Ophthalmic Clinical Trials

(current as of September 2025)

Contact Information

Phone	9382 7309 (telephone) 0412 338 075 (mobile)
Email	mrgcoordinators@groups.sydney.edu.au
Website	sydney.edu.au/save-sight-institute/retinal-clinical-trials
Fax	02 9382 7278

Please scan QR code for more details

Overview of Clinical Trials

Diabetic retinopathy

Biocryst (Recruiting)

1x Suprachoroidal injection of Avoralstat

- Previously treated (no more than 3 IVT and 8-week washout period) or Rx Naïve
- BCVA 6/7.5 – 6/48
- DMO with CST > 350µm-600µm
- CI DME needing Tx within 6 months
- 24 weeks duration
- HbA1c <10%

VANTAGE (Recruiting)

VX-01 ORAL TABLET

- Previously treated (12 months prior to screening) or Rx Naïve
- BCVA 6/12 or better
- Moderate to severe NPDR
- Non CI-DME
- CST <325µm
- HbA1c ≤ 12%

Barolo (Recruiting)

IVT EYE103 vs Ranibizumab

- Previously treated (first IVT no longer than 3 years) or Rx Naïve
- BCVA 6/7.5 - 6/18
- DMO with CST ≥ 325µm
- 104-week duration
- HbA1c ≤12%

Therini DME (Recruiting)

3x IVT injection of THN391

- Previously treated (not more than 6 injections of IVT within 9 months) for cohort 1-3, DMO Tx naïve for cohort 2-3
- BCVA 6/12-6/120
- DMO with CST ≥ 325µm
- CI-DME with NPDR dx within 9 months
- 20-week duration
- HbA1c ≤12%

Choroidal neovascularization

BENOBIO (Recruiting)

1x IVT injection of BBC1501, a BET inhibitor

- Non-responders to at least two doses of **Eylea, Lucentis**, **Vabysmo, Avastin** (Reduction of less than 50µm)
- BCVA 6/18 and 6/120
- Washout of 6 weeks required

Macular Telangiectasia Type II

MacTel NHOR (Recruiting)

Registry study

- Blood sample and data collection
- New or existing patients to the hospital
- Single visit

Central macula oedema

(2° to NI UVEITIS, RVO, DR or Cataract Surgery)

KLARITY KIORA (Recruiting)

An intravitreal injection (IVT) of KIO-104, an active pharmaceutical ingredient (API)

- BCVA 6/9-6/240
- CST ≥ 350
- ME secondary to non-infectious uveitis, RVO, DR or cataract surgery
- 20 weeks

Intermediate to Late Dry AMD

I-SIGHT2 (Recruiting)

A Microcurrent Stimulation (MCS) therapy

- ≥60 years
- BCVA 6/12-6/60
- Presence of at least one large druse >125 microns in diameter due to AMD
- 14 months

Autosomal Dominant Optic Atrophy

Myrtle (Opening soon)

Single and Repeat Dose Cohorts of IVT PYC-001

- Adult participants confirmed *OPA1* gene mutation-associated ADOA
- ≥18 years
- BCVA 6/12 to 6/60
- Rx Treatment naive participants with mild to moderate VF loss and RNFL loss in study eye as determined by GMPE RNFL and visual field structure function data

Diabetic retinopathy

BIOCRYST

A Phase 1B Study to Evaluate the Safety, Tolerability, and Preliminary Efficacy of a Suprachoroidal Injection of Avoralstat In Participants With Diabetic Macular Edema

Trial details:
This is a Phase 1b clinical study to evaluate the safety, tolerability, preliminary efficacy, and PK of avoralstat in participants with DME. Study 111 is an open-label, single ascending dose study in which participants will receive a single SCh dose of avoralstat given at one of 3 ascending dose levels.

The primary objective is to investigate the safety and tolerability of avoralstat in participants with diabetic macular edema (DME). The secondary is to assess the therapeutic potential of avoralstat in participants with DME.

