THULITE, a Phase II, randomised, double-masked, placebo-controlled trial of BI 1815368 in patients with centre-involved diabetic macular edema: Rationale and study design

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Background and study aim

- DME (also called DMO) is a leading cause of vision loss in individuals with diabetes and can severely impact their daily activities and quality of life[1]
- There is an unmet need for less invasive and more effective treatments for DME that prevent vision loss and reduce lifelong disease burden[1–3]

BI 1815368 is an **oral treatment** that demonstrated a good safety profile in Phase I trials with 185 healthy volunteers[4–8]

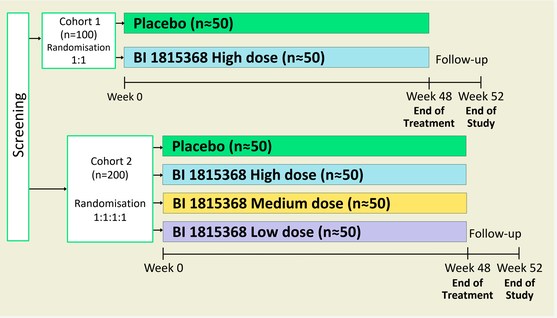
The aim of this Phase II study (NCT06962839) is to evaluate the efficacy, safety and tolerability of oral BI 1815368 in patients with CI-DME[9]

Mechanism of action of BI 1815368

- Diabetes is a metabolic disorder marked by chronic hyperglycaemia. The systemic effects of diabetes cause widespread vascular damage at the endothelial level[2]
- In the diabetic retina, increased blood vessel permeability leads to DME[2]
- **BI 1815368** is a first-in-class **vascular modulator** that may treat and improve vision in patients with DME

Trial design

- This study will have a total of ≈300 participants in 4 arms
- Recruitment starts with Cohort 1 to allow an interim analysis for potential efficacy and safety signals. Once Cohort 1 is fully recruited, recruitment will continue seamlessly for Cohort 2, to characterise dose response



Inclusion/exclusion criteria

Inclusion criteria

- Age ≥18 years
- CI-DME in ≥1 eye confirmed on SD-OCT with CST ≥320 µm in the study eye at screening
- Diagnosis of type 1 or type 2 DM
  - HbA1c <12%
  - Stable medication for DM for ≥30 days prior to Day 1
- BCVA ETDRS letter score of 24–78 in the study eye at screening (Snellen equivalent range 20/320 to 20/32)

Exclusion criteria

- Macular edema considered due to causes other than CI-DME in the study eye
- PDR or iris neovascularisation in the study eye
- Anti-VEGF treatment within:
  - 6 months before Day 1 for faricimab or aflibercept 8 mg, or
  - 4 months for any other anti-VEGF, and/or
- More than 4 prior anti-VEGF injections in the study eye
- History of panretinal photocoagulation treatment, macular laser photocoagulation, vitreoretinal surgery, IVT or periocular corticosteroid treatment (within 12 months before Day 1)

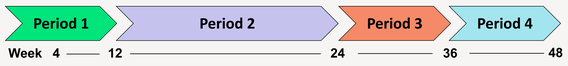
Study endpoints

Primary endpoint	• Occurrence (yes/no) of a gain of ≥10 ETDRS letters compared with baseline in the study eye at Week 48
Secondary endpoint	• Occurrence (yes/no) of gain of ≥15 ETDRS letters compared with baseline in the study eye at Week 48 • Absolute change from baseline of central subfield foveal thickness as measured by SD-OCT in the study eye at Week 48 • Occurrence (yes/no) of drug-related adverse events over the treatment period through end of study

Rescue therapy

SoC IVT injections will be used as rescue therapy in the study eye.† These will start based on the following criteria:

Weeks 4–12	Weeks 13–24 *Either/or*		Weeks 25–36	Weeks 37–48
Worsening in BCVA‡ of ≥10 letters compared with Day 1	Any/no change in BCVA	Worsening in BCVA‡ of ≥5§ letters compared with Day 1	Worsening in BCVA‡ of ≥5§ letters compared with Day 1	Worsening in BCVA‡ of ≥5§ letters compared with Day 1
OR	**AND**	**AND**	**OR**	**OR**
CST worsening by ≥20% compared with Day 1	CST worsening by ≥10% compared with Day 1	Any CST worsening compared with Day 1	CST decrease by ≤5% (with fluid present¶) compared with Day 1	CST decrease by ≤10% (with fluid present¶) compared with Day 1



†Fellow eyes that require treatment can be treated with IVT route of administration SoC, as per investigator discretion. ‡Due to DME. §Changes of 5–9 letters need to be confirmed on 2 consecutive visits at least 1 week apart. ¶Within central 1 mm visible on SD-OCT.

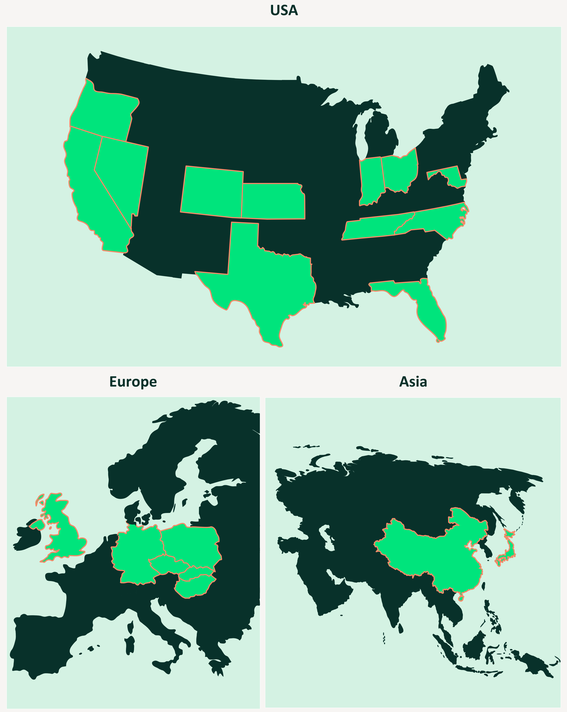
Summary

The Phase II THULITE study will provide data on the **safety, efficacy and tolerability** of **oral** BI 1815368 in patients with **CI-DME**

THULITE will help confirm whether **BI 1815368 has the potential to treat and improve sight** in people with **CI-DME**

The results of this study will potentially contribute to **addressing the need** for **effective, non-invasive treatments for CI-DME**

A global trial with 81 sites



Abbreviations
BCVA, best-corrected visual acuity; CI-DME, centre-involved diabetic macular edema; CST, central subfield thickness; DM, diabetes mellitus; DME, diabetic macular edema; DMO, diabetic macular oedema; ETDRS, Early Treatment Diabetic Retinopathy Study; HbA1c, haemoglobin A1c; IVT, intravitreal; PDR, proliferative diabetic retinopathy; SD-OCT, spectral-domain optical coherence tomography; SoC, standard of care; VEGF, vascular endothelial growth factor.

References
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Disclosures
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