

DENALI Phase 3 Study U.S. Sub-population Overview and Outcomes

Nora Lee Cothran, OD, FAAO
Doug Hubatsch, MSc, BS
Siobhan Garbutt, PhD
Craig A. Sponseller, MD

October 1, 2026
American Academy of Optometry
Anaheim, California

Financial Disclosures

- Abbvie (S/C)
- Alcon (S/C,R)
- Bausch + Lomb (S/C,R)
- Glaukos (S/C)
- Kowa Pharmaceuticals America, Inc. (C)
- LENZ (S)
- Nicox Ophthalmics, Inc. (R)
- Spyglass (C)
- Sight Sciences (C)

DENALI Phase 3

Background

- Glaucoma is a progressive, neurodegenerative disease and the leading causes of irreversible blindness in the United States and worldwide.¹
- Lowering intraocular pressure (IOP) is the only known method to mitigate disease progression.²
- Prostaglandin analogues (PGAs) are the current first-line topical therapy for OAG and OHTN, however they do not target the trabecular meshwork, the primary avenue of aqueous outflow.²
- NCX 470, bimatoprost grenod 0.1%, is a single molecule, nitric oxide-donating bimatoprost designed to lower IOP through dual outflow pathways (trabecular meshwork and uveoscleral).
- NCX 470 met the primary endpoint at all timepoints in MONT BLANC, the first Phase 3 study.
- A Phase 3b study recently confirmed the molecule's role in conventional aqueous outflow.³
- The Phase 3 DENALI trial was conducted as a second, independent evaluation of NCX 470 per the requirements for FDA NDA submission.

OAG, open-angle glaucoma; OHTN, ocular hypertension

DENALI Phase 3

Purpose

- The DENALI trial was a randomized, double-masked, active-controlled, parallel-group study conducted at 90 clinical sites worldwide.
 - United States – 65 sites
 - China – 25 sites
- DENALI investigated mean IOP reduction with NCX 470, bimatoprost grenod 0.1%, and latanoprost 0.005% in subjects with open-angle glaucoma (OAG) or ocular hypertension (OHT).



DENALI Phase 3

Methods – Global Study Design^{1,2}

Inclusion Criteria

- Adults with bilateral OAG or OHT with untreated elevated IOP following washout of prior IOP-lowering treatments
 - ≥ 26 mmHg at 8AM
 - ≥ 24 mmHg at 10AM
 - ≥ 22 mmHg at 4PM
- Baseline IOP ≤ 36 mmHg in both eyes at all timepoints
- BCVA of $+0.7$ logMAR or better

Exclusion Criteria

- Advanced glaucoma or C/D ratio > 0.8
- Narrow or closed angles, congenital glaucoma, or a history of angle closure
- CCT $< 480\mu\text{m}$ or $> 620\mu\text{m}$
- Prior MIGS
 - Durysta, iStent, or Hydrus
- Prior incisional glaucoma surgery
 - Trabeculectomy, tube, or shunt
- Any laser within 6 months of screening
 - ALT, SLT, MLT, or YAG

ALT, argon laser trabeculoplasty; BCVA, best corrected visual acuity; CCT, central corneal thickness; C/D, cup to disc; MIGS, minimally invasive glaucoma surgery; MLT, micropulse laser trabeculoplasty; SLT, selective laser trabeculoplasty; YAG, yttrium aluminum garnet.

DENALI Phase 3

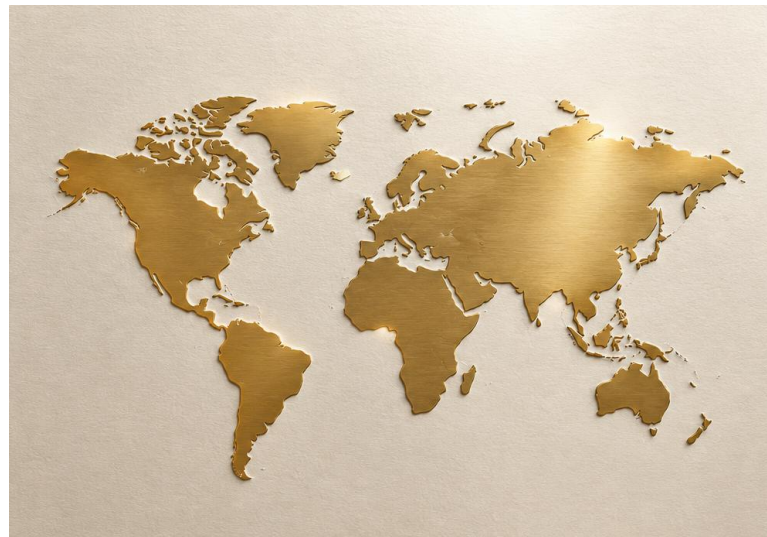
Methods – Global Study Design

Primary Endpoint

- Non-inferiority of mean IOP reduction from time-matched baseline at 8AM and 4PM at Weeks 2 and 6 and Month 3 (ITT population) (up to 3 months)