The planned dose cohorts:

- Cohort 1: 100 µg avoralstat via SCh injection
- Cohort 2: 250 µg avoralstat via SCh injection
- Cohort 3: 500 µg avoralstat via SCh injection

Inclusion:
1. Male or female aged 18 years or older
2. Glycated hemoglobin A (HbA1c) < 12% at screening
3 . Diagnosis of DME with center involvement requiring medical treatment within 6 months of screening and decreased visual acuity attributable to DME
4. Mild-to-severe non-proliferative diabetic retinopathy (NPDR) with DRSS < 61 in the study eye at screening
5. BCVA between 40 and 80 ETDRS letters (20/25 to 20/160 Snellen equivalent), inclusive, in the study eye at screening
6. CST measured by Heidelberg OCT between 350 and 600 µm in the study eye at screening
7. IOP ≤ 25 mmHg at screening
8. For women of childbearing potential, agreement to use highly effective contraception methods during the study specified in Section 5.3; women of nonchildbearing potential defined as postmenopausal ≥ 12 months or have had a hysterectomy, bilateral salpingectomy, or bilateral oophorectomy
9. Ability to provide written informed consent
10. Ability to comply with all required study procedures and restrictions as determined by the opinion of the investigator

Exclusion:
1. Participants who have previously received more than 3 anti-VEGF injections (including bevacizumab) or an anti-VEGF injection within 8 weeks of screening in the study eye
2. Any history of retinal surgery or other surgical intervention (pan-retinal, macular focal, or grid laser photocoagulation) for diabetic ocular complications or anticipated need for use of laser photocoagulation course of any of the procedures listed in the criteria in the study eye during the study period
3. Current medically untreated diabetes mellitus or previous medically untreated diabetes mellitus with initiation of oral or injectable anti-diabetic medication (including glucagon-like peptide-1 agonists) ≤ 3 months prior to screening
4. Active intraocular or periocular infection or active intraocular inflammation in the study eye
5. Intraocular surgery (including cataract surgery, trabeculectomy, or other filtration surgery, including microinvasive glaucoma surgery [MIGS], or laser trabeculoplasty) ≤ 1 year prior to screening or anticipated need for ocular surgery in the study eye during the study period

6. Vitreomacular traction or epiretinal membrane in the study eye evident biomicroscopically or on OCT that is thought to affect central vision
7. Autoimmune idiopathic inflammatory eye disease such as anterior uveitis or history or signs of chronic inflammation in either eye
8. Epiretinal membrane (ERM) in the central fovea that could affect visual acuity, full thickness macular hole, or retinal detachment in the study eye
9. Diagnosed glaucoma in either eye at screening
10. Diagnosed glaucoma in either eye at screening
11. Yttrium-aluminum garnet (YAG) laser capsulotomy ≤ 2 months prior to screening
12. Proliferative diabetic retinopathy, including presence of any neovascularization, including of the disc, in the periphery, or of the iris in the study eye
13. Structural damage to the center of the macula in the study eye that is likely to preclude improvement in BCVA following the resolution of macular edema, including atrophy of the retinal pigment epithelium, subretinal fibrosis or scar, significant macular ischemia, or organized hard exudates
14. Macular edema due to causes other than DME in the study eye
15. Monocular participants or BCVA < 35 letters in the fellow eye
16. Ocular media of insufficient quality to obtain fundus and OCT images
17. The use of corticosteroids as follows:

a. Use of systemic steroids ≤ 4 months prior to screening or anticipated need for use
b. Use of topical (drops) steroids ≤ 6 months prior to screening or anticipated need for use
c. Use of intraocular or periocular (eg, sub-Tenon's, subconjunctival) steroids ≤ 2 years prior to screening in phakic eyes, ≤ 9 months prior to screening in pseudophakic eyes, and/or throughout the remainder of the study period

