First-in-Human Evaluation of TH103, a Novel Dual-Targeting VEGF/HSPG Biologic: Phase 1 Single Ascending Dose Study in Treatment-Naïve Neovascular AMD

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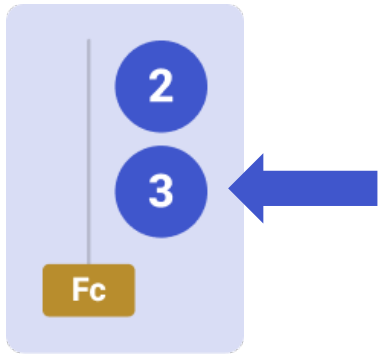
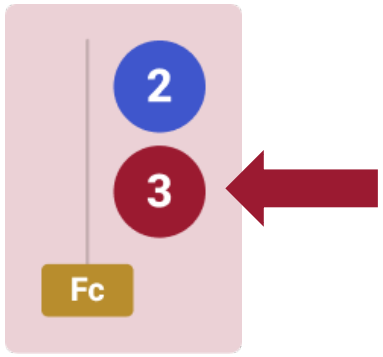
VEGFR1 domain 3 enables potential TH103 binding to retina

TH103



aflibercept



Domain 3 from VEGFR1:

Binds **strongly to HSPG** which are present in all retinal layers, thereby sequestering TH103 in the eye

In contrast, domain 3 from VEGFR2:

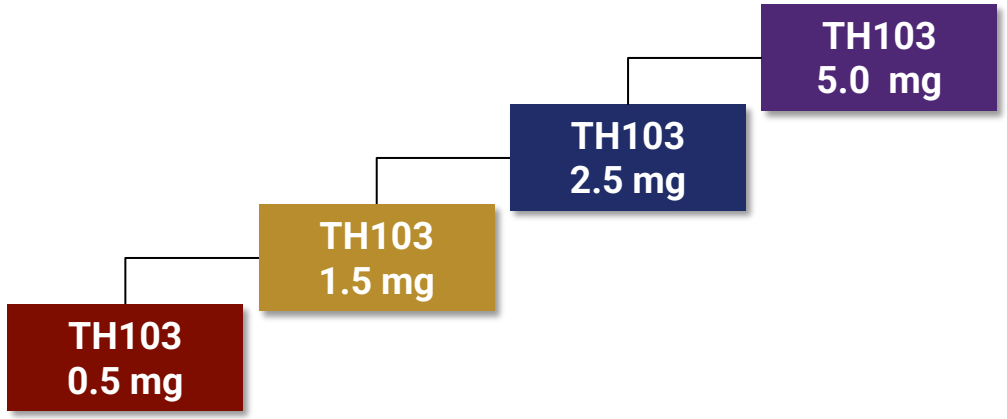
Binds less strongly to HSPG, leading to reduced tissue sequestration (preferred for systemic circulation, e.g., ZALTRAP®, but suboptimal for ocular retention)[2]

VEGFR1-domain # VEGFR2-domain #

Source: 1) Xin H, Biswas N, Li P, et al. 2021. 'Heparin-binding VEGFR1 variants as long-acting VEGF inhibitors for treatment of intraocular neovascular disorders', Proc Natl Acad Sci U S A, 118.; 2) Holash, J., Davis, S., Papadopoulos, N., Croll, S. D., Ho, L., Russell, M., ... & Rudge, J. S. (2002). VEGF-Trap: a VEGF blocker with potent antitumor effects. Proceedings of the National Academy of Sciences, 99(17), 11393-11398.

Phase 1a Single Ascending Dose (SAD) Study in Treatment-Naïve nAMD

Multi-center U.S. study to evaluate safety, tolerability, pharmacokinetics, and anti-VEGF activity following a single injection of TH103



Study Details

- Primary timepoint for analysis at Month 1
- Frequent follow-up visits within the first month; patients then followed monthly out to Month 6

Criteria for retreatment with aflibercept

- Increase of > 50 µm thickness in CST on SD-OCT compared to the lowest previously measured CST
- New macular hemorrhage due to nAMD

CST = Central Subfield Thickness
SD-OCT = Spectral-Domain Optical Coherence Tomography