Secondary Endpoint

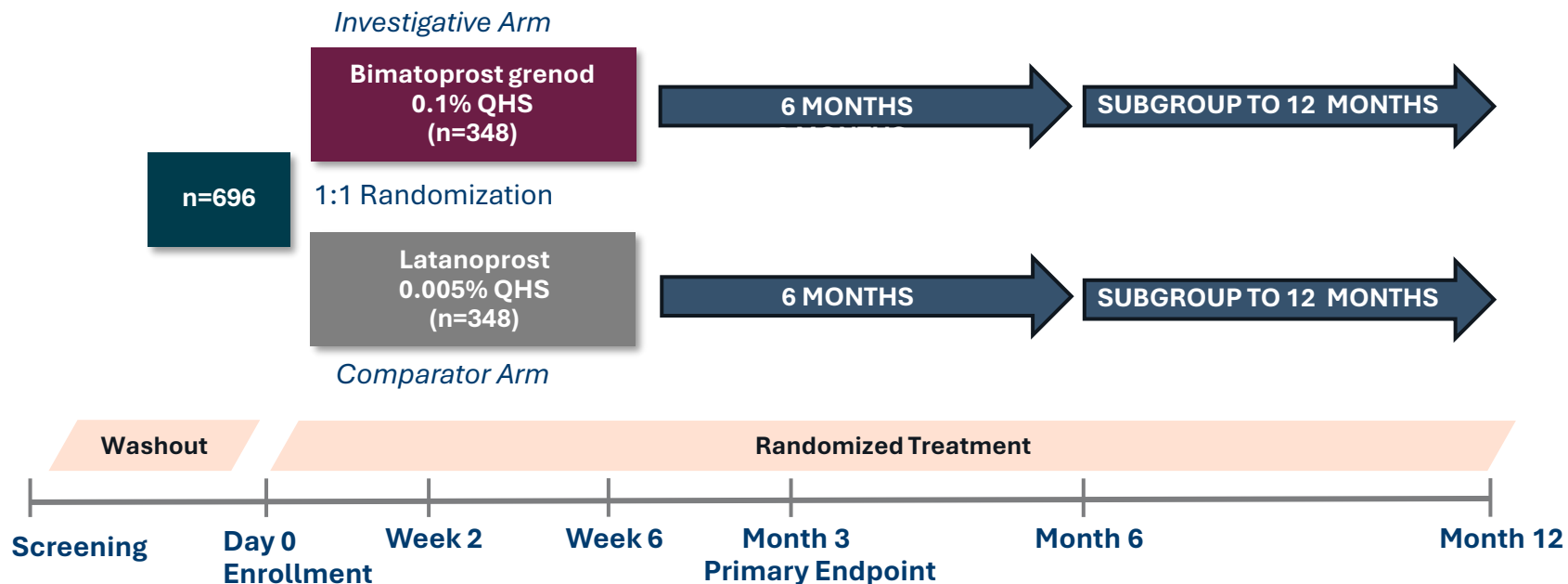
- Mean diurnal IOP change from baseline at the Week 2, Week 6 and Month 3 Visits in the study eye (up to 3 months)
- Frequency and incidence of treatment-emergent adverse events (up to 12 months)
- Rate of discontinuation (up to 12 months)



