NG101 Low-dose AAV Gene Therapy for wet AMD: First-in-human, 52-week Safety and Efficacy Data

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Introduction

• Wet (neovascular) age-related macular degeneration (wAMD) is a progressive retinal disease driven by excessive vascular endothelial growth factor (VEGF), leading to pathological neovascularization, retinal edema, and vision loss.

• Although repeated intravitreal anti-VEGF injections are effective, treatment burden and suboptimal long-term compliance continue to define an unmet clinical need.

• NG101 is an adeno-associated virus serotype 8 (AAV8)-based gene therapy designed to achieve durable intraocular expression of aflibercept after a single subretinal administration.

Figure 1. Schematic of NG101 Genome

• As shown in **Figure 1**, NG101 incorporates a proprietary CAT311 promoter with enhancer and regulatory elements to support robust and sustained expression while minimizing immunogenicity.

• NG101 is currently being evaluated in an ongoing Phase 1/2a, open-label, dose-escalation study in patients with wAMD requiring frequent anti-VEGF treatment.

Methods

• SENSE (A Phase 1/2a open-label **S**tudy to **E**valuate Safety, Tolerability, and Preliminary Efficacy of **N**G101 AAV Gene Therapy in **S**ubjects with W**E**t Age-Related Macular Degeneration, NG101WA-01) is an ongoing multicenter study (NCT05984927) (**Figure 2**).

• NG101 was administered as a single subretinal injection at 1×10^9 vg/eye (Cohort 1), 3×10^9 vg/eye (Cohort 2), or 8×10^9 vg/eye (Cohort 3); these doses are notably lower than those in current AAV gene therapies for wAMD.

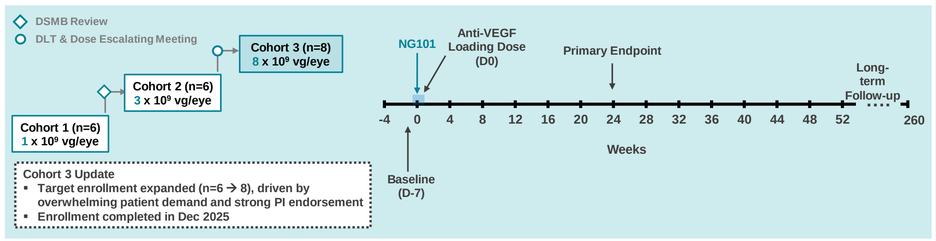


Figure 2. SENSE Study (NG101WA-01) Design (NCT05984927)

Key Eligibility

- Age: 50 to 89 years old
- Choroidal Neovascularization (CNV) due to wAMD
- Best Corrected Visual Acuity (BCVA) between 20/40 and 20/400
- At least 3 anti-VEGF injections in the past 6 months

Primary Endpoint (Safety)

Incidence and severity of ocular and non-ocular adverse events (Week 24)

Secondary Endpoint (Safety and Efficacy)

- Incidence and severity of ocular and non-ocular adverse events (Weeks 52 and 104)
- The cumulative number of rescue therapy treatments
- Change in Best Corrected Visual Acuity (BCVA)
- Change in Central Subfield Thickness (CST)
- Change in immunogenic responses in serum

Criteria for Supplemental Anti-VEGF Injection

- Increased subretinal or intraretinal fluid leading to OCT central subfield thickness (CST) increases of ≥100 µm due to active CNV, regardless of visual acuity.
- BCVA loss of more than 10 ETDRS letters associated with the presence of intraretinal or subretinal fluid on OCT that is attributable to active CNV.
- New subretinal hemorrhage, intraretinal hemorrhage, or lipid exudation observed on clinical examination or fundus photography attributable to active CNV.
- Worsening exudative macular degeneration not meeting the aforementioned criteria but deemed a threat to patient safety at the discretion of the investigator.