Note: Data safety monitoring oversight occurred before dose-escalations

Key baseline characteristics of patients in Phase 1a SAD trial of TH103

		Tx.-Naïve (efficacy analysis population)			Including Tx-Experienced	
		Dec. 2025 Data Release (n=13)	Additional Tx-Naïve Patients (n=4)[4]	All Tx.-Naïve Patients (n=17)	Tx.-Experienced[2] (n=3)	All Patients[2] (n=20)
Age (mean)		**78**	**76**	**78**	**81**	**78**
Sex (female | male)		**9 | 4**	**3 | 1**	**12 | 5**	**2 | 1**	**14 | 6**
BCVA[1] (ETDRS letters, mean, range)		**58** (36-73)	**66** (57-71)	**60** (36-73)	**63** (53-69)	**60** (36-73)
Lesion Type	**Type 1**	**5** (38%)	**3 (75%)**	**8 (47%)**	**2** (67%)	**10** (50%)
	Type 2	**1** (8%)	-	**1 (6%)**	**1** (33%)	**2** (10%)
	Type 3[3]	**6** (46%)	**1 (25%)**	**7 (41%)**	-	**7** (35%)
	Ungradable	**1** (8%)	-	**1 (6%)**	-	**1** (5%)
CST[1] (µm, mean, range)		**477** (310-657)	**478** (390-528)	**477** (310-657)	**472** (391-577)	**476** (310-657)

No study dropouts and 100% protocol adherence

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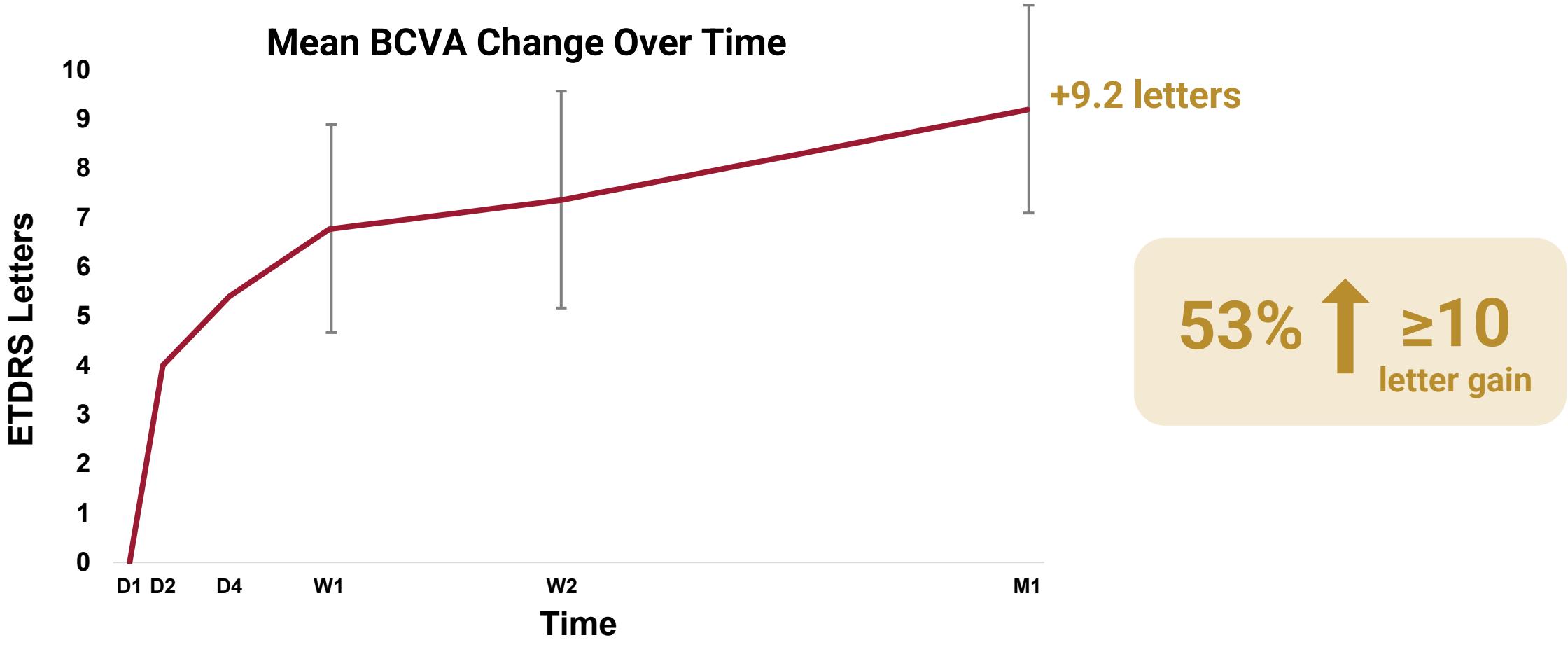
Notes: 1) BCVA and CST readings as of the day patients received their first dose of TH103; 2) Includes 3 treatment-experienced patients that are excluded from efficacy analyses that were administered either 2.5mg or 5mg of TH103; 3) Also called retinal angiomatous proliferation, or RAP; all but one of the Type 3 lesions were determined to be Stage 3; 4) Patients administered single 2.5mg dose of TH103

