GEMINI 1 Phase 3: Safety and Efficacy of AGN-190584 in Participants with Presbyopia

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AGN-190584 is not an FDA approved drug

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Objective and Study Design

Objective

- To evaluate the efficacy, safety, and tolerability of AGN-190584 (pilocarpine HCl 1.25%) administered bilaterally, once-daily, for 30 days in participants with presbyopia
- To evaluate the primary and secondary efficacy endpoints for near vision improvement without loss in distance vision with AGN-190584 vs vehicle

Study Design

- Multicenter, double-masked, randomized, vehicle-controlled, phase 3 study (NCT03804268)
- 323 participants (40-55 years of age) with presbyopia were randomized to receive 1 drop (both eyes) of topical AGN-190584 (N=163) or vehicle (N=160) once daily at 8:00 AM in both eyes for 30 days

Key Inclusion Criteria

Subjective complaints of poor near vision that impacts daily living activities with:

- Best distance correction of spherical −4.00 D to +1.00 D and cylinder ≤±2.00 D with photopic, high-contrast corrected-distance visual acuity (CDVA) 20/25 or better in each eye
- Mesopic, high-contrast DCNVA 20/40 (J3) to 20/100 (J10)

Visit Schedule: Screening and Days 1 (baseline), 3, 7, 14, and 30

Key Assessments and Procedures

- Distance Corrected Near Visual Acuity (DCNVA) - 40 cm (mesopic and photopic)
- Distance Corrected Intermediate Visual Acuity (DCIVA) - 66 cm (mesopic and photopic)
- Corrected Distance Visual Acuity (CDVA) - 4 m

[a] Mesopic condition is defined as lighting 10-11 lux, measured at the target. [b] Photopic condition is defined as lighting ≥251 lux, measured at the target.

Methods

Efficacy and Safety Endpoints

Distance-corrected near vision acuity (DCNVA) was assessed binocularly

- Primary endpoint:
  - Participants (%) with ≥3-line improvement in mesopic[a] DCNVA at **Hour 3**, Day 30
- Key secondary endpoint:
  - Participants (%) with ≥3-line improvement in mesopic[a] DCNVA at **Hour 6**, Day 30
- Prespecified endpoints:
  - Participants (%) achieving photopic,[b] DCNVA of 20/40 or better vision at Hours 1 and 3, Day 30
  - Participants (%) achieving ≥2-line gain in mesopic, high-contrast, binocular DCNVA at Hours 1 and 3, Day 30

