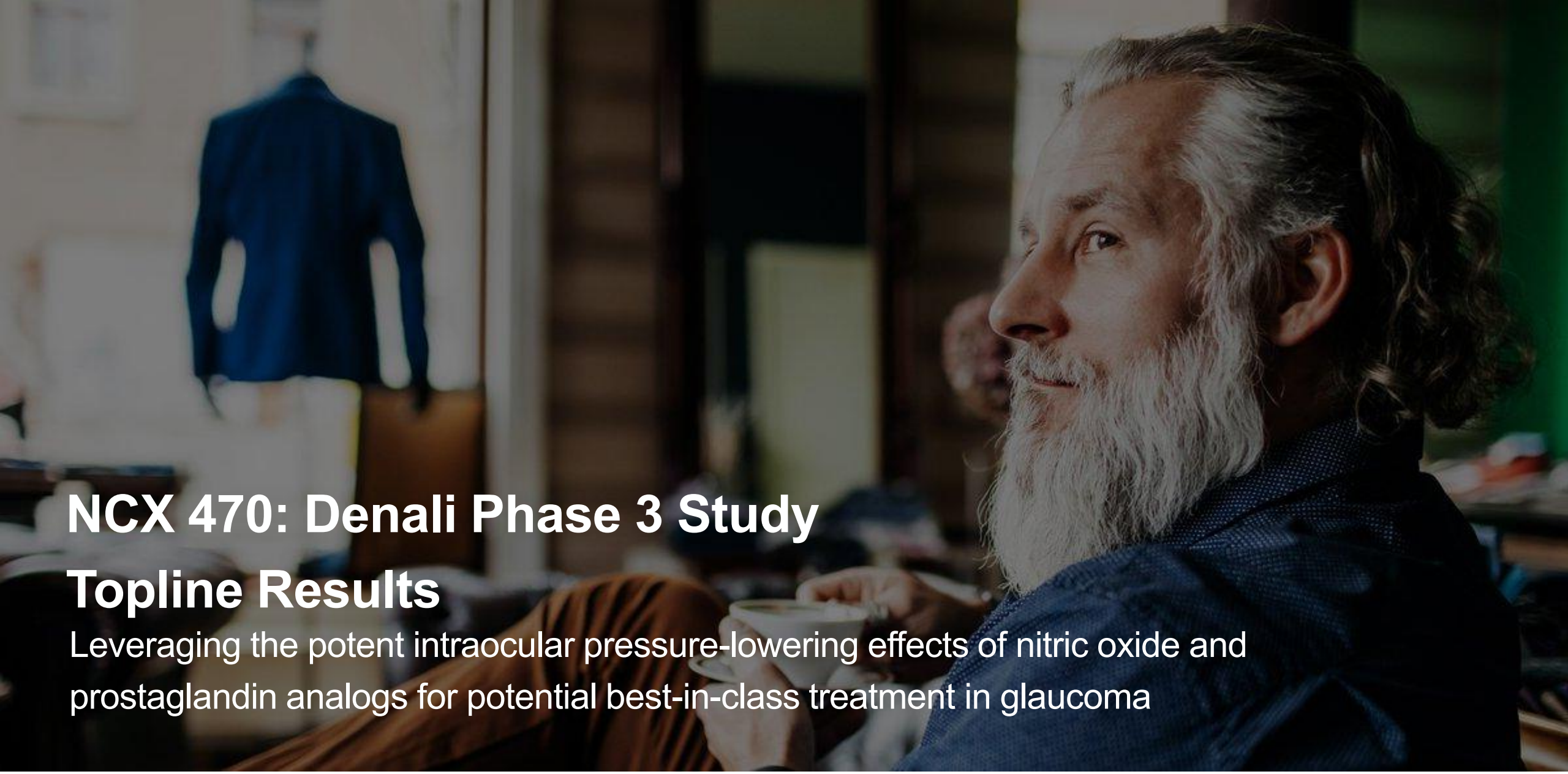


NCX 470: Denali Phase 3 Study Topline Results

Leveraging the potent intraocular pressure-lowering effects of nitric oxide and prostaglandin analogs for potential best-in-class treatment in glaucoma

nicox
visible science

Positive Topline NCX 470 Denali Results Released August 21, 2025

Phase 3 Program Intended to Support Planned U.S. & China NDA Submissions

NCX 470 0.1% demonstrated both non-inferiority, and superiority at certain timepoints, over latanoprost 0.005%, defined by intraocular pressure reduction from time-matched baseline IOP at 8 AM and 4 PM at Week 2, Week 6 and Month 3