ITT, intention to treat

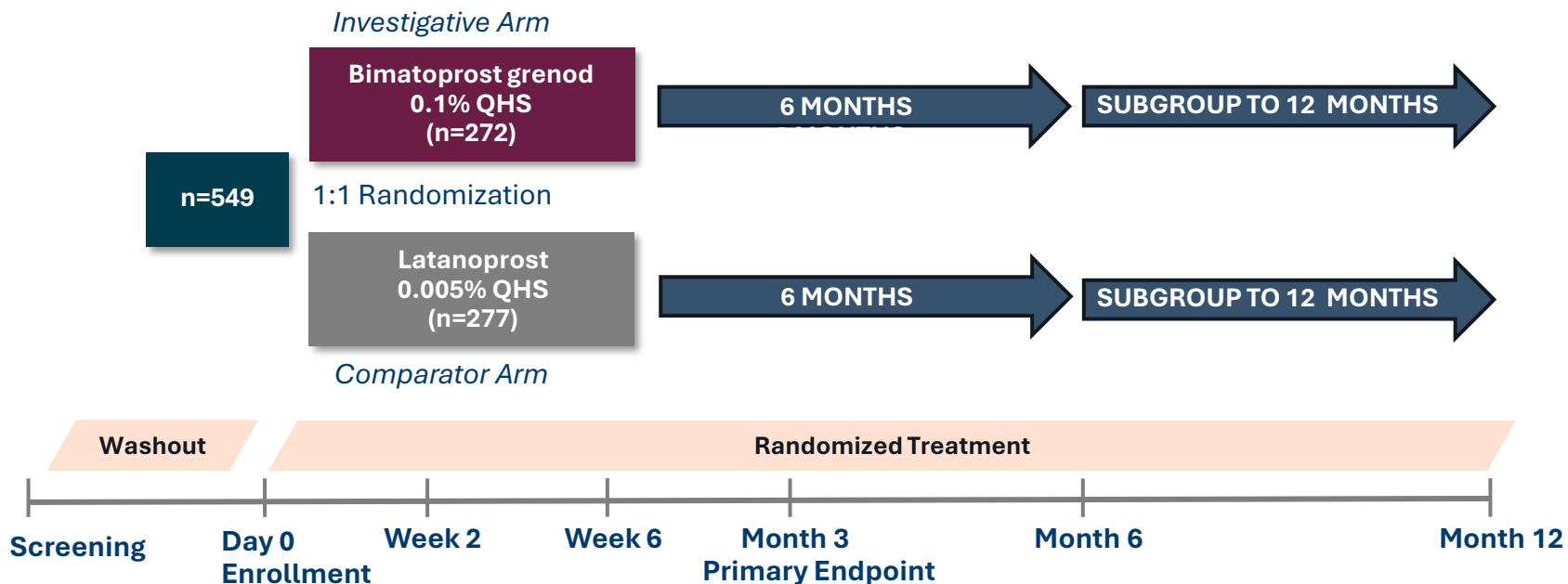
DENALI Phase 3

Methods – Global Study Design



DENALI Phase 3

Methods – U.S. Sub-population



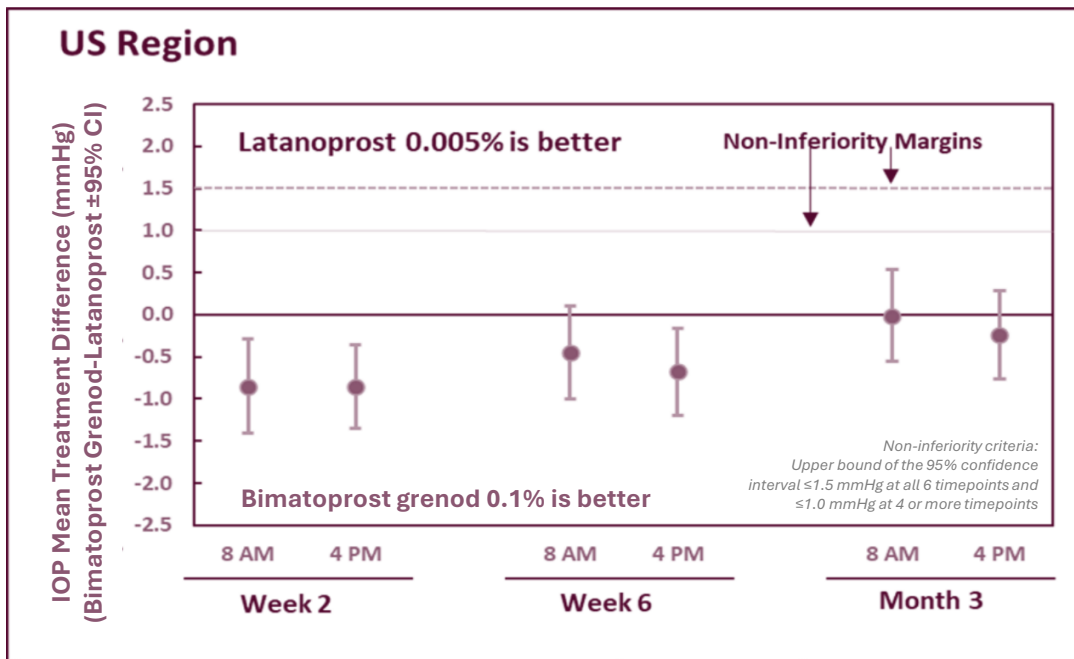
DENALI Phase 3

Baseline Characteristics – U.S. Sub-population

Baseline Characteristics		Bimatoprost grenod 0.1% (n = 272)	Latanoprost 0.005% (n = 277)
Age	Mean (SD)	64.8 (11.1)	63.8 (10.2)
Sex	n (% Female)	143 (52.6%)	147 (53.1%)
Race	n (%)		
White		180 (66.2%)	196 (70.8%)
Asian		8 (2.9%)	11 (4.0%)
Black or African American		82 (30.1%)	68 (24.5%)
Other		2 (0.7%)	2 (0.7%)