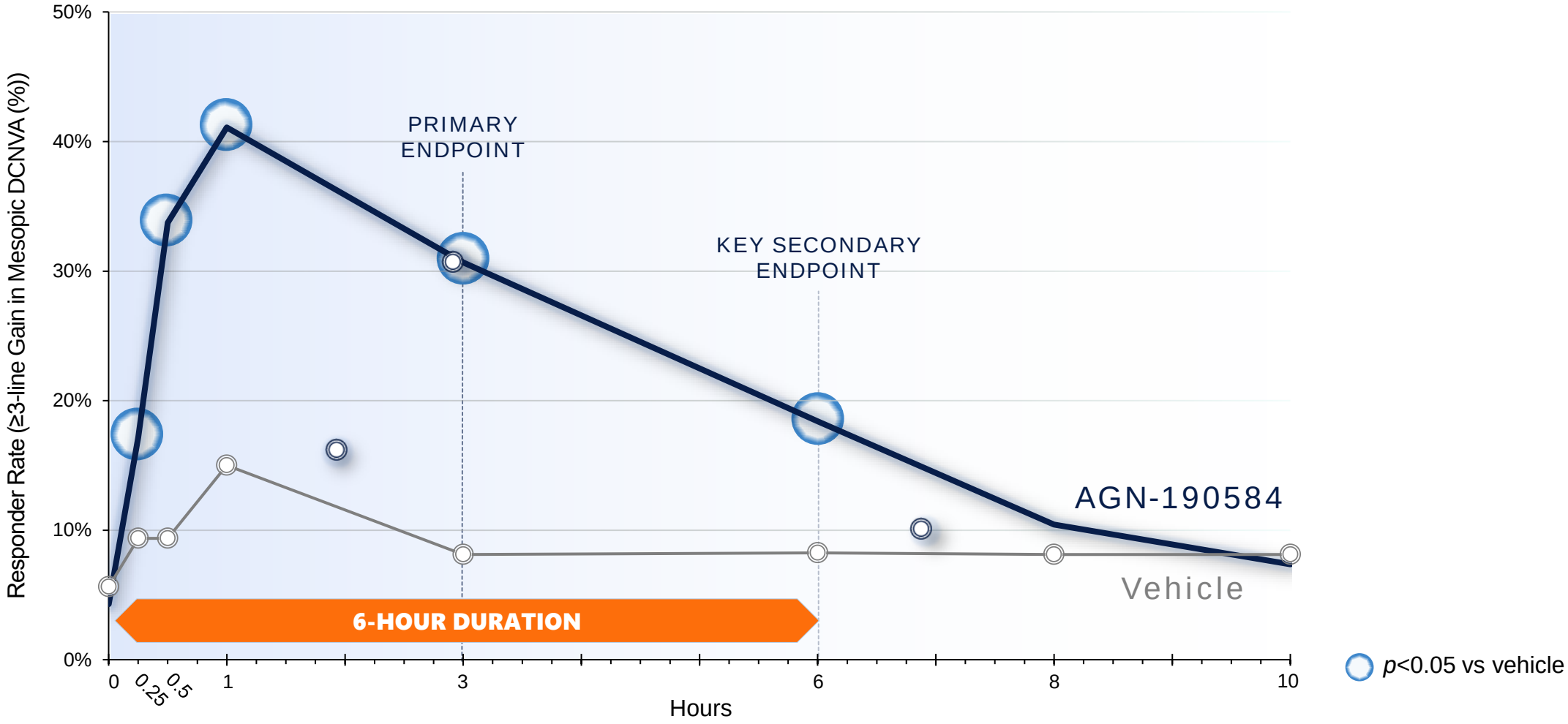
Safety profile assessed

- Treatment emergent adverse events (TEAEs), visual analog scale (VAS) assessment of headache, biomicroscopy, ophthalmoscopy, and IOP
- Mean change from baseline in mesopic corrected distance visual acuity (CDVA)

[a] Mesopic condition is defined as lighting 10-11 lux, measured at the target. Near visual acuity was assessed at 40 cm.
[b] Photopic condition is defined as lighting ≥251 lux, measured at the target.

Results

GEMINI 1 Met Primary Efficacy Endpoints ≥ 3-line Gain at Hour 3 and Key Secondary Endpoint ≥3-line Gain at Hour 6 at Day 30



Results

Significantly Higher Responder Rates for Other Predefined Efficacy Endpoints

- More patients achieved 20/40 or better in photopic, high-contrast, binocular DCNVA with AGN-190584
- More patients achieved ≥2-line gain in mesopic, high-contrast, binocular DCNVA

Endpoints at Day 30	Time Point	AGN-190584 (N=163)	P value*
Participants achieving **20/40 or better** in photopic, high-contrast, binocular DCNVA, %	Hour 1 Hour 3	92.5 84.5	0.0114 0.0171
Participants achieving **≥2-line gain** in mesopic, high-contrast, binocular DCNVA, %	Hour 1 Hour 3	74.8 58.3	<0.0001 <0.0001

[a] Mesopic condition is defined as lighting 10-11 lux, measured at the target. Near visual acuity was assessed at 40 cm.
[b] Photopic condition is defined as lighting ≥251 lux, measured at the target.
* *P* value vs vehicle

AGN-190584 is Safe and Well Tolerated, with Low Discontinuation

- Most common treatment-emergent adverse events[a] (safety population)

System Organ Class Preferred Term	AGN-190584 (N=163) % (n)	Vehicle (N=159) % (n)
Eye disorders		
Visual impairment	7 (4.3)	1 (0.6)
Conjunctival hyperemia	4 (2.5)	4 (2.5)
Vision blur	4 (2.5)	2 (1.3)
Eye irritation	4 (2.5)	1 (0.6)
Eye pain	4 (2.5)	1 (0.6)
Lacrimation increased	4 (2.5)	0 (0.0)
Punctate keratitis	1 (0.6)	5 (3.1)
Nervous system disorders		
Headaches	23 (14.1)	15 (9.4)
Gastrointestinal disorders		
Nausea	4 (2.5)	0 (0.0)
Discontinuations due to AEs	2 (1.2%)	1 (0.6%)

