Pioneering Life Changing Treatments for Diabetic Retinal Disease

Oxurion NV (Euronext: OXUR)

Company Presentation
September 2023

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YOUR VISION IS OUR VISION™

Forward Looking Statement

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Oxurion At-a-Glance

Aiming to **grow** the $5B+ diabetic macular edema (DME) market

THR-149 | potential SOC for the up to 50% of DME patients not doing well on anti-VEGFs, large unmet need

Near-term value drivers| Phase 2 topline data in **Q4 2023**

THR-687 | potential to compete/compliment all anti-VEGF, currently paused

Accomplished senior leadership | R&D team with deep ophthalmic expertise

Long-term IP protection | Composition of matter protection (2034-39)

Experienced Management Team

Seasoned leadership with deep biotech expertise

Tom Graney

CFA, MBA

Chief Executive Officer

generation bio

VERTEX

Johnson & Johnson

Andy De Deene

MD, MBA

Chief Development Officer

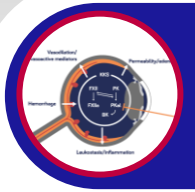
INNOGENETICS

BIOTECHNOLOGY FOR HEALTHCARE

janssen

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Differentiated Molecules, in **Validated Pathways**, with Novel Mechanisms of Action and First-in-Class Potential



Plasma kallikrein inhibitor

THR-149

Potential to be new **standard of care** for the **40-50% of DME patients** who respond **suboptimally to anti-VEGFs**

First-in-Class Potential

Pan-RGD integrin antagonist

THR-687

Potential to **disrupt** the entire **anti-VEGF market**

Currently paused

First-in-Class Potential

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Abbreviation(s): DME, diabetic macular edema; RGD, arginylglycylaspartic acid; VEGF, vascular endothelial growth factor

THR-149

Highly potent plasma kallikrein (PKal) inhibitor targeting a VEGF-independent pathway

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DME is a Large and Growing Public Health Concern

DME is the leading cause of blindness in **working-age adults**

Patients with diabetes

	2021	2045
	537 million Adults (20-79 years)	**783 million** Adults (20-79 years)

Patients with …

	2021	2045
Any DR	**120 million**	**174 million**
DME	**22 million**	**33 million**

Note(s): worldwide estimates

Abbreviation(s): DME, diabetic macular edema; DR, diabetic retinopathy

Source(s): International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: 2021. Available at: https://www.diabetesatlas.org; Teo et al. Ophthalmology 2021

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DME: Serious Sight-Threatening, Life-Altering Disease

Significant patient and caregiver burden • **Compelling health economic story**

Loss of Visual function

Disabilities

Negative impact of QoL

* Scotoma is a partial loss of vision or blind spot within the visual field

Abbreviation(s): DME, diabetic macular edema; QoL, quality of life

Source(s): pictures from The Angiogenesis Foundation. Advocating for improved treatment and outcomes for DME. 2014

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SOC Therapy is Suboptimal for up to 50% DME Patients

Anti-VEGF treatment is the mainstay but…

1st-line Anti-VEGF therapy

- **40-50% of patients treated with anti-VEGF therapies do not achieve clinically meaningful vision gain**
- Current & upcoming anti-VEGF therapies have reached a plateau in terms of efficacy
- Durability is currently targeted by upcoming anti-VEGF therapies, addressing only treatment burden & convenience

2nd-line Steroid therapy

- Usually second-line therapy (after anti-VEGF treatment)
- Mainly based on IVT sustained-release corticosteroids
- **Well-known side-effect profile incl. cataract formation and progression and/or risk of intraocular pressure increase**

Abbreviation(s): DME, diabetic macular edema; IVT, intravitreal; VEGF, vascular endothelial growth factor

Source(s): Sun JK & Kampol LM. *Ophthamic Res* 2019;62:225-230

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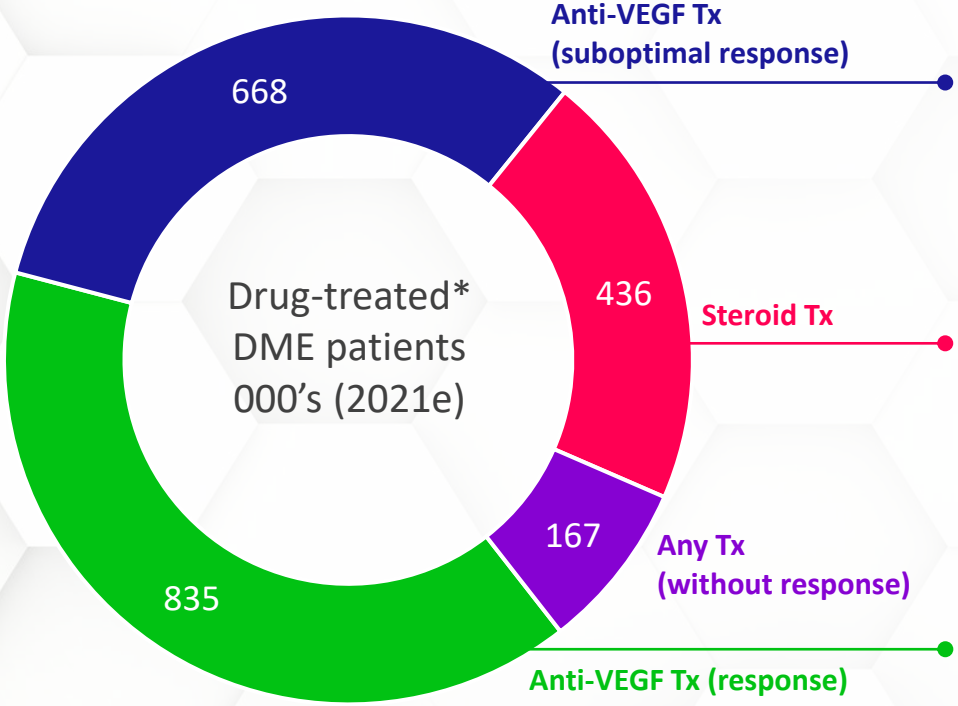
Disruptive Growth Driven by Better Treatment

Multiple opportunities for THR-149 in DME in a wide range of patient types



Potential THR-149 use		Potential TAM for THR-149
Replace anti-VEGF therapy in patients with suboptimal response	Primary opportunity	**$4B+**
Displace steroid therapy (when used as second-line therapy)	Primary opportunity	**$1B+**
In combination with anti-VEGF therapy	Secondary opportunity	**++**

* Incl. combinations with non-pharmacological therapy

Note(s): market includes 7 major markets (US, France, Germany, Italy, Spain, United Kingdom & Japan)

Abbreviation(s): DME, diabetic macular edema; e, estimates; TAM, total addressable market; Tx, therapy; US, United States; VEGF, vascular endothelial growth factor

