THR-687, a Potent and Highly Selective RGD Integrin Inhibitor in Development for the Treatment of DME

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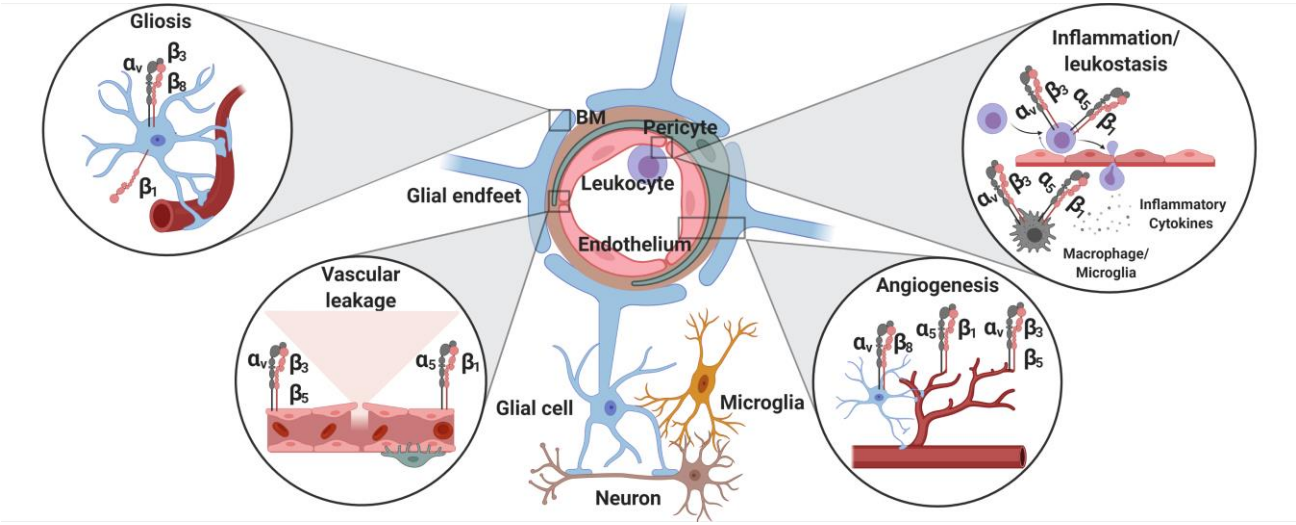
Disclosure

- ALLERGAN
- BAYER
- BOEHRINGER-INGELHEIM
- FIDIA SOOFT
- HOFMANN LA ROCHE
- NOVARTIS
- NTC PHARMA
- SIFI
- OXURION
- ZEISS

Selective RGD Integrin Antagonist | THR-687

Small molecule targeting a broad spectrum of disease hallmarks of DR/DME, nAMD and ME-RVO



- In the eye, integrins have been shown to play an important role in neovascularization, vascular permeability, inflammation, fibrosis, and gliosis
- By selectively antagonizing disease-related integrin receptors, THR-687 is expected to inhibit pathological processes at multiple points[1]

[1] Van Hove I et al. Targeting RGD-binding integrins as an integrative therapy for diabetic retinopathy and neovascular age-related macular degeneration. Prog Retin Eye Res 2021, 85: 100966.

Abbreviations: BCVA, best-corrected visual acuity; DME, diabetic macular edema; DR, diabetic retinopathy; ETDRS, Early Treatment of Diabetic Retinopathy Study; ME-RVO, macular edema following retinal vein occlusion; RGD, arginine-glycine-aspartate; VEGF, vascular endothelial growth factor; nAMD, neovascular age-related macular degeneration