18. Use of the following medications or substances within the specified timeframes below and/or throughout the remainder of the study period:

a. Systemic anti-VEGF or pro-VEGF treatments
b. Systemic, approved, or off-label drugs or devices for treatment of DME
c. Any investigational drug or device ≤ 16 weeks or 5 half-lives (whichever is longer) prior to screening, inclusive of systemic or ocular studies
d. Tobacco- or nicotine-containing products (eg, cigarettes, cigars, chewing tobacco, snuff, vapes) ≤ 12 weeks of screening e. Drugs that may affect the retina or optic nerve (eg, quinolones, thioridazine, deferoxamine, ethambutol, vigabatrin, pentosan, hydroxychloroquine, and prostaglandin inhibitors such as latanoprost) ≤ 4 weeks of screening

18. Bariatric surgery ≤ 1 year of screening
20. Malignancies ≤ 3 years of screening
21. Renal failure requiring dialysis or renal transplan
22. Current pregnancy or engagement in breastfeeding or intention to become pregnant during the study period
23. Concurrent disease in the study eye other than central-involved DME that could require medical or surgical intervention during the study period or confound interpretation of results (eg, cataracts)
24. Any condition that could confound the ability to detect the efficacy of the IMP product
25. Uncontrolled hypertension at rest, defined as systolic pressure ≥ 180 mmHg or diastolic pressure ≥ 110 mmHg despite maximum medical treatment
26. Known hypersensitivity to avoralstat or any of its formulation excipients or fluorescein dye
27. Anything that, in the opinion of the investigator or sponsor, would interfere with the participant's ability to enroll in the study or increase the risk of study enrollment for that participant.

VANTAGE

A Phase 2, Double-Masked, Randomised, Placebo-Controlled, Parallel Design Study to Evaluate the Efficacy and Safety of Orally Administered VX-01 in Diabetic Retinopathy of Non-Proliferative Type (NPDR)

Trial details:
This is a multi-centre, double-masked, randomised, placebo-controlled, parallel group study that will evaluate the efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of VX-01 as standalone treatment for NPDR (without CI-DME). The primary objective of the study is to evaluate the efficacy of daily oral doses of VX-01 versus placebo following 52 weeks of treatment. Approximately 100 male and female subjects aged ≥ 18 years with a documented diagnosis of T1DM or T2DM with moderate to severe NPDR (without CI-DME) will be enrolled, if they meet all the eligibility criteria for the study.

Subjects will be randomised 1:1 to 1 of 2 study cohorts:

- Cohort 1 (n = 50): VX-01 (film-coated tablets, 150 mg administered BID)
- Cohort 2 (n = 50): Placebo (film-coated tablets, administered BID)

Subjects will be stratified by the presence or absence of proliferative diabetic retinopathy (PDR) and by glycated haemoglobin (HbA1c) of ≥ 8.5% or < 8.5% at Screening.

All subjects will take 1 tablet of VX-01 or placebo BID for 52 consecutive weeks. All subjects will be followed for 12 weeks after completion of treatment at Week 52