DENALI: Completed, Positive Results

N=696; 65 clinical sites in the U.S. & 25 in China

Includes a 12-month safety extension

NCX 470 was statistically superior to latanoprost 0.005% in IOP reduction from baseline at 3 of the 6 timepoints

Jointly conducted and financed with Ocumension Therapeutics

Denali Phase 3 Efficacy Trial Design[1]

Designed to Evaluate NCX 470 vs. Established Therapy, Latanoprost

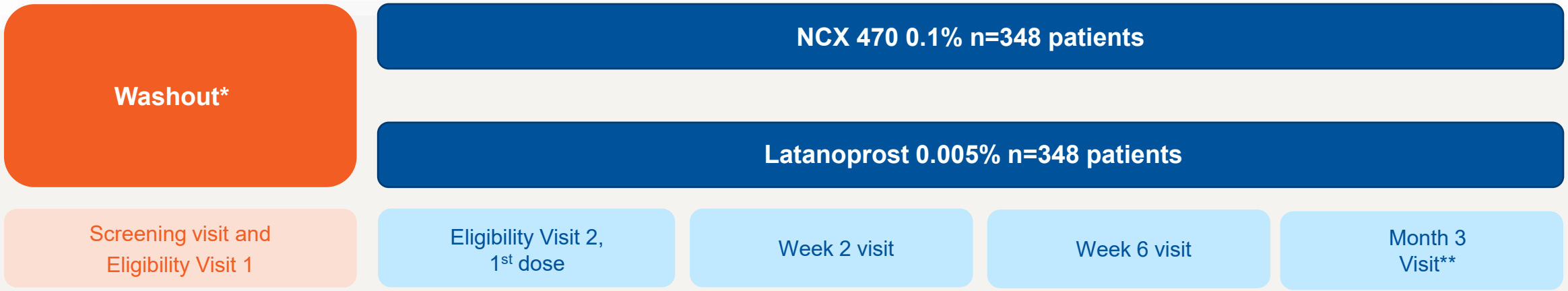
Randomized, controlled, double-masked, parallel design trial. Patients with open angle glaucoma or ocular hypertension were randomized 1:1 to once-daily treatment with NCX 470 0.1% or latanoprost 0.005%

Primary Endpoint:

Mean intraocular pressure reduction from time-matched baseline at 8AM and 4PM at the Week 2, Week 6 and Month 3 Visits

Enrollment:

The trial enrolled 696 patients across the two arms



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

** All subjects continued through 6M and a portion of patients continued for 12M in a safety extension

1. This schematic reflects the first 3 months of the study i.e., up to the primary end point

Denali Key Inclusion and Exclusion Criteria

Main Key Inclusion Criteria

- Subjects with a diagnosis of OAG or OHT in both eyes
- Meet IOP eligibility criteria:
  - IOP ≥ 26 mmHg at 8AM, ≥ 24 mmHg at 10AM, and ≥ 22 mmHg at 4PM in the study eye
  - IOP ≤ 36 mmHg in both eyes at all 3 measurement time points
- BCVA of +0.7 logMAR units or better

Main Key Exclusion Criteria

- Subjects with advanced glaucoma or subjects with a cup/disc ratio greater than 0.8
- Subjects with narrow angles and subjects with angle closure, congenital glaucoma, or a history of angle closure in either eye
- Subjects with a central corneal endothelial cell density < 2000 cells/mm^2 in either eye
- Subjects with history of previous glaucoma or angle surgery or subjects with SLT, YAG, ALT or MLT within 6 months prior to the Screening Visit