Source(s): Datamonitor Healthcare, 2017-2020; Decision Resources Group, 2019, GlobalData, 2021

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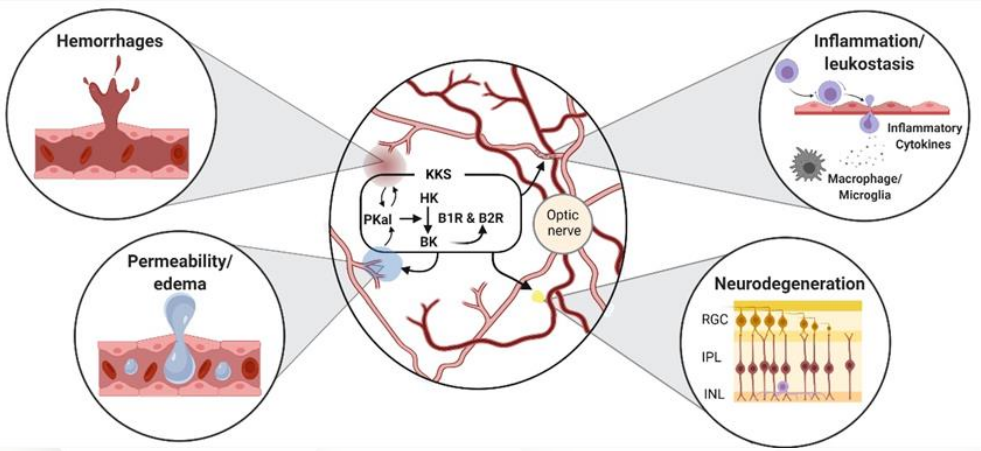
THR-149: Highly Potent PKal Inhibitor for DME

Selective and stable peptide



- PKal is a mediator of vascular leakage, inflammation, micro-hemorrhages and neurodegeneration.
- Human vitreous shows elevated PKal levels in DME patients.
- THR-149, a potent and selective PKal inhibitor[1], has the potential to reduce the hallmarks of DME.

Abbreviation(s): BK, bradykinin; B1R,bradykinin receptor 1; B2R, bradykinin receptor 2; DME, diabetic macular edema; HK, High molecular weight kininogen; INL, inner nuclear layer; IPL, inner plexiform layer; KKS, kinin kallikrein system; PK, PreKallikrein; PKal, plasma kallikrein; RGC, retinal ganglion cell

Source(s): [1] Teufel et al. *J Med Chem* 2018;61(7):2823-2836; Sun JK & Kampol LM. *Ophthamic Res* 2019;62:225-230

Image created with BioRender.com

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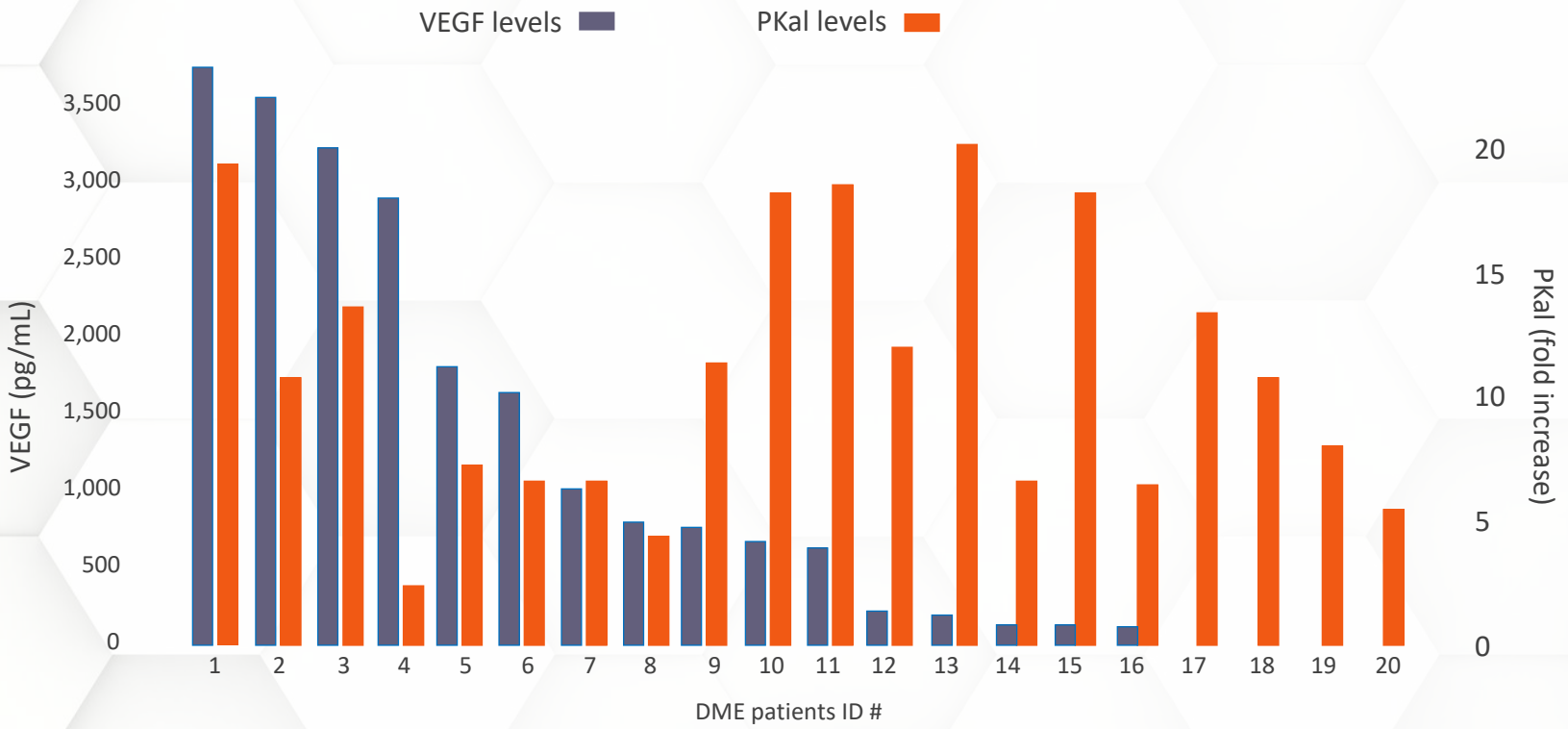
Rationale for Targeting PKal in DME

Two distinct pathways linked to DME: not all patients have elevated VEGF levels



- PKal is a key driver in the pathogenesis of DME
- PKal inhibitors have potential to address suboptimal responders to anti-VEGF

Abbreviation(s): DME, diabetic macular edema; PKal, plasma kallikrein; SoC standard of care; VEGF, vascular endothelial growth factor