Inclusion:
1. Written informed consent must be obtained from the subject prior to any study-related procedures.
2. Subject must be aged > 18 years at the time of Screening.
3. Subject must have a body mass index (BMI) of between 18 and 40 kg/m2 , inclusive.
4. Subject has a documented diagnosis of T1DM or T2DM.
5. Subject has moderate to severe NPDR, DRSS level 43 to level 53, as determined by a Central Reading Centre (CRC) using DRSS in at least one eye (see Table S1).
6. Subject must have clear ocular media and be able to undergo adequate pupil dilation to allow adequate fundus imaging of both eyes.
7. Female subject must be either: a. Of non-childbearing potential: i. post-menopausal (defined as at least 1 year without any menses and confirmed via follicle-stimulating hormone [FSH] levels at Screening), or ii. documented surgically sterile post hysterectomy (at least 1 month prior to Screening) b. Or, if of childbearing potential, i. must have a negative serum pregnancy test at Screening (and a negative urine pregnancy test at Baseline [Visit 2]), and ii. must use 2 acceptable forms of contraception (at least one of which must be a barrier method) starting at Screening and throughout the study period and for 28 days after the final IP administration.
8. Female subject must not be breastfeeding at Screening or during the study period, and for 28 days after the final IP administration.
9. Male subject must be surgically sterile (> 30 days since vasectomy with no viable sperm), or if engaged in sexual relations with a female of childbearing potential, the couple should agree to use 2 acceptable contraceptive methods (at least one of which must be a barrier method) from Screening, during the study, and for 28 days after last IP administration.
10. Female subject must not donate ova or male subject must not donate sperm starting at Screening and throughout the study period, and for 28 days after the final IP administration.
11. Subject must have Best Corrected Visual Acuity (BCVA) assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) protocol letters score of ≥ 70 letters (Snellen equivalent 20/40 or better) in study eye, and ≥ 20 letters (Snellen equivalent 20/400 or better) in the non-qualified fellow eye.
12. Subject must have the ability, in the opinion of the Investigator, and willingness to return for all scheduled visits and perform all assessments.

13. Subject agrees not to participate in another interventional study after signing the informed consent and until the End of Study (EOS) visit has been completed.

Exclusion:

Ophthalmic:

1. Presence of CI-DME (with central subfield thickness [CST] measured greater than 325 µm on spectral domain optical coherence tomography [SD-OCT]) threatening the centre of the macula (within 1,000 µm of the foveal centre) in either eye, or presence of DME requiring treatment.
2. Presence of moderate to high-risk PDR (DRSS level 65 or higher).
3. Any prior treatment (in either eye) with:
a. Focal or grid laser photocoagulation within the past 6 months prior to Screening or pan-retinal photocoagulation (PRP) at any time.
b. Systemic or intravitreal anti-vascular endothelial growth factor (VEGF) agents within the last 12 months prior to Screening.
c. Intraocular, sub-tenon or periocular steroids, including triamcinolone and dexamethasone implant within the last 6 months, or suprachoroidal triamcinolone within the last 3 months prior to Screening.
d. Fluocinolone implant within the last 3 years prior to Screening.
e. Prior treatment for NPDR with any other treatment which is not labelled for NPDR within 1 year prior to Screening (e.g., calcium dobesilate, fibrate medication).
f. Vitrectomy at any timepoint prior to Screening.
g. Yttrium-Aluminium-Granate (YAG) capsulotomy within 3 months prior to Screening.
4. Active uveitis, vitritis, or infection in either eye including infectious conjunctivitis, keratitis, scleritis, or endophthalmitis.
5. History of corneal transplant and/or vitrectomy or any other ocular incisional surgery in either eye (e.g., shunt surgery). Note: Subjects who have had cataract or refractive surgery in either that was more than 3 months prior to Screening may be permitted at the discretion of the Investigator.
6. Uncontrolled glaucoma, as evidenced by intraocular pressure (IOP) > 25 mmHg despite up to 4 glaucoma medications, or evidence of glaucomatous visual field loss or has advanced glaucoma (e.g., prior shunt surgery) in either eye.
7. Clinically significant ocular disease in either eye that in the opinion of the Investigator would preclude participation in the study.
8. Presence of macular or retinal vascular disease including DME and/or retinopathy from causes other than diabetes, age-related macular degeneration, pattern dystrophy, choroidal neovascularisation of any cause, retinal vein occlusion, retinal artery occlusion in either eye.
9. History of retinal detachment or full-thickness macular hole post intraocular surgery in either eye, or idiopathic or autoimmune uveitis in either eye.
10. Any other ocular disease that may cause substantial reduction in BCVA.