Demographics and Disposition

	NCX 470 0.1% N = 348	Latanoprost 0.005% N = 348
Gender, n (%) Female Male	 173 (49.7%) 175 (50.3%)	 170 (48.9%) 178 (51.1%)
Age, Years (SD)	59.49 (15.421)	58.96 (14.706)
Race, n (%) White Asian Black or African American Other	 180 (51.7%) 83 (23.9%) 82 (23.6%) 3 (0.9%)	 196 (56.3%) 82 (23.6%) 68 (19.5%) 1 (0.3%)
Completed the Study	313 (89.9%)	325 (93.4%)
Discontinued Prior to Study Completion	35 (10.1%)	23 (6.6%)
Reasons for Discontinuation		
Withdrawal by Subject	14 (4.0%)	11 (3.2%)
Lack of Efficacy	6 (1.7%)	4 (1.1%)
Lost to Follow-up	6 (1.7%)	2 (0.6%)
Adverse Event	3 (0.9%)	1 (0.3%)
Lack of Compliance	3 (0.9%)	0
Protocol Violation	2 (0.6%)	2 (0.6%)
Sponsor or IRB Decision	1 (0.3%)	1 (0.3%)
Physician Decision	0	1 (0.3%)
Other	0	1 (0.3%)

Table 14.1.1.1 and Table 14.1.2.1

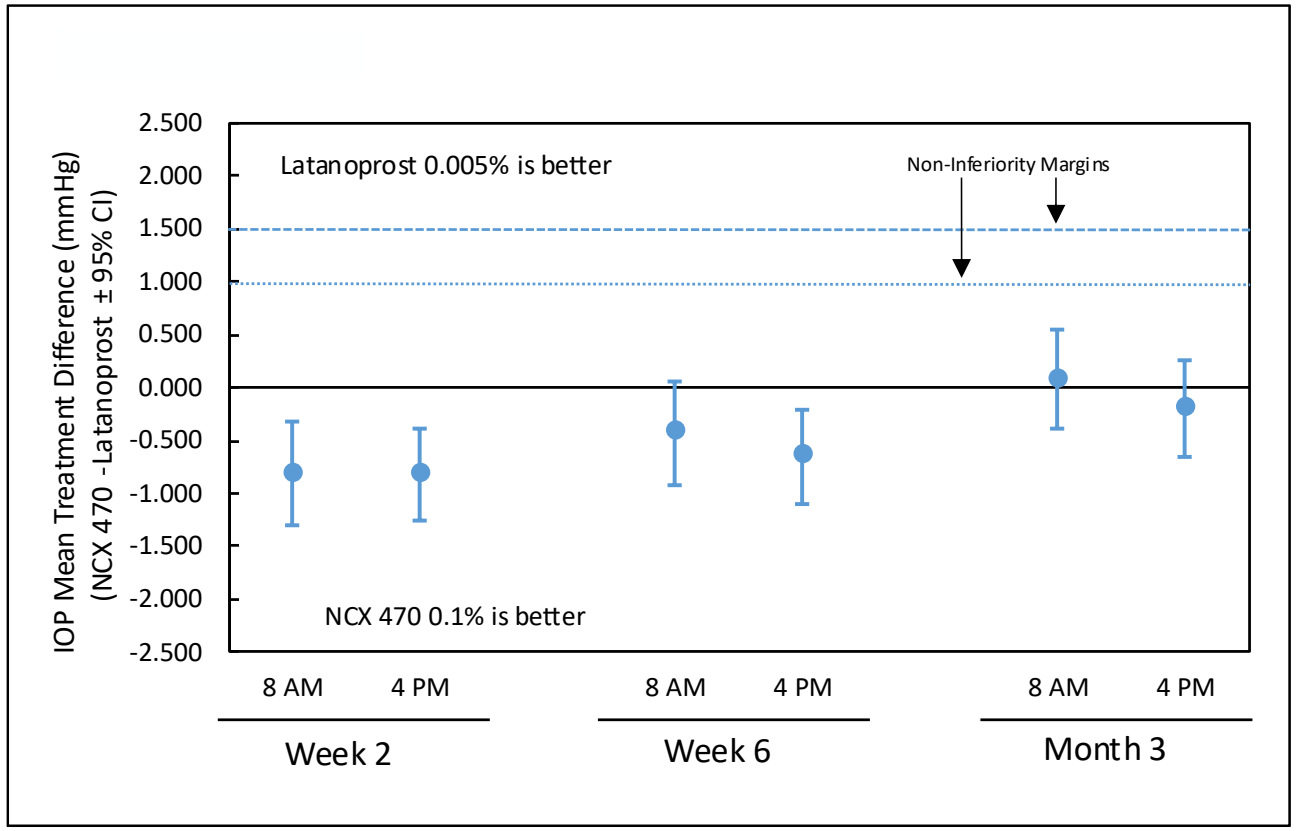
Baseline Characteristics

	NCX 470 0.1% N = 348	Latanoprost 0.005% N = 348
Baseline IOP (mmHg)		
Time Matched IOP		
8 AM (SD)	28.142 (2.1074)	28.025 (1.9096)
10 AM (SD)	26.892 (2.2970)	26.846 (2.1662)
4 PM (SD)	25.364 (2.3468)	25.458 (2.4558)
Mean Diurnal IOP	26.753 (1.9855)	26.741 (1.9753)
Central Corneal Thickness (um)		
Mean, (SD)	555.1 (32.51)	556.4 (32.98)
Central Corneal Endothelial Cell Density (cells/mm^2)		
Mean (SD)	2636.7 (318.72)	2641.1 (280.96)
Cup to Disk Ratio		
Horizontal (SD)	0.49 (0.172)	0.50 (0.180)
Vertical (SD)	0.50 (0.173)	0.52 (0.182)
Conjunctival Hyperemia		
Mean (SD)	0.23 (0.345)	0.25 (0.351)
BCVA		
Mean (SD)	0.048 (0.1257)	0.054 (0.1325)