Source(s): graph adapted from Kita T et al. *Diabetes* 2015;64:3588-3599

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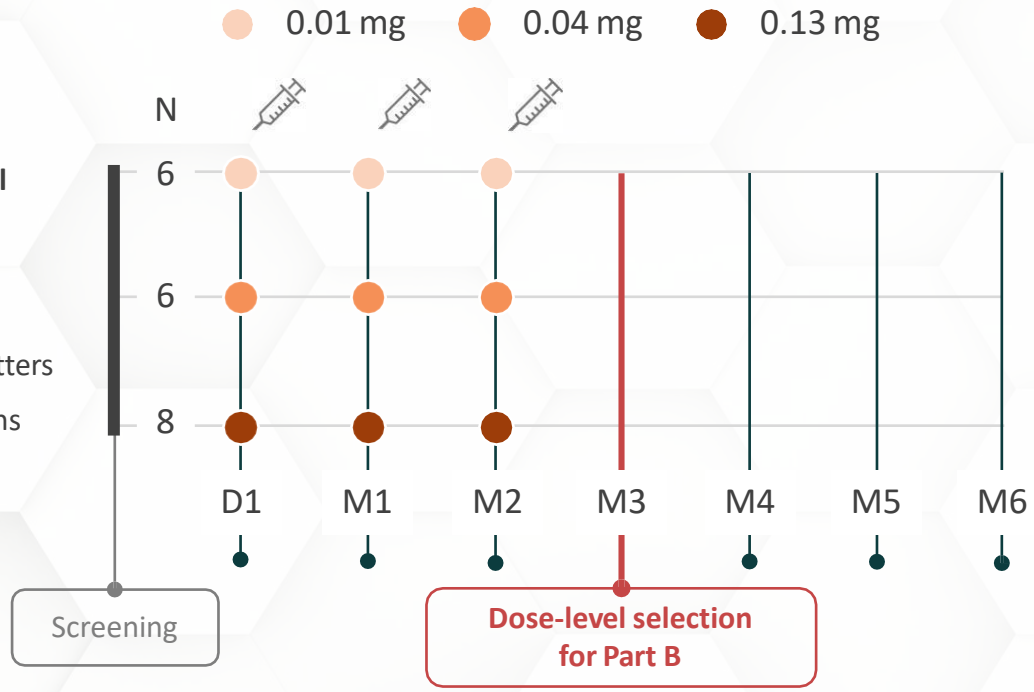
KALAHARI Phase 2 Part A:
Dose Selection Suboptimal Responders to anti-VEGF

Primary endpoint BCVA, secondary endpoints CST, AEs

Part A ● Dose level selection THR-149
N=20, rando 1:1:1



Anti-VEGF suboptimal responders:

Center-involved DME;
CST ≥ 320 µm (OCT)

BCVA ≤ 73 and ≥ 39 letters

≥ 5 anti-VEGF injections

Phase 2 ● Part A

- First time multiple IVT of THR-149 in DME patients who respond suboptimally to anti-VEGF (per inclusion criteria)
- Confirmation of safety & efficacy for the highest dose
- Confirming proof of concept

* Per protocol set

Abbreviations: AE, adverse event; 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; VEGF, vascular endothelial growth factor

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KAHALARI Phase 2 Part A Clinical Trial

High dose (0.13 mg) selected for Part B, based on safety and efficacy at Month 3

Treatment safety

- **Favorable safety profile** with no serious ocular AEs at any dose
- **No inflammation** in the study eye of any patient at any dose

High dose outcome

- **No rescue medication need**
- **6.1 letter improvement in mean BCVA at Month 3**
- **Stable CST**

Note(s): safety data set, N=23 patients; efficacy data set, N=20 patients; high-dose efficacy data set, N=8 patients
Abbreviations: AE, adverse event; BCVA, best-corrected visual acuity; CST, central subfield thickness
Source(s): data on file

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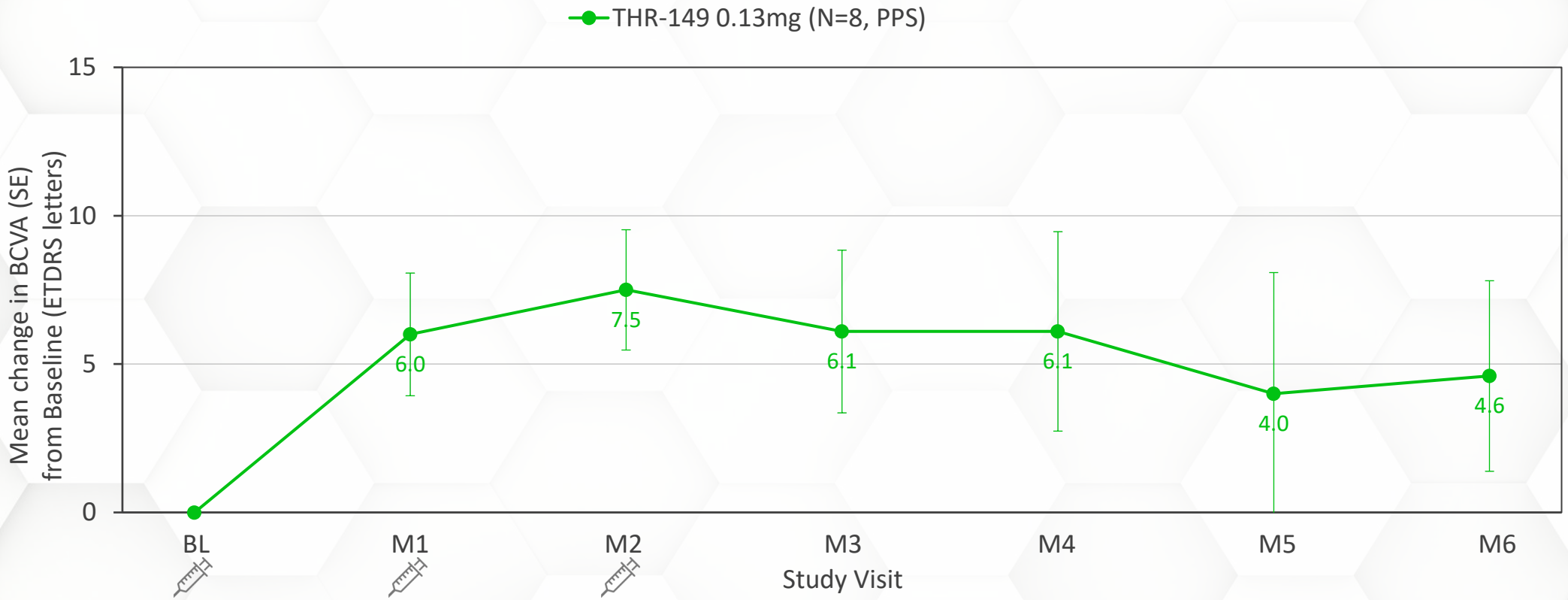
Mean Change in BCVA from Baseline in High Dose Group [a]

