properties.

1. Bastia et al., J Ocul Pharmacol Ther. 2022, 38: 496-504;
2. Sgambellone et al., Transl Vis Sci Technol. 2023, 1;12(9):22.

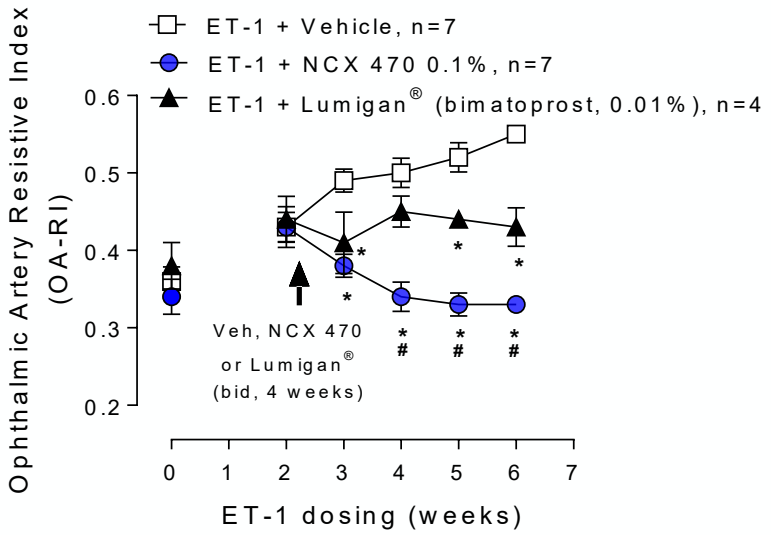
Nitric Oxide May Protect the Retina



NCX 470 Shows Retinal Cell Protection in a Nonclinical Model[1,2]

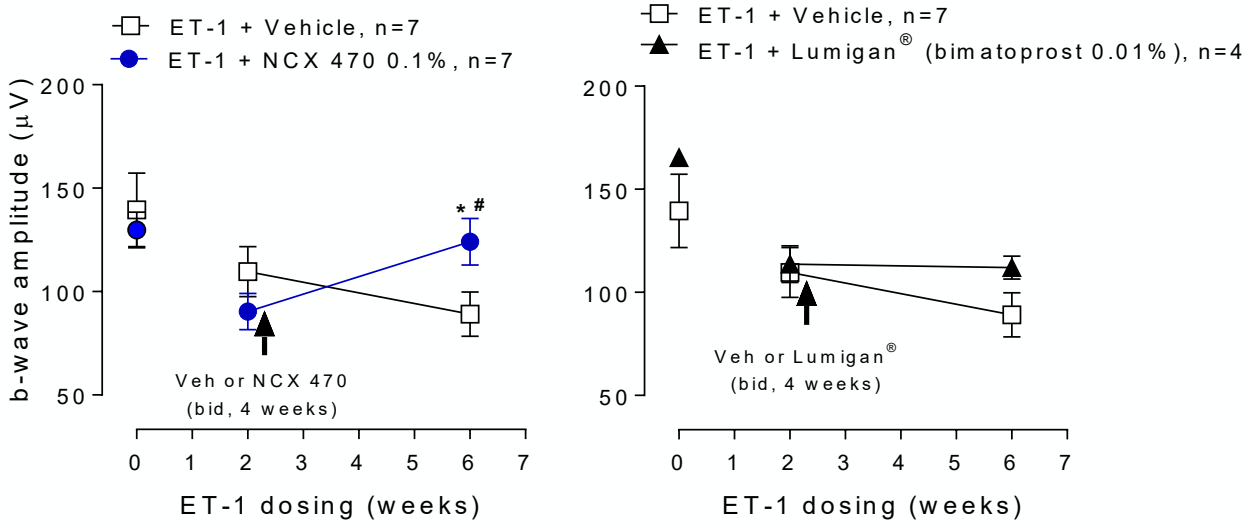
Improved ocular perfusion and retinal function in damaged eyes vs. Lumigan®

Ocular hemodynamics
(Echo-doppler - Ophthalmic artery)



Detrimental effect of ET-1 on ophthalmic artery hemodynamics reversed in eyes receiving NCX 470. Lumigan® only was only partially effective

Retinal function
(Scotopic Electroretinogram - rod/cone responses)



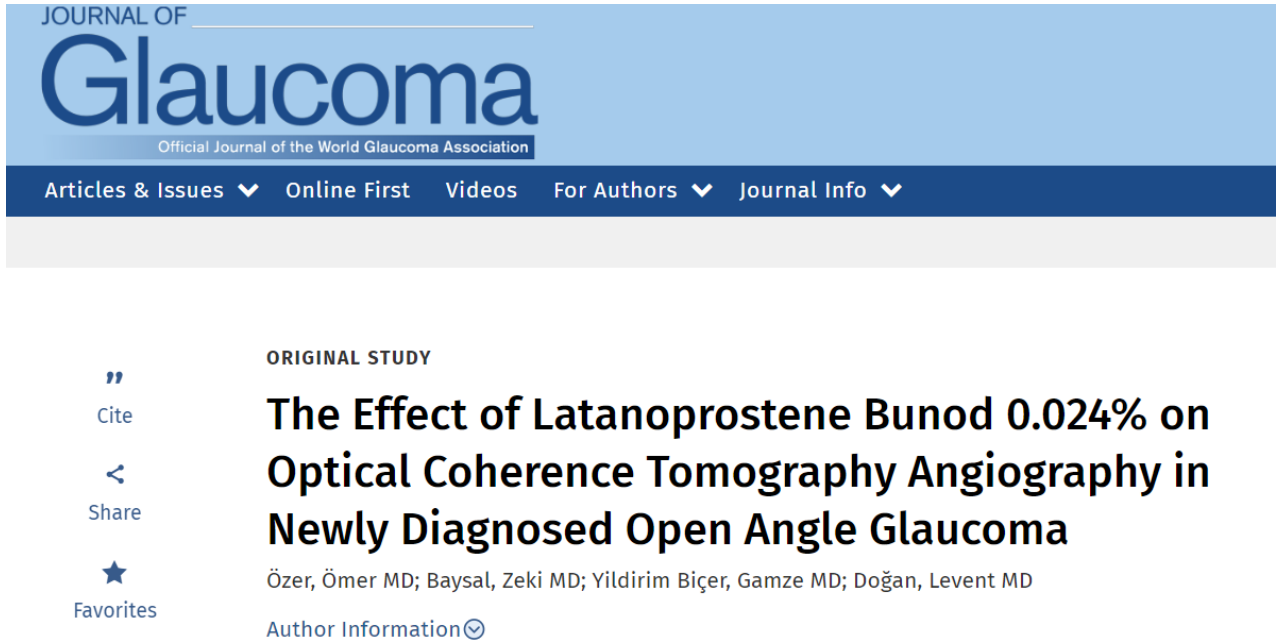
Photoreceptor response decline induced by ET-1 was almost completely reversed in eyes treated with NCX 470.
Lumigan® had no significant effect

* p<0.05 vs. vehicle at the same time point, # p<0.05 vs. Lumigan® Student's t-test

1. Bastia et al., J Ocul Pharmacol Ther. 2022, 38: 496-504;
2. Impagnatiello et al. ARVO 2023, abstract # 2580

Recent Literature Supporting the NO Retina Hypothesis

...an IOP-independent mechanism by which LBN modulates the risk of glaucoma progression by the enhancing ocular microcirculation



...the importance of LBN in the treatment of glaucoma is likely to be that it increases macular microcirculation, possibly via NO, independent of its IOP-reducing effect.

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