The figure was created with BioRender.com

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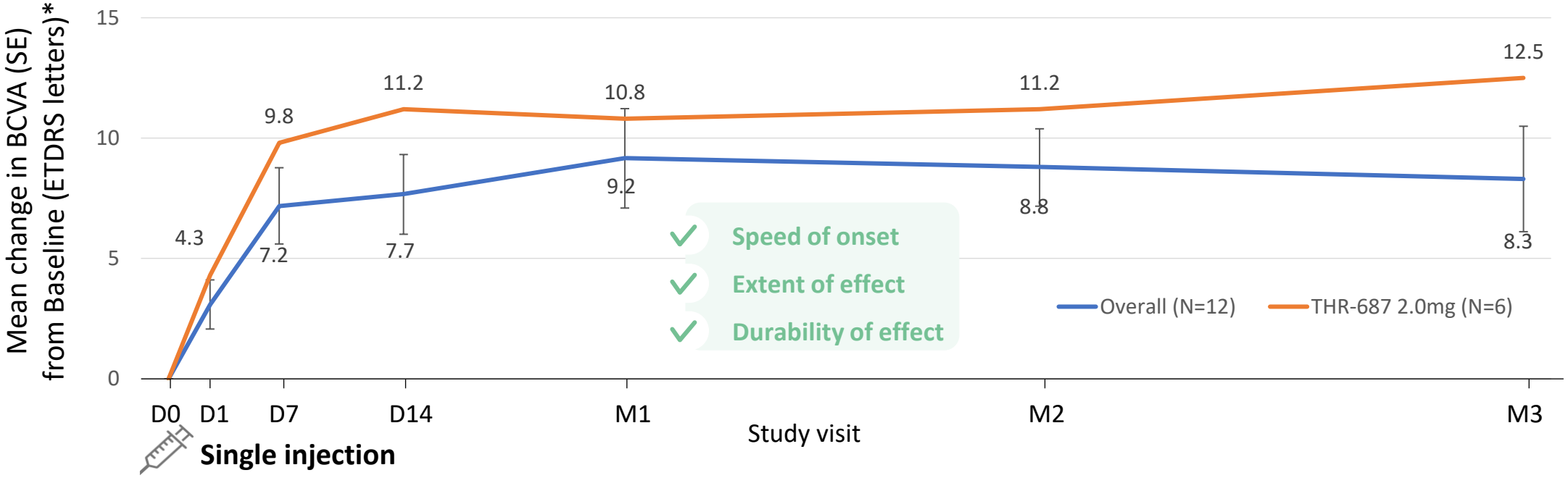
THR-687 Phase 1 • Clinical evidence

Safety and efficacy after one single injection of THR-687

- THR-687 was safe and well-tolerated | No dose limiting toxicities, no serious adverse events occurred in the study
- All treatment-related adverse events were unrelated to THR-687
- Three subjects received rescue medication; 1 in the middle dose group at M2 and 2 in the high dose group (one at M1 and one at M2)