Clinically meaningful improvement with impressive durability



[a] No rescue treatment was given in the high dose group

Abbreviations: BCVA, best-corrected visual acuity; BL, baseline; CRC, central reading center; ETDRS, early treatment diabetic retinopathy study; M, month; N, number of subjects in the analysis set; OCT, optical coherence tomography; PPS, per protocol set; SE, standard error

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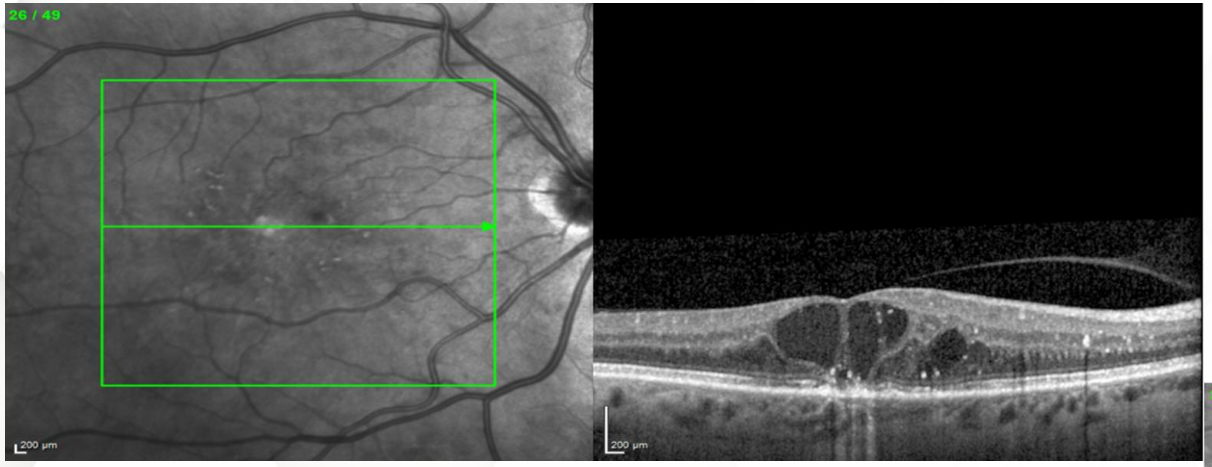
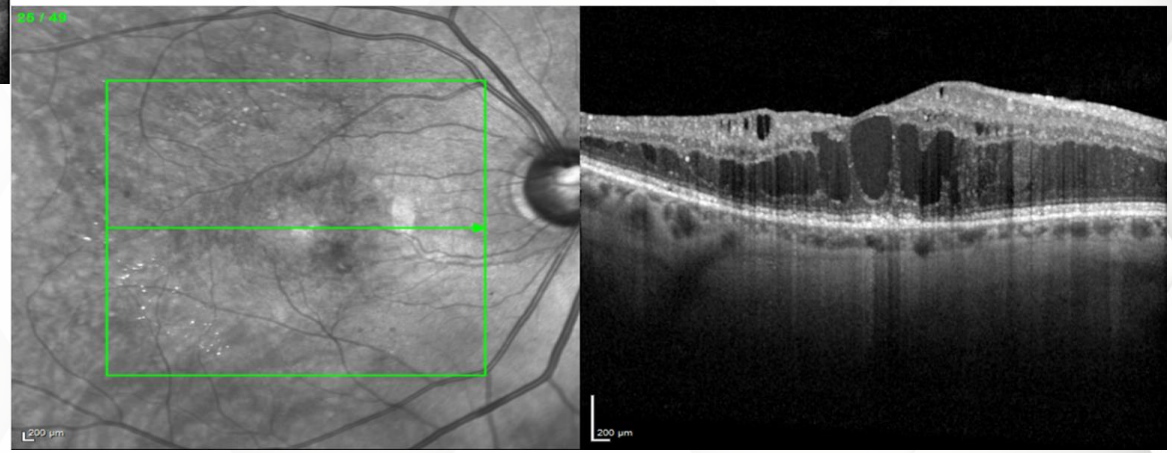
CRC, masked to clinical data including BCVA, identified 2 subjects with abnormalities on OCT

Subfoveal atrophy (EZ or ELM disruption), and severe cysts in the central 1mm occupying and disrupting all the retinal layers

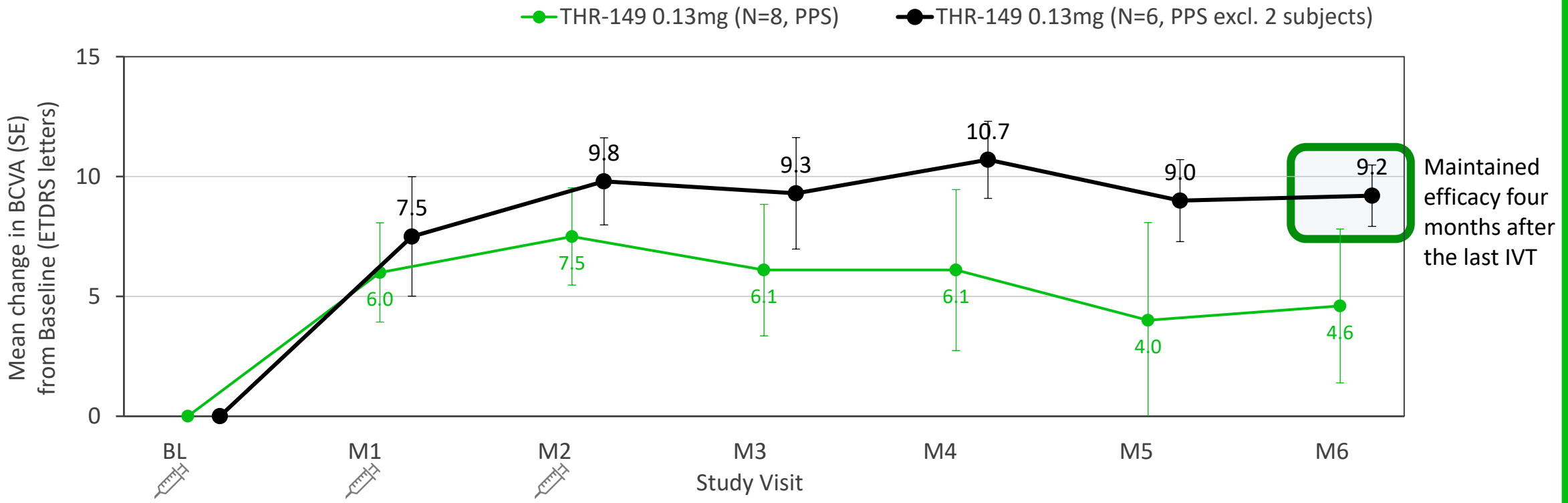




Mean Change in BCVA from Baseline in High Dose Group [a]