Systemic exclusion:

11. Known, suspected hypersensitivity or contraindication to IP.
12. Uncontrolled diabetes mellitus with HbA1c of ≥ 12%.
13. Initiation of treatment with glucagon-like peptide-1 (GLP-1) modulators for glycaemic control and other indications within the last 3 months prior to Screening.
14. Initiation of intensive insulin treatment (a pump or multiple daily injections) within 3 months prior to Screening or plans to do so in the next 3 months.
15. Current use of coumarin anticoagulants (Coumadin/Warfarin).
16. On dialysis or an estimated glomerular filtration rate (eGFR) of < 30 mL/min/1.73m2 as per CKDEPI evaluation at Screening. (Active Diabetic Ketoacidosis or Hyperglycemic Hyperosmolar Nonketotic State).
17. Hypertension with resting diastolic blood pressure (BP) > 100 mmHg or systolic BP > 180 mmHg on 2 consecutive measurements at least 5 minutes apart. Note: If the result is out of range, the assessment may be repeated once prior to randomisation for confirmation.
18. Resting heart rate outside the specified range (50 to 110 beats per minute). Note: If the result is out of range, the assessment may be repeated once prior to randomisation for confirmation.
19. History of chronic liver disease or presence of elevated (defined as > 3 × upper limit of normal) alanine aminotransferase (ALT) and aspartate aminotransferase (AST) consistent with such diagnosis.
20. Known to be immunocompromised or receiving immunosuppressive therapy. Note: Subjects receiving low dose corticosteroids may be eligible, at the discretion of the Investigator.

21. Currently receiving treatment with a strong inhibitor of the P-glycoprotein transporter (see Section 6.4.2), which may interfere with the IP.
22. History of allergy to fluorescein.
23. Any disease or medical condition that in the opinion of the Investigator would interfere with the study, prevent the subject from successfully participating in the study, or which might confound the study results.
24. Participation in any investigational study within 30 days prior to Screening or planning to participate in any other investigational drug or device clinical trials within 30 days of study completion.
25. History of blood transfusion or severe blood loss within 3 months prior to Screening, known hemoglobinopathy, and severe anaemia.

BAROLO

A Randomized, Double-masked, Multi-center, 3-Arm Pivotal Phase 2/3 Study to Evaluate the Efficacy and Safety of Intravitreal EYE103 Compared with Intravitreal ranibizumab (0.5mg) in Participants with Diabetic Macular Edema

Trial details:
This study is a randomized, double-masked, active-controlled pivotal Phase 2/3 study to evaluate the efficacy, safety, pharmacokinetics (PK), and immunogenicity of 2 dose levels of EYE103 in comparison with the active control, ranibizumab, in participants with diabetic macular edema (DME).

The primary objective of the study is to demonstrate that EYE103 (0.5 mg or 0.8 mg) is non-inferior to ranibizumab 0.5 mg, as measured by the mean change in BCVA up to and including Week 52. This change will be measured using the standardized ETDRS chart from Day 1 to Year 1 (average of Weeks 48 and 52).

Approximately 960 participants with DME will be randomized in a 1:1:1 ratio to one of the following 3 treatment groups:

- 0.5 mg of EYE103 via intravitreal injection (IVT)
- 0.8 mg of EYE103 via IVT
- 0.5 mg of ranibizumab via IVT.

Inclusion:
1. Be willing and able to understand the study procedures and the risks involved and provide written informed consent before the first study-related activity.
2. Be male or female ≥18 years of age.
3. If female, have a negative serum pregnancy test at screening and further negative urine tests immediately before each dose of study medication if the participant is a female of childbearing potential (including those with <2 years since the onset of menopause, amenorrhea for <1 year, or not surgically sterile); such participants must agree to use a highly effective method of contraception for 30 days after the last dose of study drug (see Appendix B). She must also agree not to donate oocytes from the time of the first dose and for 30 days after the last dose of study drug.
4. If male, be surgically sterile for at least 12 weeks, or agree to use a highly effective method of contraception, such as a condom and a second highly effective method of contraception from screening up to and including 90 days after the last dose of study drug (see Appendix B). He must also agree not to donate sperm from the time of the first dose until 12 weeks after the last dose of study drug.
5. Have type 1 or type 2 diabetes mellitus and a HbA1c of ≤12% and should be under regular investigation by a trained specialist as per local standard of care prior to and during the trial.
6. Have a BCVA ETDRS letter score between 75 and 24, inclusive, in the study eye at screening and on day 1. In the event both eyes are eligible, the worse-seeing eye should be enrolled in the trial.
7. Have a decrease in vision in the study eye determined by the investigator to be primarily the result of DME.