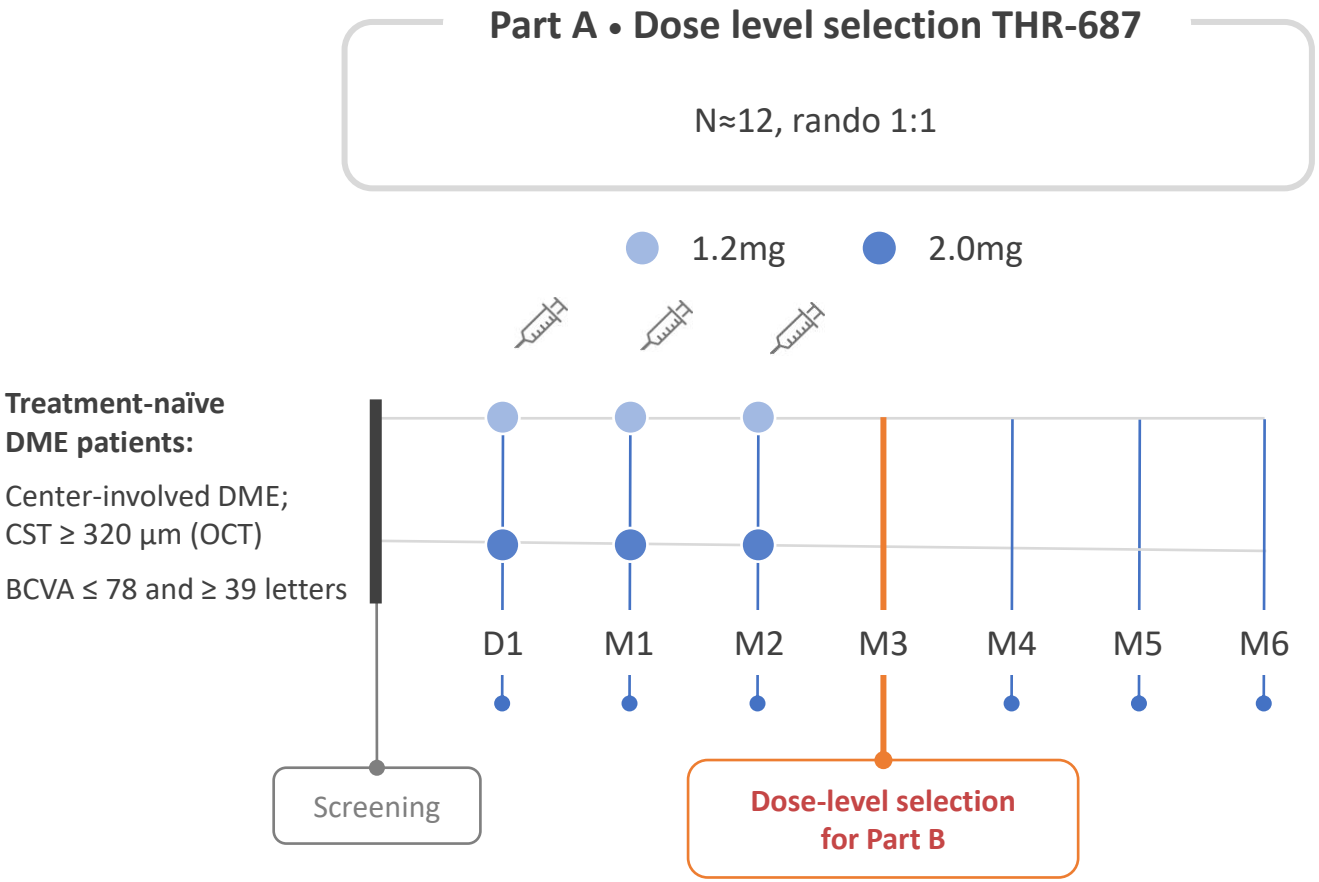
*Accounted for rescue: value before rescue carried forward. Baseline defined as the day of the injection. SE is only presented for overall data (across dose levels)

Khanani AM et al. Phase 1 study of THR-687, a novel, highly potent integrin antagonist for the treatment of diabetic macular edema. Ophthalmol Sci 2021; 1(3), 100040.

Abbreviation(s): BCVA, best-corrected visual acuity; D, day; ETDRS, early treatment diabetic retinopathy study; M, month; SE, standard error

THR-687 Phase 2 Part A Clinical Trial in DME

Primary Endpoint was BCVA • Secondary Endpoints include CST, AEs



Phase 2 • Part A

- Dose selection for Part B
- First time multiple IVT of THR-687 in treatment naïve DME patients
- Confirmation of safety multiple IVT THR-687: safe & well-tolerated
- Stacking of efficacy signal (early onset, high effect, durability of effect)
- Confirming proof of concept

Dose levels expressed as THR-687 free base, corresponding to 1.4 mg and 2.5 mg in the Phase 1 study, where dose levels were expressed as THR-687 salt

Abbreviations: BCVA, best-corrected visual acuity; CST, central subfield thickness; D, day; DME, diabetic macular edema; IVT, intravitreal; M, month; N, number; OCT, optical coherence tomography; rando, randomization

Demographics

Characteristic	**Overall** *All Treated Set* **N=16**	**Overall** *Per Protocol set* **N=14**
Gender, n (%)		
Male	9 (56)	9 (64)
Female	7 (44)	5 (36)
Race, n (%)		
Asian	2 (13)	2 (14)
Native Hawaiian or Other Pacific Islander	1 (6)	1 (7)
White	13 (81)	11 (79)
Age (years)		
Mean (SD)	62.6 (11.87)	63.2 (11.94)

- Follow-up of patients to Month 6 is still ongoing
- Only summary data are presented to protect the credibility of further data collection

Abbreviations: Max, Maximum; Min, Minimum; n, Number of Subjects in Category; N, Number of Subjects in the Analysis Set; SD, Standard Deviation