Mean 9.2 letter gain in BCVA letter score after a single TH103 injection at Month 1

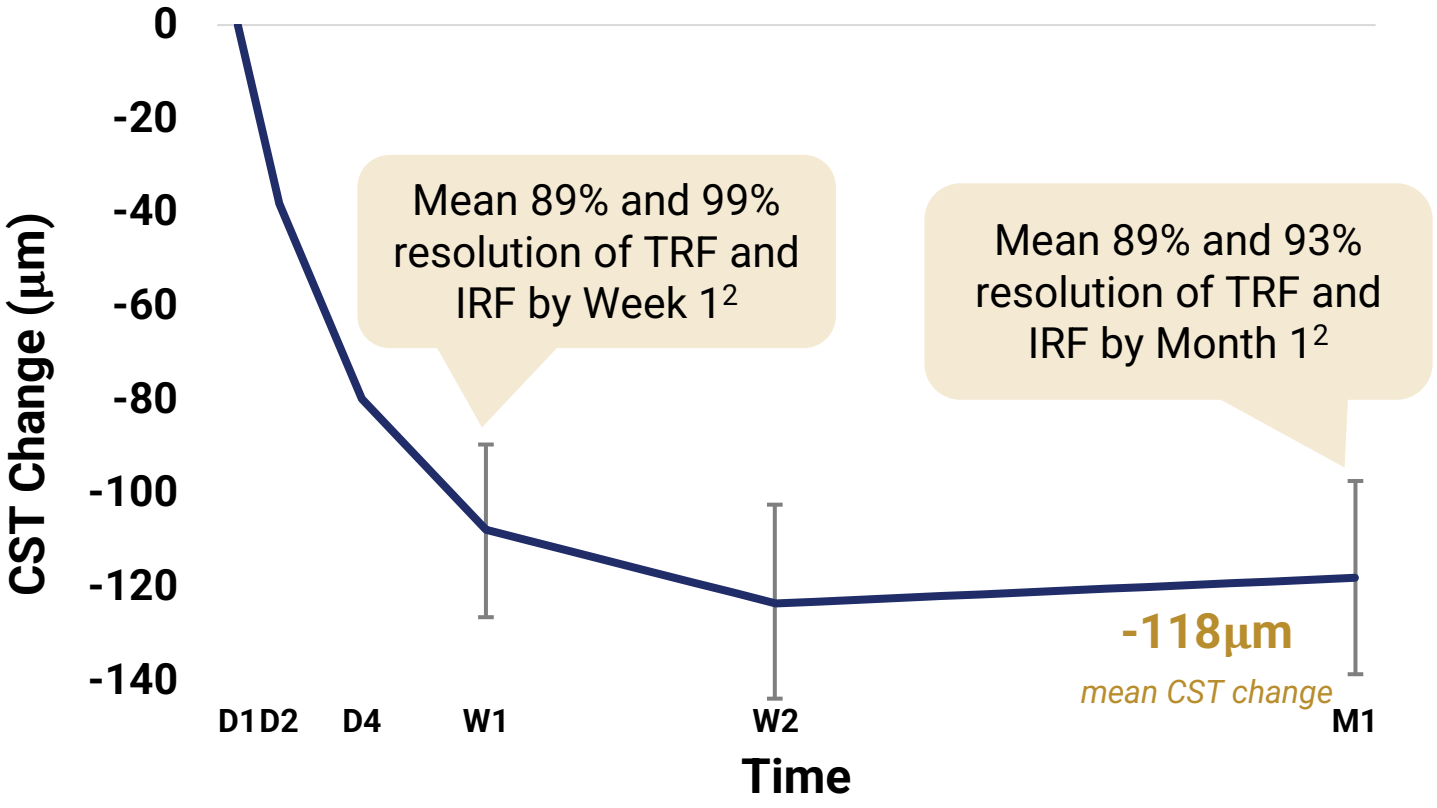


53% ↑ **≥10** letter gain

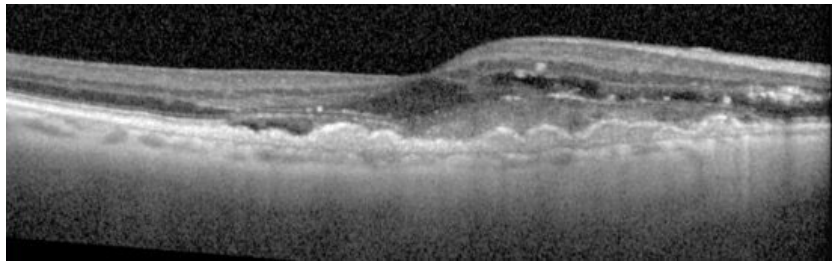
ETDRS = Early Treatment Diabetic Retinopathy Study
Note: n = 17 at all timepoints except Month 1, where n =16; one patient in the 0.5 mg cohort was treated with aflibercept at Week 2 and therefore the Month 1 data point is censored. Brackets indicate standard error

Rapid, robust improvement in CST and total retinal fluid (TRF) & intraretinal fluid (IRF) volume at Week 1 and Month 1

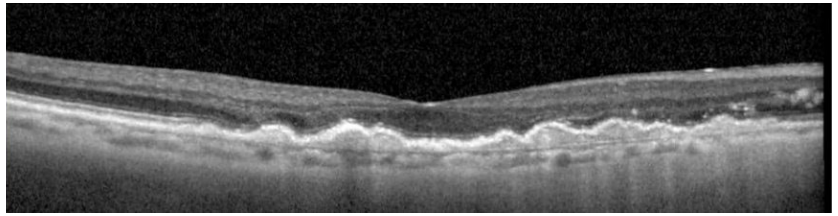
Mean CST Change Over Time[1]



Case Example (1.5 mg)



Single Dose TH103



Month 1

Note: n = 17 at all timepoints except Month 1, where n =16; one patient in the 0.5 mg cohort was treated with aflibercept at Week 2 and therefore the Month 1 data point is censored. Brackets indicate standard error.

Sources: 1) As measured by independent reading center; 2) Data from automated fluid measurement software, Notal Vision Inc.; percentage change in mean central subfield TRF volume (subretinal fluid + intraretinal fluid in the central subfield, measured in nanoliters) or IRF volume (intraretinal fluid in the central subfield) from Day 1 to Week 1 & Month 1

