Inhibition of Complement C3 in Geographic Atrophy with NGM621:
Phase 1 Dose-Escalation Study Results

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- A. DePaoli, P. Chandra, E. Henry, H. Younis are employees (E) of NGM Biopharmaceuticals, South San Francisco, CA, USA

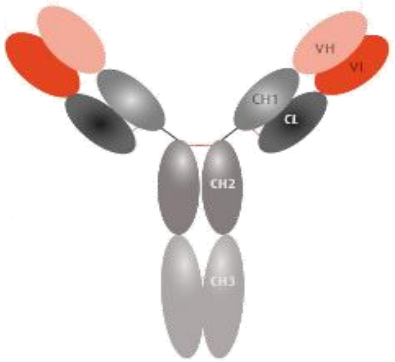
Study Disclosures:

- This study includes research conducted on human subjects
- Institutional Review Board approval was obtained prior to study initiation
- Funding was provided by NGM Biopharmaceuticals

C, consultant/advisor; E, employee; L, lecture fees; O, equity owner; P, patents, royalty; S, grant support.

NGM621: A Potent Anti-Complement C3 Antibody

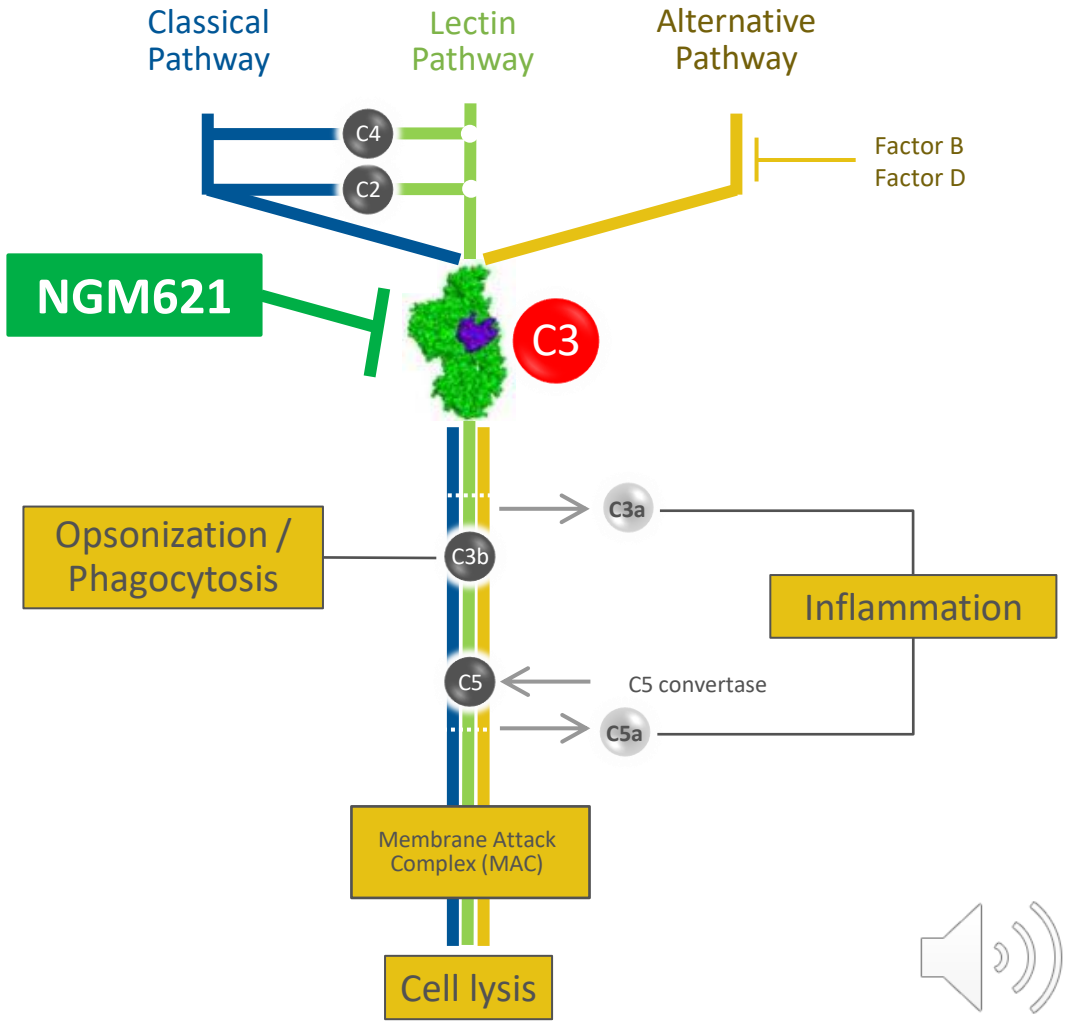
NGM621 MOLECULE ATTRIBUTES



NGM621

Type	Humanized IgG1 monoclonal antibody
Target	Complement C3
MW	~150 kDa
Affinity	K_D = 340pM
Effector Function	Fc mutations eliminating effector function