(post hoc analysis Feb. 2022)

- CRC, masked to clinical data including BCVA, identified 2 subjects with abnormalities on OCT
- **Post-hoc analysis** excluding these 2 subjects showed a mean gain in **BCVA of > 9 letters** up to Month 6
- Part B protocol amended to **refine the target population** and exclude subjects with these abnormalities on OCT



[a] No rescue treatment was given in the high dose group

BCVA, Best-corrected Visual Acuity; BL, Baseline; CRC, Central Reading Center; ETDRS, Early Treatment Diabetic Retinopathy Study; M, Month; N, Number of Subjects in the Analysis Set; OCT, Optical Coherence Tomography; PPS, Per Protocol Set; SE, Standard Error

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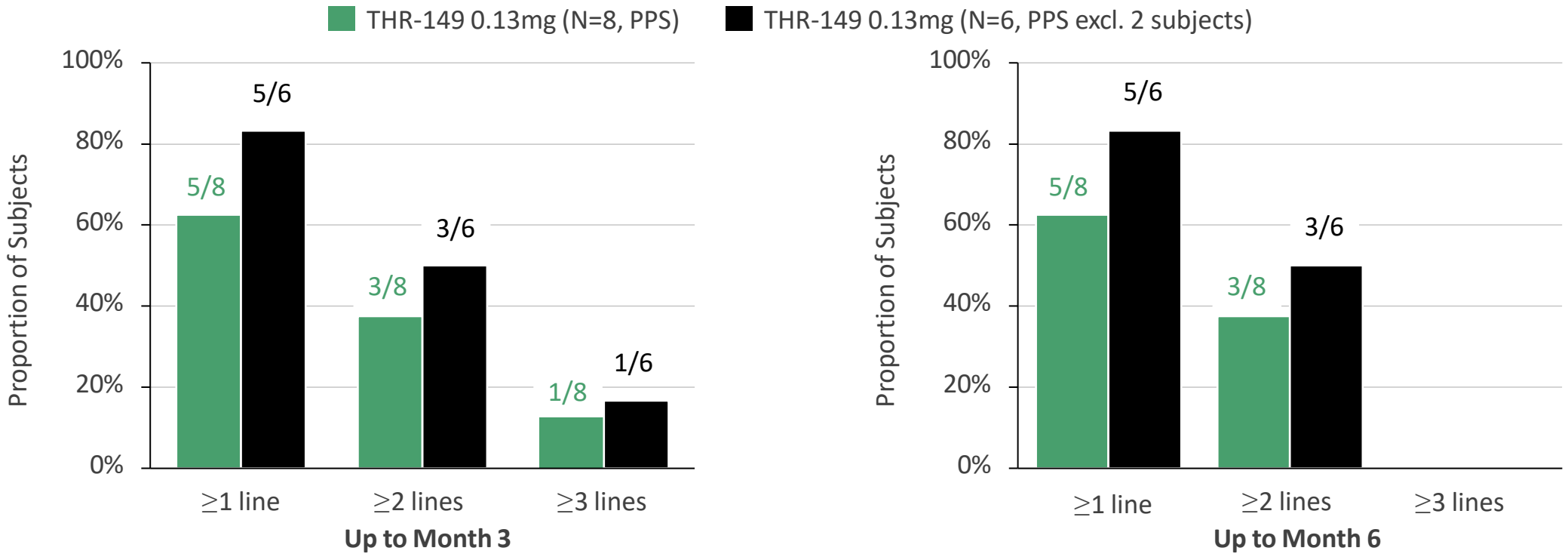
Categorical Gain in BCVA from BL in the High Dose Group [a]

(post hoc analysis Feb. 2022)

- 3/6 (50%) subjects had at least a 2-line improvement up to Month 6, without the need for rescue treatment, 4 months after their last THR-149 injection



[a] No rescue treatment was given in the high dose group

Abbreviations: BCVA, best-corrected visual acuity; BL, baseline; N, number of subjects in the analysis set; PPS, per protocol set

KAHALARI Phase 2 Part B Clinical Trial

Phase 2 Part B multiple injections

Multicenter, randomized, 2-part study

128 targeted patients (Part A, 20; **Part B, 108)**

81 targeted sites (US & EU)

Part A High dose selected for Part B

Part B Compare THR-149 to aflibercept

Topline Part B data **Q4 2023**

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Abbreviation(s): DME, diabetic macular edema; EU, Europe; US, United States

KALAHARI Phase 2 Part B

Evaluate THR-149 against anti-VEGF market leader aflibercept for DME

Part B of the KALAHARI trial building on Part A in/exclusion criteria learnings:

- Primary endpoint BCVA
- Secondary endpoint CST
- 80% powered for superiority vs. aflibercept
- Interim analysis December 2022; IDMC recommends continuation
- Enrollment completed May 2023
- Topline results expected Q4 2023

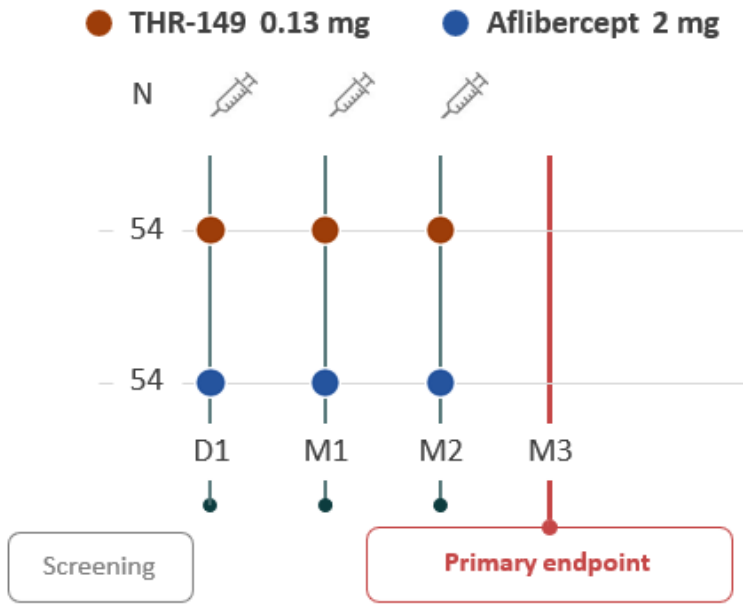
Anti-VEGF suboptimal responders:

Center-involved DME; CST ≥ 320 µm (OCT)

BCVA ≤ 73 and ≥ 24 letters

≥ 5 anti-VEGF injections

Part B • Topline Data
N=108, rando 1:1 4Q 2023



Abbreviations: BCVA, best-corrected visual acuity; CST, central retinal thickness; DME, diabetic macular edema; N, number; OCT, optical coherence tomography; VEGF, vascular endothelial growth factor

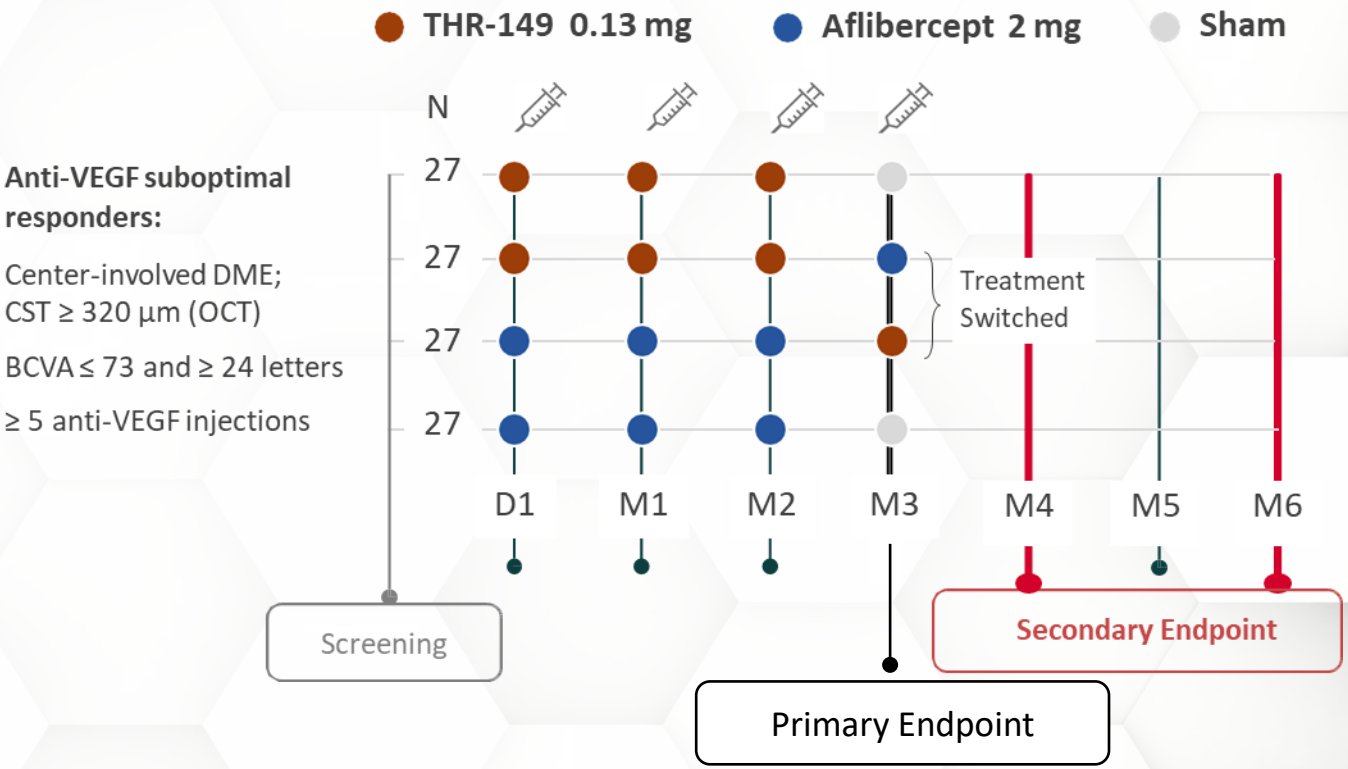
KALAHARI Phase 2 Trial: Part B

Evaluate THR-149 in combination with anti-VEGF therapy

Optimizing trial design protocol to evaluate THR-149 in combination with anti-VEGF market leader aflibercept:

- Primary endpoint BCVA at Month 3
- 80% powered for superiority vs. aflibercept
- Secondary endpoint CST
- Interim analysis December 2022; IDMC recommends continuation
- Topline results expected Q4 2023

Provide preliminary data on use of THR-149 in combination with anti-VEGF therapy through a flip-over injection at Month 3



Abbreviations: BCVA, best-corrected visual acuity; CST, central retinal thickness; DME, diabetic macular edema; N, number; OCT, optical coherence tomography; VEGF, vascular endothelial growth factor

THR-687

Pan-RGD integrin antagonist with the potential to disrupt the entire anti-VEGF market

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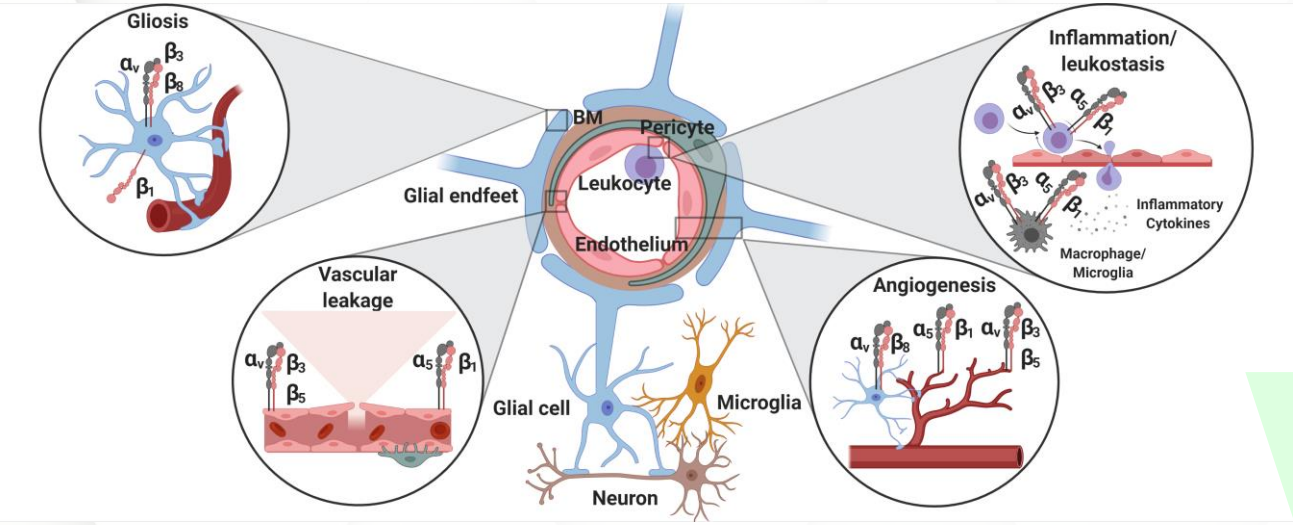
THR-687: Selective RGD Integrin Antagonist