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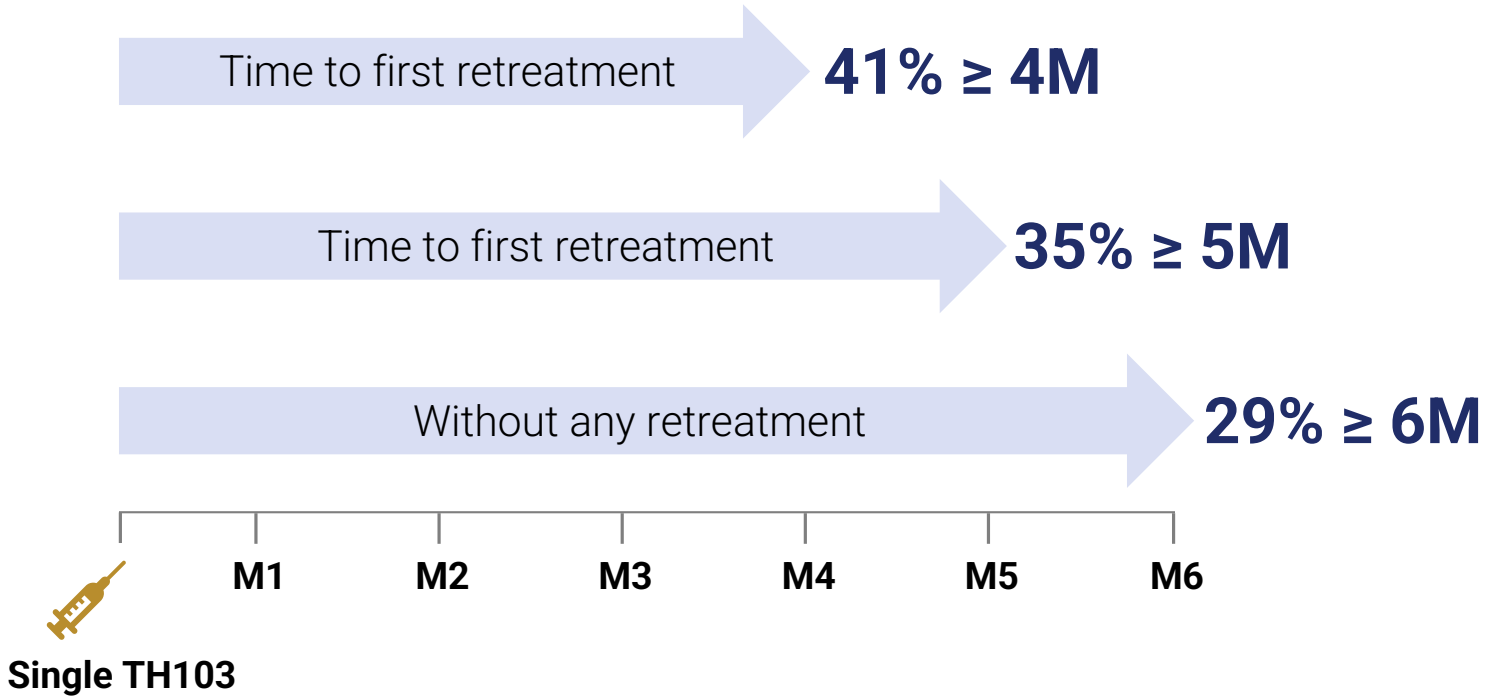
Single-dose durability signal suggests potential for stronger durability outcomes after standard four-dose loading regimen, currently being evaluated in ongoing Ph 1b/2 study

Phase 1a Single-Dose Time to Retreatment (n = 17, Tx-naïve)