COMPLEMENT CASCADE



SCIENTIFIC RATIONALE: NGM621 FOR GEOGRAPHIC ATROPHY

- Complement dysregulation is implicated in GA/AMD; C3 is the central convergence point in the complement cascade
- NGM621 is a novel monoclonal antibody that potently inhibits C3, blocking all complement pathways and associated downstream effects, with the potential for extended dosing without PEGylation

AMD, age-related macular degeneration; GA, geographic atrophy; IgG1, immune globulin G1; PEG, polyethylene glycol.

Phase 1 Study Objectives and Design

SINGLE-ASCENDING DOSE COHORTS

- 2 mg/eye — N = 3
- 7.5 mg/eye — N = 3
- 15 mg/eye — N = 3

MFD

MULTIDOSE COHORT

- 15 mg/eye Q4W X 2 — N = 6

STUDY OBJECTIVES

- **Primary:** To evaluate the safety and tolerability of single and multiple IVT injection(s) of NGM621 in patients with GA
- **Secondary:** To characterize the PK of single or multiple doses of and evaluate immunogenicity of NGM621 (serum ADA levels) NGM621

COHORT DESIGN

- 3 Single-Ascending Dose Cohorts of 2mg, 7.5mg, and 15mg
- 1 Multidose Cohort of 15mg NGM621 given twice, 4 weeks apart
- Patients dosed sequentially, followed for 12 weeks
- Safety review performed after sentinel patient dosed and prior to enrollment proceeded to subsequent cohorts

ADA, anti-drug antibodies; GA, geographic atrophy; IVT, intravitreal; MFD, maximum feasible dose; PK, pharmacokinetics; Q4W, every 4 weeks.
ClinicalTrials.gov NCT04014777.

Phase 1: Key Patient Eligibility and Assessments

PATIENT ELIGIBILITY

- GA secondary to AMD in at least one eye
- ≥50 years of age
- GA lesion size in the study eye of ≥2.5 mm^2
  - If the GA is multifocal, at least one lesion must be >1.5mm^2 with the total lesion size ≥2.5 mm^2 on the Screening FAF
- ETDRS BCVA between 54 and 4 letters (20/80 to 20/400 Snellen equivalent) in study eye
  - Fellow eye must have BCVA of at least 34 letters (Snellen equivalent 20/200)
- No history or evidence of CNV in either eye (including subclinical neovascular AMD)

DOSING AND KEY ASSESSMENTS

- Cohorts 1-3: Single-Ascending Dose
  - NGM621 dosed on Day 1
- Cohort 4: Multidose
  - NGM621 dosed on Days 1 and 28
- All cohorts were followed for 12 weeks (85 days)
- Key Assessments Included:
  - Slit Lamp Biomicroscopy, Fundus Exam
  - Ocular imaging: FAF, CFP, OCT/OCT-A
  - Visual Acuity: ETDRS BCVA & LLVA
  - Vitals / Labs / ECG
  - Serum / Plasma Samples

AMD, age-related macular degeneration; BCVA, best corrected visual acuity; CFP, color fundus photography; CNV, choroidal neovascularization; ECG, electrocardiogram; FAF, fundus autofluorescence; GA, geographic atrophy; LLVA, low-luminance visual acuity; OCT, optical coherence tomography.
ClinicalTrials.gov NCT04014777.