Baseline Ocular Characteristics in the Study Eye

Characteristic	Overall *All Treated Set* N=16	Overall *Per Protocol Set* N=14
DR Severity *, n (%)		
DR questionable, microaneurysms only	1 (6)	1 (7)
Mild NPDR	5 (31)	3 (21)
Moderate NPDR	4 (25)	4 (29)
Moderately severe NPDR	4 (25)	4 (29)
Severe NPDR	2 (13)	2 (14)
Time since First Known Diagnosis of DR (Months)		
Median	2.86	2.86
Time since First Known Diagnosis of DME (Months) **		
Median	1.55	1.79
HbA1c (%)		
Mean (SD)	8.34 (1.92)	8.29 (1.79)
Type of Diabetes, n (%)		
Type 2	16 (100)	14 (100)

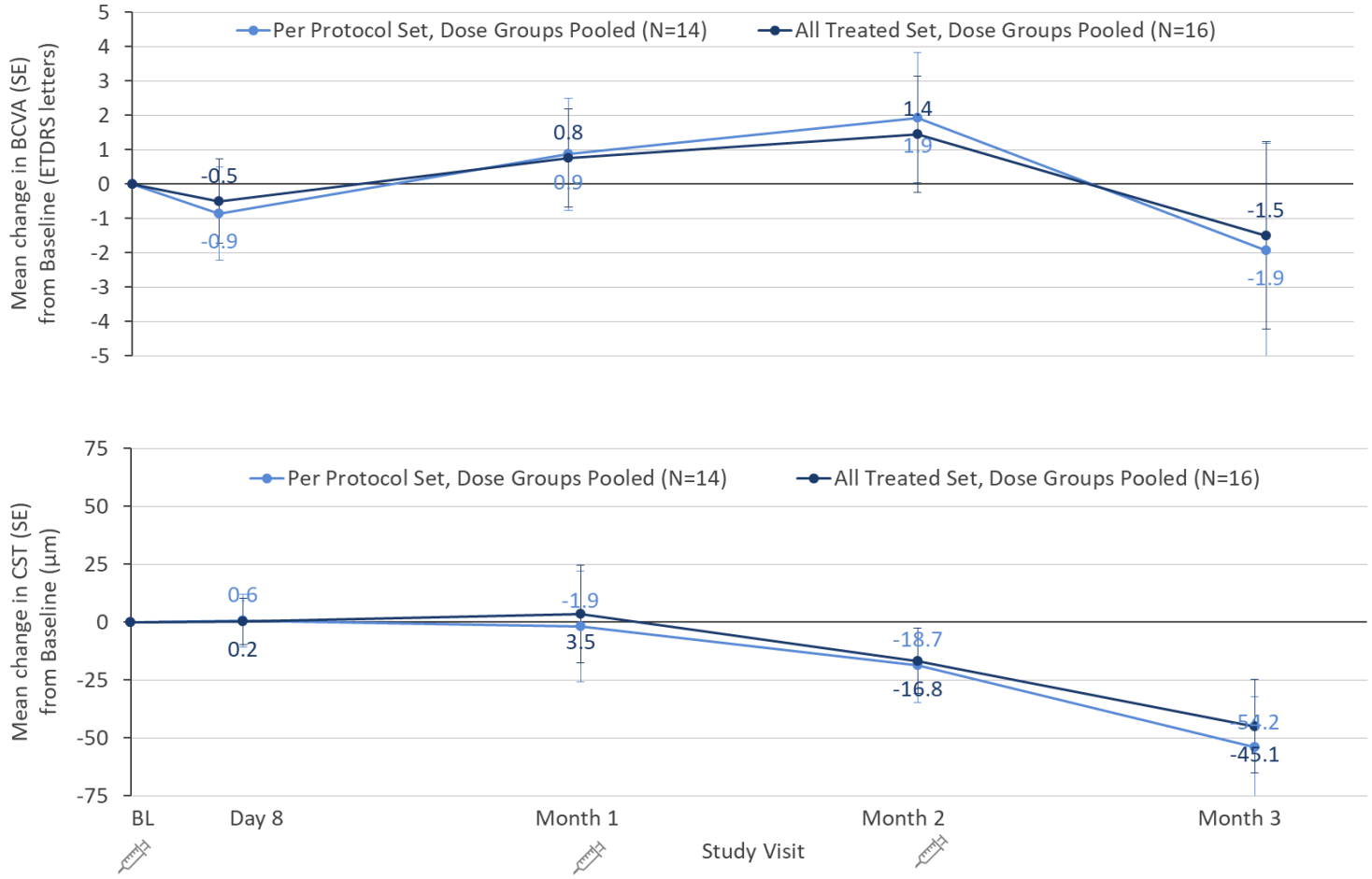
Characteristic	Overall *All Treated Set* N=16	Overall *Per Protocol Set* N=14
BCVA (ETDRS letters)		
Mean (SD)	65.2 (7.13)	63.9 (6.59)
CST (µm), as assessed by CRC		
Mean (SD)	441.9 (105.01)	446.4 (111.38)