Results

Baseline Characteristics of Cohort 1

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Average
Age (years)	78	80	73	66	80	77	76
Gender / Race	Male / White	Female / White	Female / Asian	Female / White	Female / White	Female / White	-
BCVA (ETDRS letters)	47	56	47	72	65	57	57
CST (microns)	267	305	390	295	254	256	295
Time since wAMD Diagnosis (years)	7	2	10	9	4	14	7.5
Number of Anti-VEGF Injections (1 year prior to NG101 injection)	10	10	8	13	9	9	9.8

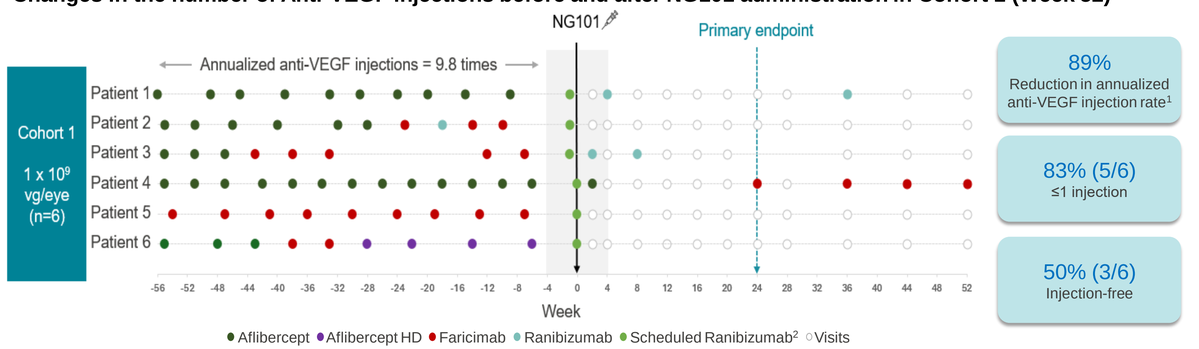
Safety

Favorable Safety and Tolerability Profile to Date

- NG101 continues to be generally well-tolerated across all subjects (n=20).
- No NG101-related serious adverse events (SAEs) or dose-limiting toxicities (DLTs).
- No NG101-related clinically significant RPE changes or retinal degeneration.
- No cases of hypotony, vascular occlusions, endophthalmitis, vasculitis, or retinitis.

Efficacy: Reduction in Treatment Burden

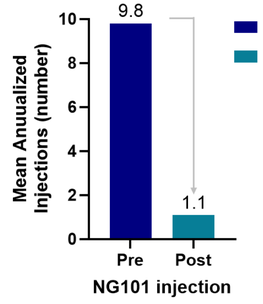
Changes in the number of Anti-VEGF injections before and after NG101 administration in Cohort 1 (Week 52)



89%
Reduction in annualized anti-VEGF injection rate[1]

83% (5/6)
≤1 injection

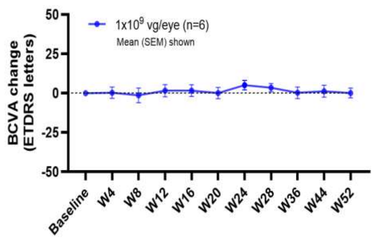
50% (3/6)
Injection-free



[1]Reduction rate was calculated by comparing the total number of anti-VEGF injections during the 52-week baseline period prior to treatment with those during the 52-week post-treatment period. Injections administered during the 4 weeks prior to treatment and the first 4 weeks post-treatment were excluded. [2]Standard of care was administered to prevent treatment gaps until NG101 achieves therapeutic levels. Injection moved from Day -7 to Day 0 starting with Patient 4 for better safety and practicality.

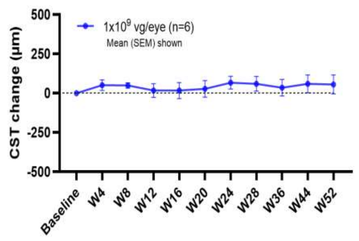
Efficacy: BCVA and OCT-CST

Best Corrected Visual Acuity



Mean BCVA change
+0 letter
from baseline to W52

Central Subfield Thickness



Mean CST change
+57 µm
from baseline to W52

Conclusions

- ✓ **NG101 has been safe and well-tolerated to date in all cohorts of patients.**
- ✓ **NG101 (1×10^9 vg/eye) resulted in an 89% reduction in mean annualized anti-VEGF injection rate in Cohort 1 through 52 weeks.**
- ✓ **Stable visual acuity and stabilization of CST were observed in Cohort 1.**
- ✓ **In Cohort 1 of this Phase 1/2a study, NG101 biofactory gene therapy demonstrated a favorable 52-week safety profile and reduced anti-VEGF treatment burden at an industry-leading low dose.**
- ✓ **These preliminary results highlight the potential of NG101 as a single-treatment option to reduce the burden of frequent anti-VEGF injections in wAMD patients.**

Acknowledgement

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