Phase 1: Patient Demographics and Baseline Characteristics

	SAD Cohort 1 NGM621 2mg (N = 3)	SAD Cohort 2 NGM621 7.5mg (N = 3)	SAD Cohort 3 NGM621 15mg (N = 3)	MD Cohort 4 NGM621 15mg (N=6)	Total (N = 15)
Age Mean (SD) Years	84.3 (3.06)	79.0 (9.64)	76.7 (4.04)	76.5 (7.04)	78.6 (6.66)
Sex					
Male	100.0%	100.0%	33.3%	33.3%	60.0%
Female	0	0	66.7%	66.7%	40%
Race					
White	100.0%	100.0%	100.0%	100.0%	100.0%
BCVA, Mean (SD) ETDRS letter score	19.3 (16.3)	23.7 (16.1)	36.7 (13.3)	38.8 (12.8)	31.5 (14.7)
Snellen Equivalent	20/400	20/320	20/200	20/160	20/250
GA lesion size, Mean (SD) mm^2	5.7 (3)	9.6 (8.5)	21.4 (14.5)	18.7 (11.2)	14.9 (10.8)
Unifocal lesions	66.7%	100%	100%	66.7%	80%
Foveal-involved GA (Yes)	66.7%	100%	100%	83.3%	86.7%

BCVA, best corrected visual acuity; GA, geographic atrophy; MD, multidose cohort; SAD, single ascending dose cohort; SD, standard deviation.

Primary Analysis: Key Safety & Tolerability Observations

- No safety or tolerability signals observed in any cohort
  - No safety events attributed to study drug
  - No SAEs or deaths
  - No endophthalmitis or IOI
  - No cases of CNV in either eye
  - Ocular AEs were representative of those seen with intravitreal injections
- No vision-related safety signals detected
  - On average, patients maintained their visual acuity over the 12-week follow-up

SUMMARY OF ADVERSE EVENTS BY DECREASING FREQUENCY*

	SAD Cohort 1 NGM621 2 mg (N = 3)	SAD Cohort 2 NGM621 7.5 mg (N = 3)	SAD Cohort 3 NGM621 15 mg (N = 3)	MD Cohort 4 NGM621 15 mg (N = 6)	Total (N = 15)
At least one AE	3	3	2	6	14
Conjunctival hemorrhage	0	0	0	3	3
Eye pruritus	0	1	0	1	2
Basal cell carcinoma	1	0	0	0	1
Benign prostatic hyperplasia	1	0	0	0	1
Diarrhea	0	1	0	0	1
Diverticulitis	0	1	0	0	1
Headache	0	0	0	1	1
Hypaesthesia	0	0	0	1	1
Pneumonia	1	0	0	0	1
Sciatica	0	0	1	0	1
Ventricular extrasystoles	0	0	1	0	1

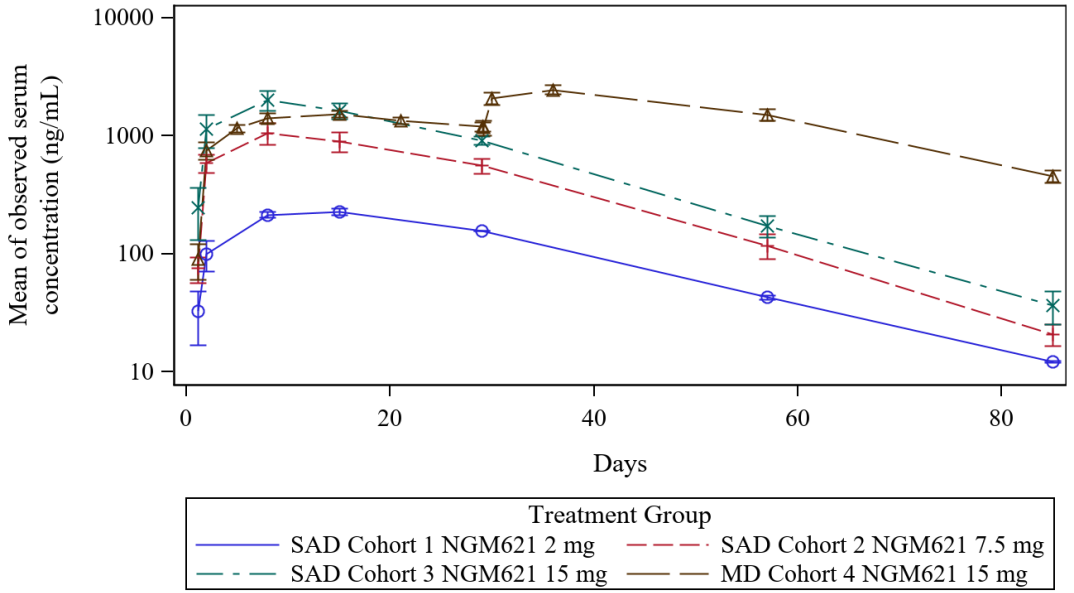
AEs, adverse events; CNV, choroidal neovascularization; IOI, intraocular inflammation; MD, multidose cohort; SAD, single ascending dose cohort; SAEs, serious adverse events.
*Defined as treatment emergent events; includes any events not present prior to initiation of drug treatment or events that were already present that worsen intensity or frequency.