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, 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

Image created with BioRender.com

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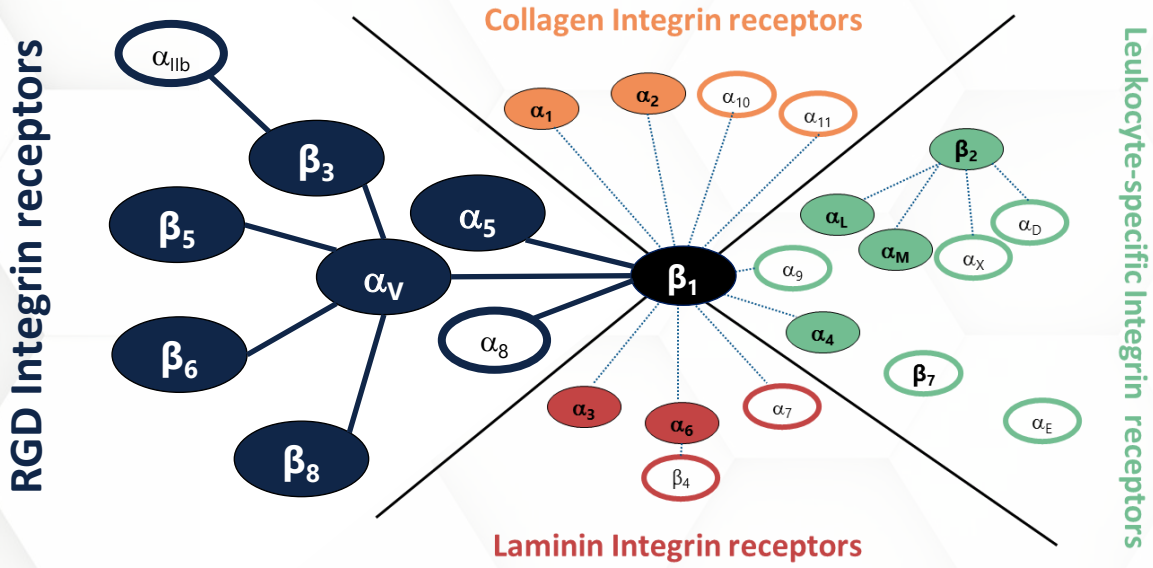
THR-687: Highly Selective & Potent RGD-Integrin Antagonist

Strong binding to *"efficacy"* receptors and weak binding to potential *"side effect"* receptors



Integrin	Integrin Receptor Class	THR-687 IC_{50} ± SD (nM)
$\alpha_v\beta_3$	RGD binding	4.4 ± 2.7
$\alpha_v\beta_5$		1.3 ± 0.5
$\alpha_5\beta_1$		6.8 ± 3.2
$\alpha_v\beta_6$		9.0 ± 5.3
$\alpha_v\beta_8$		1.5 ± 0.7
$\alpha_v\beta_1$		3.2 ± 1.3
$\alpha_{IIb}\beta_3$*		2,000 ± 1,500*
$\alpha_4\beta_1$	Leukocyte-specific	3,800 ± 1,700
$\alpha_2\beta_1$	Collagen binding	121,000 ± 25,000
$\alpha_3\beta_1$	Laminin binding	> 5,000,000

* THR-687 did not affect platelet aggregation up to 100 µM (fibrinogen as inducer)

Abbreviation(s): IC50, half maximal inhibitory concentration; RGD, arginylglycylaspartic acid; SD, standard deviation

Source(s): Hu TT et al. *Exp Eye Res* 2019;180:43-52

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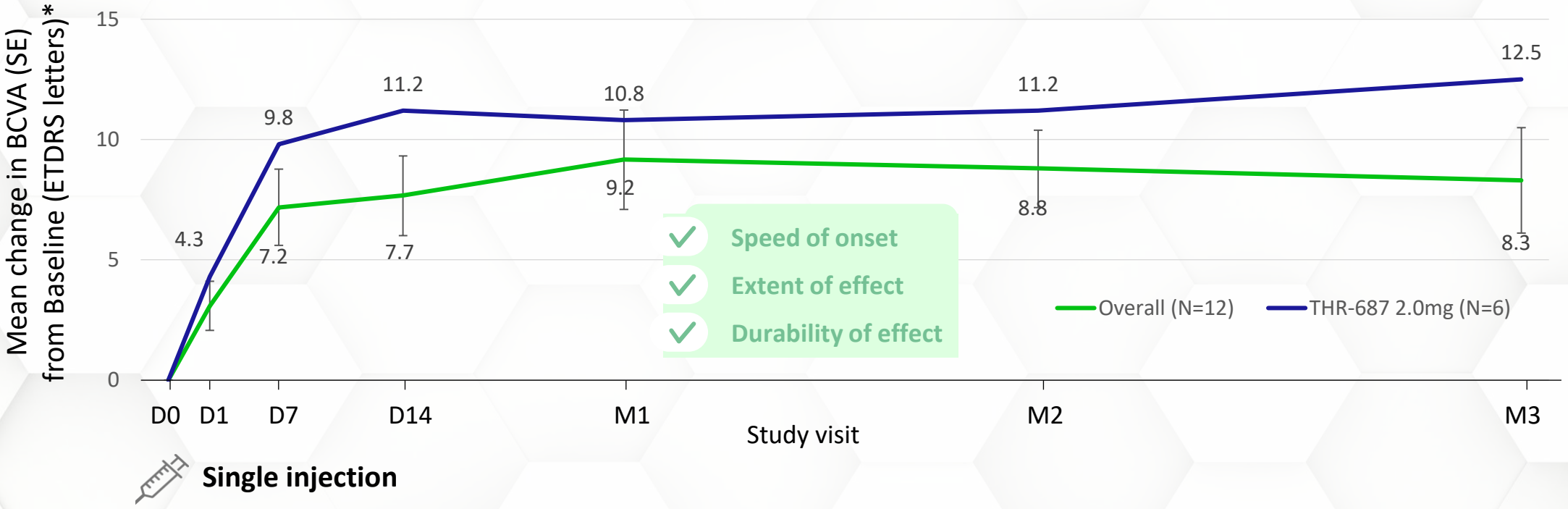
THR-687 Phase 1 • Clinical Evidence (treatment experienced)

Safety and efficacy after a 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