8. For participants who are treated naive for DME, the diagnosis must have been made within 9 months of screening. For all treatment-experienced participants, the first treatment should have been no longer than 3 years prior to the screening visit. If the participant has received anti-VEGF therapy previously, the last treatment must have been ≥90 days prior to the screening visit. For patients treated previously with 8 mg aflibercept (EYLEA HD) or faricimab (VABYSMO), treatment must have been ≥120 days prior to the Screening visit.
9. Have a CST of ≥325 µm in the study eye on SD-OCT as determined by the IRC at screening.

Exclusion:
1. Be pregnant or breastfeeding.
2. Have been committed to an institution by virtue of an order issued either by the judicial or the administrative authorities.
3. Have had renal failure requiring renal transplant, hemodialysis, or peritoneal dialysis or have renal failure anticipated to require hemodialysis or peritoneal dialysis at any time during the study
4. Have uncontrolled blood pressure, defined as systolic ≥180 mmHg and/or diastolic ≥100 mmHg while a participant is at rest.
- If a participant's initial reading exceeds these values, a second reading may be obtained later the same day or on another day during the screening period.
- If the participant's blood pressure is controlled by antihypertensive medication, the participant should be taking the same medication continuously for at least 30 days prior to Day 1.
5. Have history of stroke (cerebral vascular accident) or myocardial infarction within 180 days prior to Day 1.
6. Have any active malignancy.
7. Have any history of organ transplant.
8. Newly diagnosed or previously untreated diabetes mellitus and initiated oral or injectable anti-diabetic medication within 3 months prior to Day 1. (This does not impact any changes to a participant's medication regimen that may be deemed necessary for optimal glycaemic control over the course of the study.)
9. If treatment-experienced for DME have a history of any of the following treatments within the noted time windows:
- Have had prior treatment with 8 mg aflibercept (EYLEA HD) or faricimab (VABYSMO) within 120 days prior to the Screening visit in the study eye
- Have had an IVT with other anti-VEGF treatments (ranibizumab, bevacizumab, aflibercept [2 mg], brolucizumab, pegaptanib sodium) in the study eye within 90 days of the Screening visit
- Had prior IVT investigational agents in either eye at any time
- Had treatment with ocriplasmin (JETREA®) in the study eye at any time
- Had previous use of ILUVIEN® at any time, of OZURDEX® IVT implants within 180 days of the Screening visit, or any other intraocular or periocular corticosteroids in the study eye within 90 days of the Screening visit
10. Are currently using drugs with known retinal toxicity (e.g., Hydroxychloroquine, pentosan polysulfate sodium, and amiodarone).
11. Have history of cataract surgery and/or minimally invasive glaucoma surgery in the study eye within 90 days of screening.
12. Have any treatment for complications of cataract surgery with steroids or yttrium-aluminum garnet (YAG) laser capsulotomy within 90 days of Screening.
13. Have had pan-retinal photocoagulation or focal/grid thermal laser photocoagulation in the study eye within 90 days of screening.
14. Have tractional retinal detachment in the study eye.
15. Have advanced or uncontrolled glaucoma (defined as IOP ≥25 mmHg despite treatment with antiglaucoma medication) in the study eye.
16. Have had glaucoma-filtering surgery (trabeculectomy or tube shunt) in the study eye.
17. Have any history of retinal detachment or treatment or surgery for retinal detachment in the study eye.
18. Have any history of uveitis in either eye.
19. Have significant media opacities, including cataract, in the study eye that might interfere with VA, assessment of safety, OCT, or fundus photography in the opinion of the reading center.
20. Have a cataract in the study eye that, in the judgment of the investigator is expected to require surgical extraction within 4 months of screening.
21. Have aphakia in the study eye.