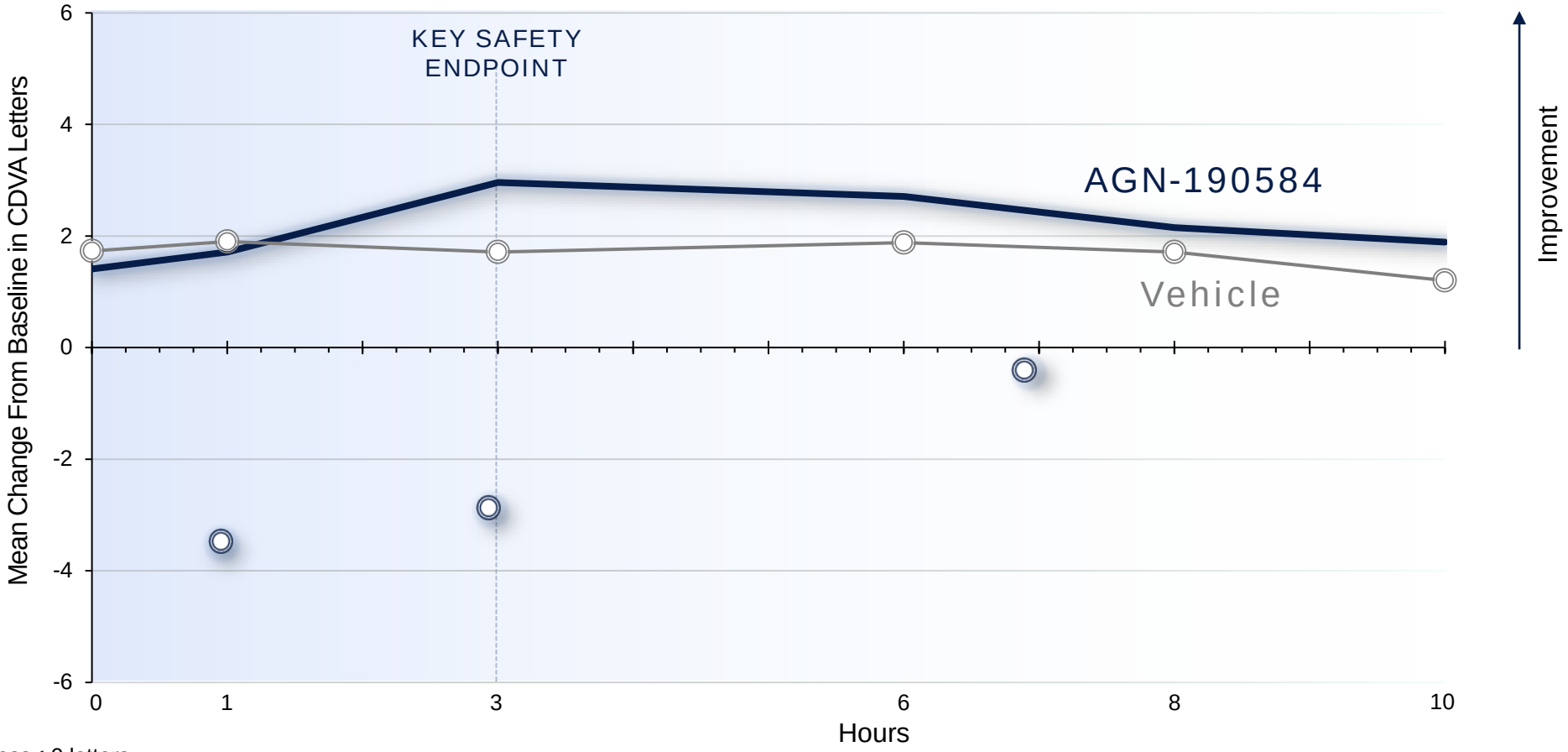
[a] Reported by at least 2% of patients in either group.

- Participants were prompted to report AEs of headaches
  - At each visit, before and after dosing, all participants were required to fill out a VAS questionnaire to rate the degrees of temporal and supraorbital headaches
  - In the study arm, headaches were mostly mild (85%), and transient, requiring no treatment
  - There were no reports of discontinuations due to headache in the treatment arm
- No retinal detachments were observed
- No serious adverse events were reported

Results

AGN-190584 does not Compromise Distance Vision

- No loss in mean distance vision was observed
- Slight numerical improvement (up to 3 letters) observed
- The mean change from baseline in mesopic corrected distance visual acuity (CDVA), in number of letters, was similar with AGN-190584 and vehicle on Day 30



Gain > 0 letters; loss< 0 letters.

Conclusions

AGN-190584 met the primary and key secondary efficacy endpoints of ≥3-line improvement in mesopic DCNVA at Day 30

- ≥3-line gain starting at 15 minutes with a duration of up to 6 hours post-administration

Additional secondary efficacy endpoints were met in GEMINI 1 at Day 30, including:

- More patients achieved 20/40 or better vision in photopic, high-contrast, binocular DCNVA with AGN-190584
- More patients achieved ≥2-line gains in mesopic, high-contrast, binocular DCNVA
- More patients demonstrated improvements in patient-reported outcomes (NVPTQ and PICQ)

AGN-190584 is safe and well tolerated

- TEAEs were predominantly mild and transient, and discontinuations rates were low

Thank you!

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