*DR severity level had to be severe NPDR or lower (ETDRS level <61) per the protocol eligibility criteria, ** Time since diagnosis of DME had to be less than 1 year prior to screening as per the protocol inclusion criteria.

Abbreviations: DME, Diabetic Macular Oedema; DR, Diabetic Retinopathy; n, Number of Subjects in Category; N, Number of Subjects in the Analysis Set; NDPR, Nonproliferative Diabetic Retinopathy; BCVA, Best-corrected Visual Acuity; CST, Central Subfield Thickness; Max, CRC, central reading center

Mean Change in BCVA and CST from Baseline [a]

Per Protocol Set and All Treated Set



[a] Missing values replaced by LOCF approach; no rescue treatment was administered.

BCVA, Best-corrected Visual Acuity; BL, Baseline; ETDRS, Early Treatment Diabetic Retinopathy Study; LOCF, Last Observation Carried Forward; N, Number of Subjects in the Analysis Set; SE, Standard Error; CST, Central Subfield Thickness

Summary of Adverse Events: up to Month 3 (1/2)

All Treated Set

Category	Overall N=16
	n [E]
Overall	
Any AE	8 [12]
Any AE in Study eye	5 [6]
Any AE in Non-Study eye	0
Any Non-Ocular AE	5 [6]
AEs Related to IMP	
Any AE	1 [1]
Any AE in Study eye	1 [1]
AEs Related to Injection Procedure	
Any AE	0
SAEs	
Any SAE	0

Abbreviations: AE, Adverse Event; E, Number of Events; n, Number of Subjects in Category; N, Number of Subjects in the Analysis Set

Adverse Events in the Study Eye: up to Month 3

All Treated Set

Adverse event	Overall N=16 n [E]
Optic Disc Hemorrhage	1 [1]
Retinal Thickening	2 [2]*
Visual Acuity Reduced	3 [3]

No IOI, endophthalmitis, vasculitis or vascular occlusion occurred.

* One of them related to IMP (no AEs were considered Related to the injection procedure)
Abbreviations: E, Number of Events; n, Number of Subjects in Category; N, Number of Subjects in the Analysis Set; IOI: intraocular inflammation

Overall Conclusions

Study population

- Study population was representative of treatment naïve DME patients based on the CRC feedback on OCT at BL
- Mean BL BCVA and CST values were aligned with naïve DME studies for other compounds

Efficacy

- There was insufficient evidence of efficacy on the key endpoints (BCVA and CST)

Safety and tolerability

- THR-687 is safe and well tolerated
- No rescue medication was administered to any of the subjects
- The ocular AEs are consistent with the progressive nature of DME, no toxic drug effects occurred

- **Oxurion has decided not to advance THR-687 to Part B of the INTEGRAL study**
- **Follow-up in Part A is still ongoing**

Abbreviations: DME, Diabetic Macular Edema; CRC, central reading center; OCT, optical coherence tomography; BL, baseline; BCVA best-corrected visual acuity; CST, central subfield thickness; AE, adverse event

Currently enrolling

- OXURION® 's other asset THR-149 is in Phase 2
- The Part B of the global KALAHARI trial in DME patients with suboptimal response to aVEGF is ongoing.

Topline results: Mid 2023