NGM621 Human Serum PK Profile and Ocular PK/PD Modeling to Support Every 8-Week IVT Dosing Regimen

PHASE 1 SERUM PK POST-IVT SINGLE & REPEAT DOSING

- The serum PK of NGM621 was linear and dose-proportional with low accumulation following every 4-week repeat IVT dosing
- NGM621 serum exposure was below concentrations that produce systemic complement inhibition at the highest IVT dose of 15mg
- All subjects were ADA negative at all timepoints

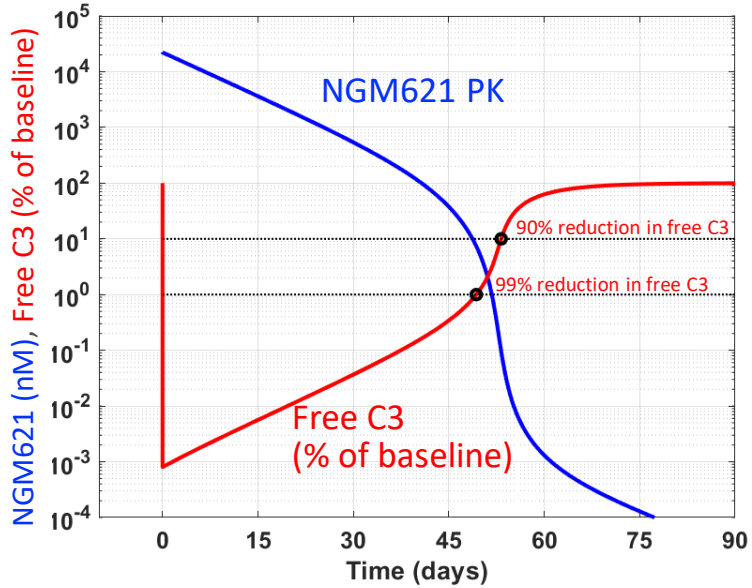
Mean Serum Concentration-time Profile post-IVT of NGM621



OCULAR PK/PD MODELING*

- NGM621 is predicted to achieve >90% C3 target engagement in the eye for 7 weeks following a single IVT dose of 15 mg based on a PK/PD model
- PK/PD modeling and simulation support an every 8-week IVT dosing regimen at the 15 mg dose level

Predicted vitreous humor PK/PD profile



ADA, anti-drug antibodies; IVT, intravitreal; MD, multidose cohort; PD, pharmacodynamics; PK pharmacokinetic; SAD, single ascending dose cohort.
*ocular PK was not collected in Phase 1; model based on pre-clinical ocular PK data.

Encouraging Phase 1 Results Support Continued Clinical Development of NGM621 for GA

- NGM621 up to 15mg was well tolerated in this first-in-human study
  - All 15 patients enrolled completed the 12-week follow-up
  - No SAEs
  - No drug-related AEs
  - No CNV developed in either eye

- NGM621 serum exposures appeared dose-proportional indicating linear PK in the studied range
  - PK/PD modeling supports NGM621 dose intervals of up to 8 weeks

THANK YOU TO THE NGM621 PHASE 1 STUDY SITES, INVESTIGATORS, AND PATIENTS!

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ADA, anti-drug antibodies; AE, adverse events; CNV, choroidal neovascularization; GA, geographic atrophy; PD, pharmacodynamic; PK, pharmacokinetic; SAEs, serious adverse events.

Now Recruiting: CATALINA Phase 2 GA Study

Dosing with NGM621 every 4 or 8 weeks vs Sham

PATIENTS WITH GA SECONDARY TO AMD; N = 240[1]

Randomized 2:1:2:1

Primary Objective	To evaluate the efficacy and safety of NGM621 IVT injections administered every 4 or 8 weeks in GA patients compared to sham control
Design	Phase 2 Multicenter, Randomized, Double-Masked, Sham-Controlled

1 Target enrollment; enrollment ongoing NCT04465955.

AMD, age-related macular degeneration; FAF, fundus autofluorescence; GA, geographic atrophy; IVT, intravitreal; Q4, every 4 weeks; Q8, every 8 weeks.