Separately, treatment-experienced patients
extended their prior treatment interval by a mean of 2-months[1]

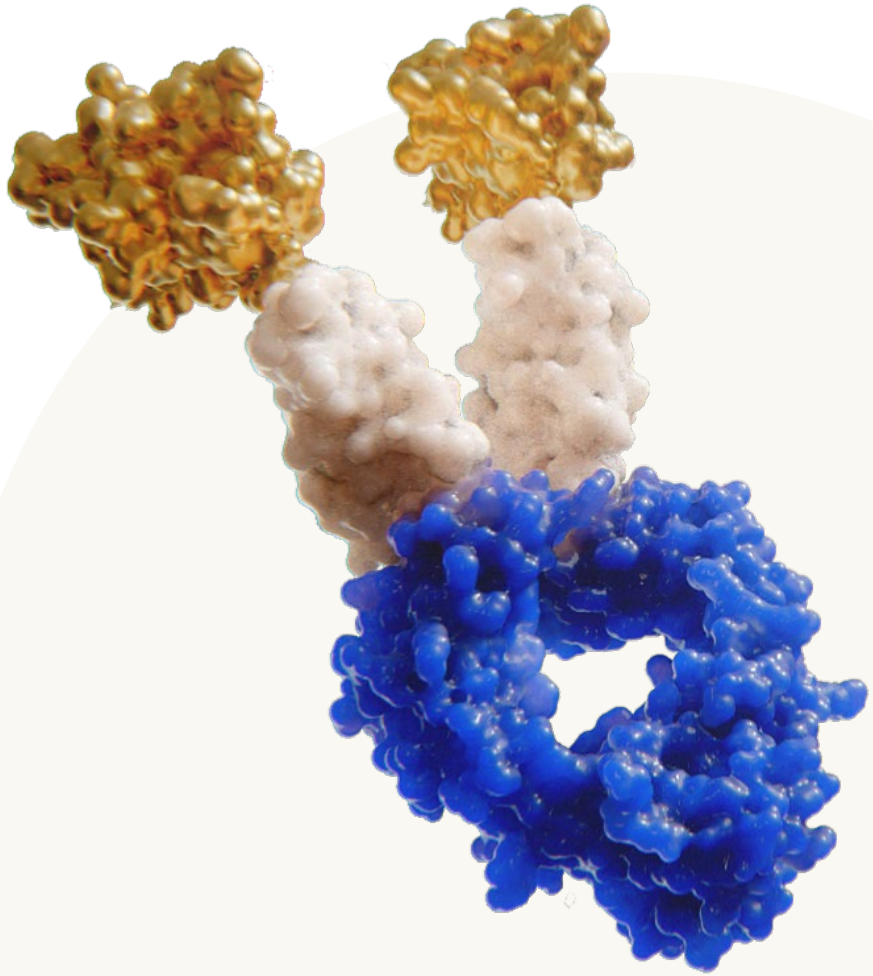
1) N=3; Mean treatment interval pre-enrollment: 2.33 months; mean time to retreatment after a single TH103: 4.33 months