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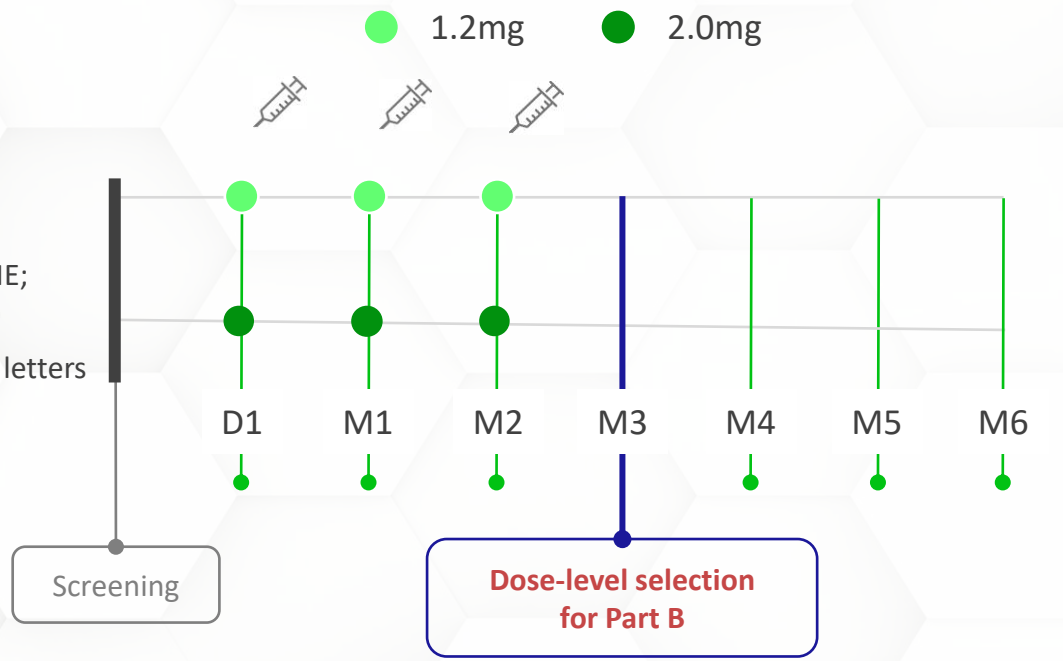
THR-687 Phase 2 Part A Clinical Trial in DME (treatment naïve)

Primary Endpoint was BCVA • Secondary Endpoints include CST, AEs

Part A • Dose level selection THR-687

N≈12, rando 1:1



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

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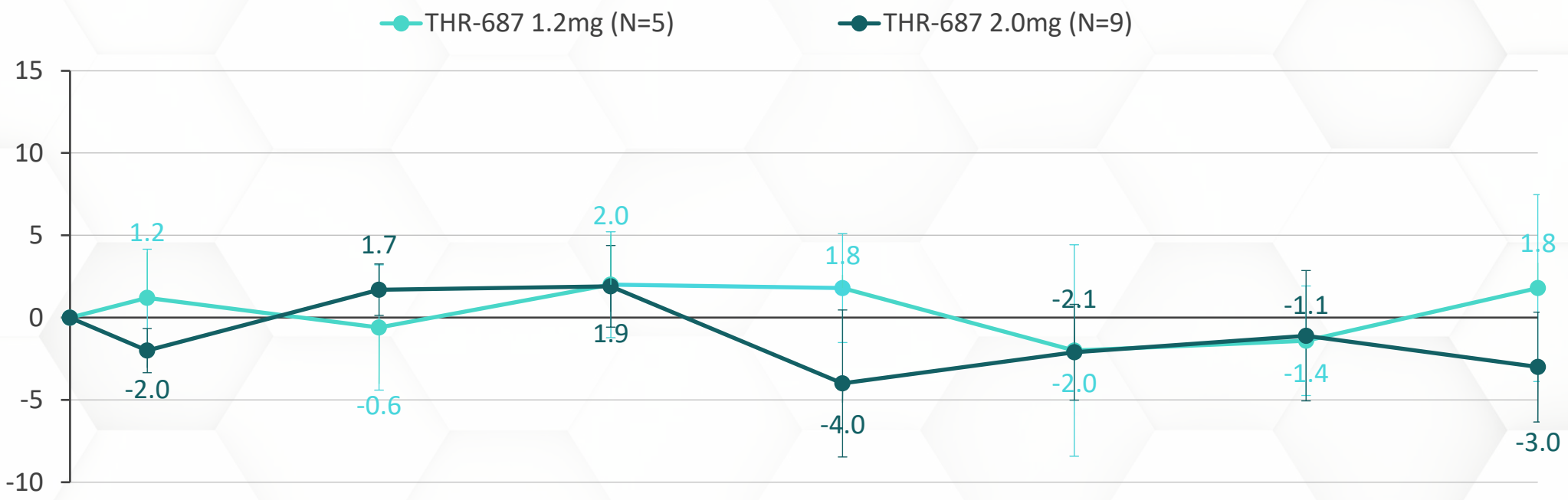
Mean Change in BCVA from Baseline[a]

Per protocol set



Program is currently paused due to a lack of capital; the next line of investigation would be multiple IVTs in pre-treated or treatment experienced patients

Missing values replaced with LOCF approach. No rescue treatment was administered.

Abbreviations: BCVA, best-corrected visual acuity; BL, baseline; LOCF, Last Observation Carried Forward

Number of Subjects in the Analysis Set: SE, standard error

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The Oxurion Opportunity

Oxurion NV (Euronext: OXUR)

Oxurion Investment Thesis

An attractive business model, relatively de-risked

Attractive value creation opportunity

- Limited competition in THR-149 MoA (first-in-class potential)
- Large addressable market
- THR-149 only novel 2nd-line DME therapy
- Already developed market
- Chronic disease - high value per patient
- Market trends (diabetes & ageing)
- High net margin business
- Capital efficient outsourced supply chain

Relatively de-risked

- Validated MoA
- Regulatory endpoints well established
- No safety signals in any clinical study
- Manufacturing; numerous quality CDMOs
- Modality (peptide)
- Payor friendly therapeutic area

Abbreviation(s): CDMO, commercial drug manufacturing organization; DME, diabetic macular edema; MoA, mechanism of action

Source(s): adapted from www.pwc.com/pharma2020

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Oxurion At-a-Glance

Aiming to **grow** the $5B+ diabetic macular edema (DME) market

THR-149 | potential SOC for the up to 50% of DME patients not doing well on anti-VEGFs, large unmet need

Near-term value drivers| Phase 2 topline data in **Q4 2023**

THR-687 | potential to compete/compliment all anti-VEGF, currently paused

Accomplished senior leadership | R&D team with deep ophthalmic expertise

Long-term IP protection | Composition of matter protection (2034-39)

Pioneering Life Changing Treatments for Diabetic Retinal Disease

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Thank you!

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YOUR VISION IS OUR VISION™