Completed the Study	n (%)	242 (89.0%)	257 (92.8%)
Baseline IOP			
8:00 AM	Mean (SD)	28.1 (2.0599)	28.1 (1.9742)
10:00 AM	Mean (SD)	26.8 (2.2797)	26.9 (2.2333)
4:00 PM	Mean (SD)	25.3 (2.3708)	25.5 (2.5601)
Diurnal IOP	Mean (SD)	26.7 (1.9787)	26.8 (2.0581)

DENALI Phase 3

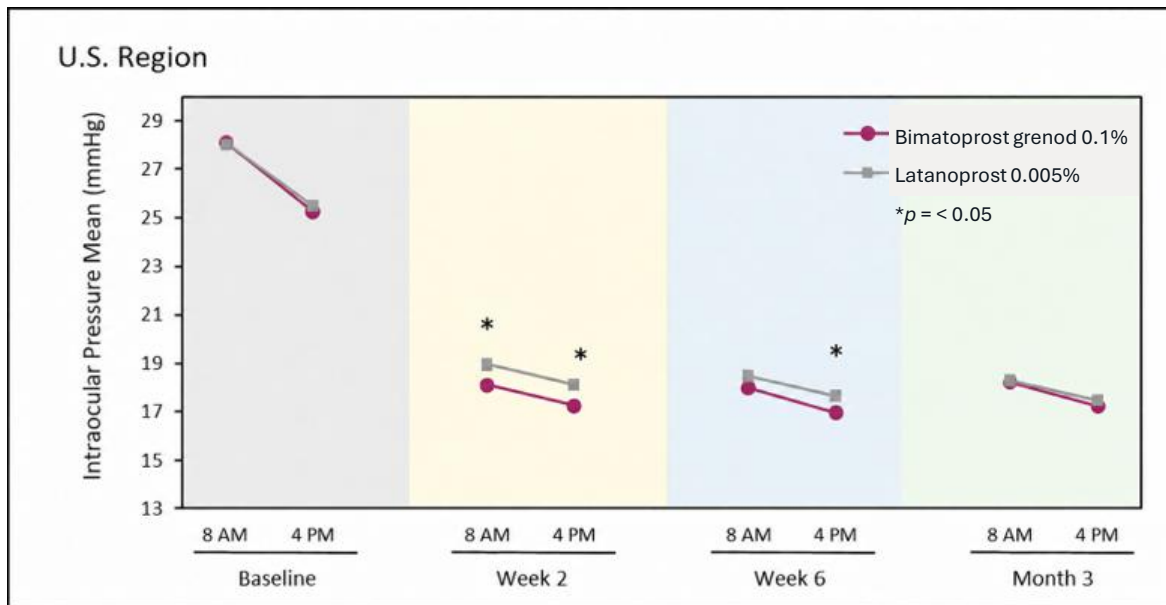
Results: U.S. Sub-population



- Bimatoprost grenod 0.1% (n=272)
- Latanoprost 0.005% (n=277)
- Non-inferiority - Mean difference in IOP reduction with 95% confidence intervals (CI) at Week 2, Week 6 and Month 3.
- Values below zero favored bimatoprost grenod 0.1%.