22. Have an allergy to fluorescein dye.
23. Have had vitrectomy in the study eye.
24. Have known or former (if the participant has undergone refractive and/or cataract surgery) refractive error with a spherical equivalent of ≥±8 diopters.
25. Have active retinal disease other than the condition (DME/diabetic retinopathy) under investigation in the study eye.
26. Have any history or evidence of a concurrent ocular condition present in the study eye that, in the opinion of the investigator, could require either medical or surgical intervention or affect macular edema or alter VA during the study (e.g., Vitreomacular traction, epiretinal membrane, choroidal neovascularization due to NVAMD or other causes, such as pathological myopia, angioid streaks, presumed ocular histoplasmosis syndrome, and multifocal choroiditis).
27. Have active or suspected ocular or periocular infection or inflammation in either eye at day 1.
28. Currently have evidence of, or a history of any clinically significant autoimmune, cardiovascular, hematologic, hepatic, metabolic, peripheral vascular, renal, or respiratory disease, which, in the opinion of the investigator, would prevent the participant from completing the required assessments for this study.
29. Have a known hypersensitivity to any of the components of EYE103 formulation or prior hypersensitivity to mAbs.
30. Have previously participated in any study of EYE103.
31. Presence of amblyopia, amaurosis or ocular disorders with BCVA <35 letters (EDTRS testing charts) in the fellow eye at screening. This includes conditions that are anticipated to be transient, such as vitreous haemorrhage.
32. Have macular edema in the study eye considered to be secondary to a cause other than DME (e.g., Retinal vein occlusion, Irvine-Gass syndrome).
33. Have active iris or angle neovascularization or neovascular glaucoma in the study eye.
34. Have active proliferative diabetic retinopathy (PDR) in the study eye (e.g., Any vitreous or preretinal hemorrhage, active neovascularization at optic disc [NVD], or active neovascularization elsewhere [NVE]) as determined by the IRC at screening.
35. Have structural damage to the center of the macula in the study eye that, in the opinion of the investigator or sponsor, is likely to preclude improvement in BCVA, including atrophy of the retinal pigment epithelium, subretinal fibrosis or scar, significant macular ischemia, organized hard exudates in the foveal center, or other evidence of chronic disruption of the macular architecture.

THERINI

A Phase 1b Open-Label, Multiple Ascending Dose Study of the Safety, Tolerability, and Biological Activity of Intravitreal THN391 in Diabetic Macular Oedema Secondary to Non-Proliferative Diabetic Retinopathy

Trial details:
The primary objective of this study is to assess the safety and tolerability of THN391 administered by intravitreal (IVT) injection every 4 weeks for a total of 3 doses in participants with centre-involving diabetic macular oedema (DMO) secondary to non-proliferative diabetic retinopathy (DR).
Intravitreal (IVT) THN391 administration reduced vascular permeability and choroidal neovascularisation lesion area in animal models of DR and neovascular AMD, suggesting a role for anti-fibrin therapy in managing retinal vascular diseases.
THN391 was safely administered intravenously in healthy volunteers in an ongoing program intended for patients with Alzheimer's Disease. This first-in-human study of IVT THN391 will evaluate the safety and tolerability of multiple ascending doses (MAD) in participants with non-proliferative DR with centre-involving DMO.

Inclusion:
Participant Inclusion:
1. Able and willing to provide written informed consent after the nature of the study has been explained and prior to the commencement of any study procedures.
2. Male or female, 18 to 80 years of age (inclusive at the time of informed consent).