Table 14.1.3.1

NCX 470 Achieved Non-Inferiority vs Latanoprost

Intent-To-Treat Population



NCX 470 N=348
Latanoprost N=348

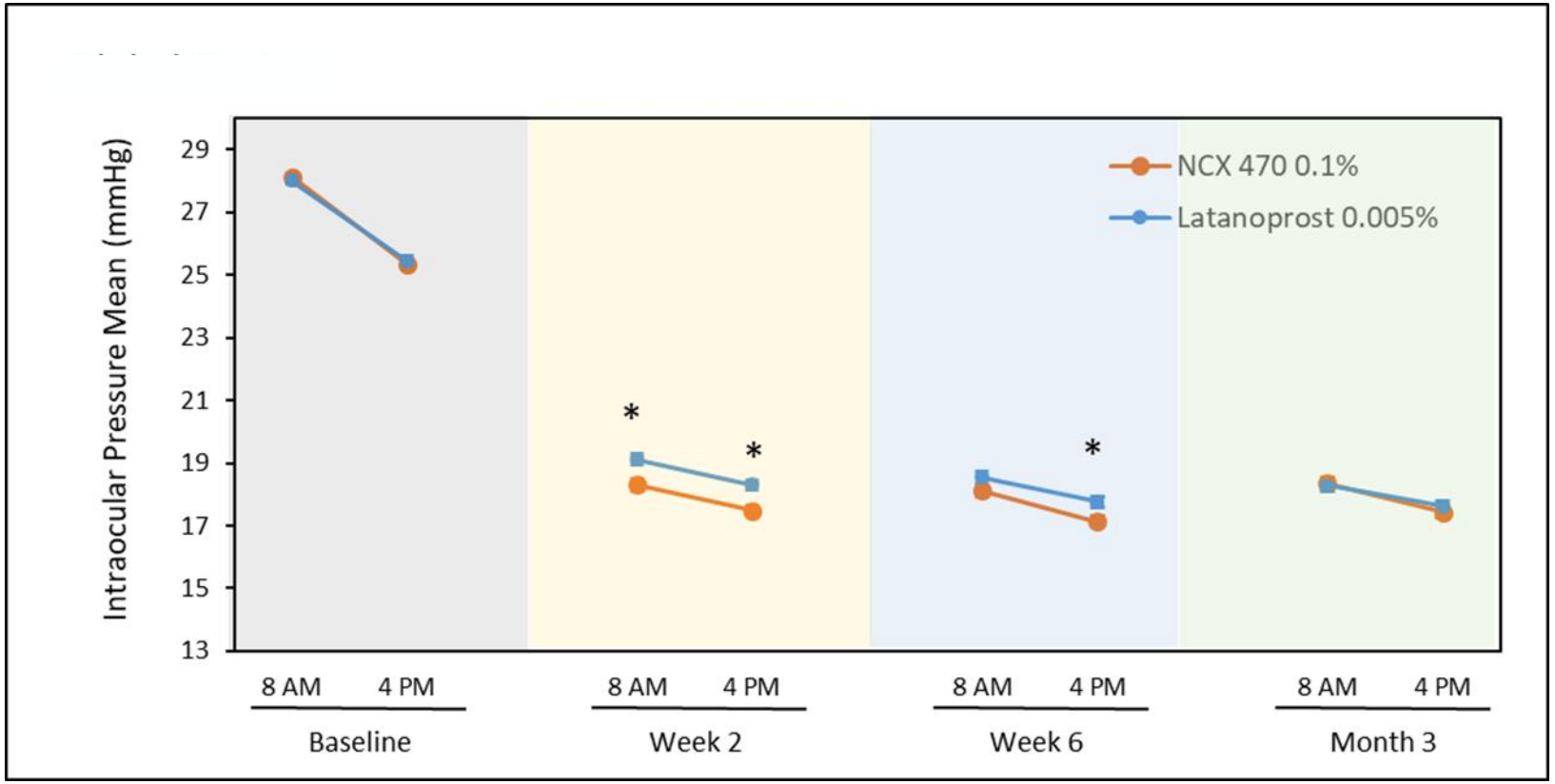
Non-inferiority criteria: The upper limit of all 6 95% confidence intervals were required to be ≤1.5 mmHg and at least 4 of 6 were required to be ≤1.0 mmHg

NCX 470 0.1% demonstrated an IOP lowering effect greater than latanoprost 0.005% of up to 0.8 mmHg

Table 14.2.1.1

NCX 470 Achieved Superiority vs Latanoprost at 3 of 6 Timepoints

Intent-To-Treat Population



NCX 470 N=348
Latanoprost N=348

* Denotes statistically significant difference between NCX 470 and latanoprost ($p<0.05$)

IOP-lowering effect from baseline was 7.9 to 10.0 mmHg for NCX 470 0.1% vs. 7.1 to 9.8 mmHg for latanoprost (reduction from baseline in time-matched IOP at 8 AM and 4 PM across the week 2, week 6 and month 3 visits)

Table 14.2.1.2

NCX 470 Denali Topline Results Demonstrates Robust Efficacy and Safety

IOP-lowering effect from baseline was 7.9 to 10.0 mmHg for NCX 470 vs. 7.1 to 9.8 mmHg for latanoprost

Measured by a change from baseline in time-matched IOP at 8 AM and 4 PM across the week 2, week 6 and month 3 visits

Statistical non-inferiority was met vs. latanoprost in the primary efficacy analysis

The upper limit of the 95% confidence limit on the difference in the treatment effect between NCX 470 and latanoprost in change from baseline in time-matched IOP to the follow-up visits (week 2, week 6, and month 3) was ≤1.5 mmHg at 6 of 6 timepoints and ≤1.0 mmHg at 6 of 6 timepoints

NCX 470 demonstrated statistically significant ($p<0.05$) superiority to latanoprost at 3 of 6 timepoints

NCX 470 was well-tolerated

- The most common adverse event was conjunctival hyperaemia in 22.0% of the NCX 470 patients vs. 9.2% of latanoprost patients
- There were no ocular or non-ocular serious adverse events related to NCX 470
- 10.1% of patients on NCX 470 discontinued compared to 6.6% on latanoprost

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