Durability signal: intraocular retention and extended treatment intervals

✓ **Pharmacokinetics:** 27–53× lower plasma Cmax/dose[1] than Eylea, Eylea HD, and Vabysmo — consistent with greater intraocular retention

✓ **Time to retreatment:**

- After one TH103 dose (n=17, treatment-naïve): 41% reached ≥4 months, 35% ≥5 months, and 29% ≥6 months without retreatment
- In treatment-experienced patients (n=3), mean time to retreatment extended by ~2 months (2.3 → 4.3 months) after a single TH103 dose



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Cmax = maximum plasma concentration; PK = Pharmacokinetics; nAMD = neovascular AMD

1) Calculated based on treatment-naïve patients receiving a single 2.5mg dose of TH103 (n=7)

Safety Summary from Phase 1a SAD Trial

- No dose limiting toxicity (DLT) or treatment-emergent serious adverse events (SAEs) observed
- Transient, mild-moderate intraocular inflammation (IOI) presented at Day 4 in 2 patients dosed at 2.5mg with TH103 manufacturing batch #1[1]
- No cases of IOI in 6 patients dosed at 2.5mg with TH103 manufacturing batch #2[2]
- One case of transient, moderate IOI that resolved without sequelae in a patient dosed at 5.0mg with TH103 manufacturing batch #2[2]

1) N = 13 patients
2) N = 7 patients, including 3 treatment-experienced patients that are excluded from the efficacy analyses. All patients completed trial including 6-month follow-up period. TH103 manufacturing batch #1 was additionally purified to generate batch #2 by reducing levels of host cell proteins in the drug product.

New Phase 1a SAD data continue to support TH103's potential as best-in-class, first-line treatment for retinal vascular diseases

✓ **Efficacy:** rapid, robust response on BCVA and OCT parameters observed across dose levels at one month

- Mean 9.2-letter BCVA improvement at Month 1 after one TH103 injection
- Mean 118µm improvement in mean CST and mean 93% resolution in CSF intraretinal fluid at Month 1

✓ **Safety:** TH103 generally well tolerated, supporting exploration of multi-dose regimen

- No dose-limiting toxicities or TH103-related SAEs observed
- 2 cases of mild/moderate IOI at 2.5mg dose level with TH103 manufacturing batch #1 material
- No cases of IOI at 2.5mg dose level (n=6) observed through ≥6 months with TH103 manufacturing batch #2
- Single case of transient, moderate IOI at 5.0mg dose level with TH103 manufacturing batch #2 material

✓ **Durability:**

- PK analysis consistent with greater TH103 intraocular retention vs. other leading agents
- Single-dose durability signal suggests potential for stronger durability outcomes after standard four-dose loading regimen

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CSF = Central Subfield