DENALI Phase 3

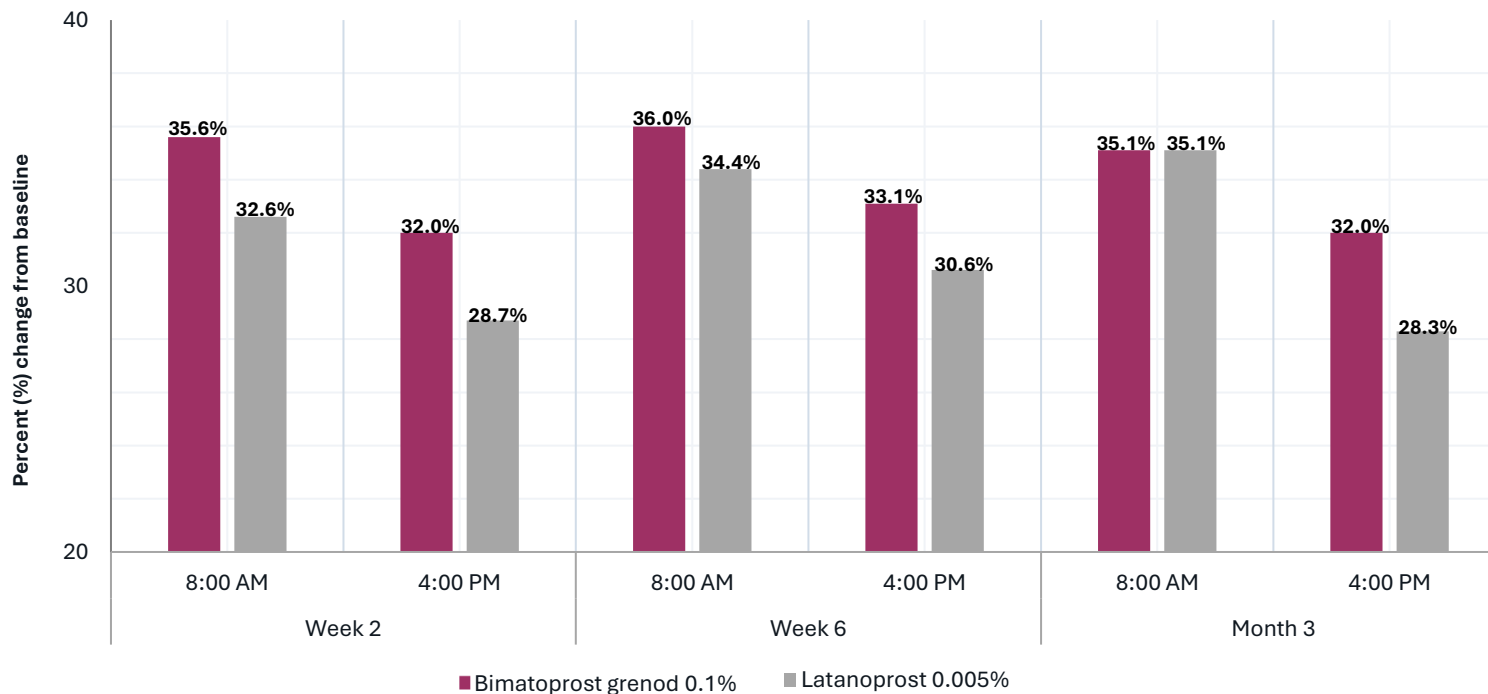
Results - Mean IOP Reductions from Baseline in U.S. Sub-population



- Primary Endpoint was met at all timepoints for bimatoprost 0.1%.
- Statistically significant ($p < 0.05$) differences in IOP-reduction were observed at 3 of 6 timepoints:
 - Week 2 (8 AM)
 - Week 2 (4 PM)
 - Week 6 (4 PM)

DENALI Phase 3

Results - Percentage IOP Reductions from Baseline in U.S. Sub-population



DENALI Phase 3 Safety

Results - Most Common Adverse Events in U.S. Sub-population

	Bimatoprost grenod 0.1%	Latanoprost 0.005%
Conjunctival hyperemia	40 (14.9%)	19 (6.9%)
Punctate keratitis	16 (5.9%)	9 (3.2%)
Eyelash growth	15 (5.6%)	1 (0.4%)
No treatment-related serious ocular adverse events were reported.		
Discontinuation due to adverse event was low for both treatment groups (1.1% vs 0.4%).		
Discontinuation due to lack of efficacy was uncommon in both treatment groups (2.2% vs 1.4%).		

DENALI Phase 3

Conclusion

- The DENALI trial demonstrated non-inferiority of bimatoprost grenod 0.1% compared to latanoprost 0.005% at all evaluated timepoints up to the primary endpoint at Month 3.
- In the DENALI U.S. sub-population, the IOP-lowering effect of bimatoprost grenod 0.1% was statistically superior ($p<0.05$) to latanoprost 0.005% at 3 of 6 timepoints.
- Bimatoprost grenod 0.1% was well-tolerated and exhibited robust efficacy, with mean IOP reduction of **8.1-10.1 mmHg** in the U.S. sub-population.
- The trabecular meshwork is responsible for up to 80% of aqueous outflow, thus agents that target this primary pathway are ideal first-line glaucoma therapies.
- Future studies may investigate attributes unique to bimatoprost grenod 0.1%.
- These efficacy and safety data are consistent with the MONT BLANC Phase 3 trial.
- The NDA has been submitted to the FDA for review with a PDUFA date in April 2027.

THANK YOU