3. Females must not be pregnant or lactating. Women of childbearing potential (WOCBP) must have a negative pregnancy test at Screening and Day 1 and be willing to have additional pregnancy tests as required throughout the study. WOCBP must agree to use acceptable, highly effective contraception from Screening until 90 days after the last dose of IP. WOCBP with same-sex partners (abstinence from penile-vaginal intercourse) or who are abstinent from heterosexual intercourse are not required to use contraception when this is their preferred and usual lifestyle. Women not of childbearing potential must be postmenopausal for ≥ 12 months (postmenopausal status is to be confirmed through testing of follicle-stimulating hormone [FSH] levels ≥ 40 IU/L at Screening for amenorrhoeic female participants) or surgically sterile. Women who are not of childbearing potential are not required to use contraception.
4. Males must either be surgically sterile (> 30 days since vasectomy with no viable sperm) or, if engaged in sexual relations with a WOCBP, either his partner must be surgically sterile (eg, tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy) or an acceptable, highly effective contraceptive method must be used from Screening until 90 days after the last dose of IP. Males with same-sex partners (abstinence from penile-vaginal intercourse) or who are abstinent from heterosexual intercourse are not required to use contraception when this is their preferred and usual lifestyle. Males must not donate sperm from the first dose of IP until at least 90 days after the last dose of IP.
5. Able and willing to attend the necessary visits to the study site.
6. Diagnosis of diabetes mellitus (Type 1 or Type 2), according to the American Diabetes Association and/or World Health Organization criteria.

Study Eye Inclusion:

7. Centre-involving macular oedema associated with non-proliferative DR in the study eye, diagnosed within 9 months before Screening and confirmed by the CRC.
8. Decreased visual acuity in the study eye attributable primarily to centre-involving DMO, in the opinion of the PI.
9. BCVA between 70 and 35 letters, inclusive, using Early Treatment Diabetic Retinopathy Study (ETDRS) testing (approximately 20/40 to 20/200, inclusive, by Snellen chart) in the study eye.
10. Central subfield thickness of ≥ 325 µM confirmed by the CRC.

11. For DMO treatment-experienced participants (Cohorts 1 to 3): Prior DMO treatment not exceeding 6 injections of VEGF antagonists within 9 months before Screening in the study eye.
12. For DMO treatment-naïve participants (Cohorts 2 and 3 only): No prior treatment for DMO in the study eye.

Participant Exclusion:

1. Major illness or major surgical procedure within 1 month prior to Day 1.
2. Uncontrolled diabetes, in the opinion of the PI or indicated by glycosylated haemoglobin (HbA1c) > 12% at Screening.
3. Uncontrolled blood pressure, in the opinion of the PI, or > 180 mmHg systolic and/or > 100 mmHg diastolic blood pressure.
4. History of uveitis, retinitis, other autoimmune eye illnesses, or any clinically significant ocular complaints, in the opinion of the PI.
5. Prior use of medications known to be toxic to the retina, lens, or optic nerve (eg, deferoxamine, chloroquine/hydrochloroquine, chlorpromazine, phenothiazines, tamoxifen, and ethambutol).
6. History of significant hypersensitivity, intolerance, or allergy to any drug compound or other substance, unless approved by the PI.
7. History of severe allergic or anaphylactic reactions, or sensitivity to the IP or its constituents, or to any components used in the protocol-defined study procedures (eg, fluorescein).
8. Receipt of any IP within the 30 days prior to Screening or 5 half-lives of the IP, whichever is longer.
9. Clinically significant abnormal laboratory parameters at Screening, including alanine aminotransferase (ALT), aspartate aminotransferase (AST) or total bilirubin > 1.5 × upper limit of normal (ULN); estimated glomerular filtration rate (eGFR) < lower limit of normal or creatinine > 1.5 × ULN. Repeat testing at Screening is acceptable for out-of-range values following approval by the PI or designee.
10. A recent (within 1 year of Screening) clinically significant history of drug or alcohol use, abuse or dependence that, in the opinion of the PI, could interfere with the participant's participation or compliance in the study.
11. Anything that the PI considers that would jeopardise the safety of the participant, prevent complete participation in the study, or compromise interpretation of study data.

12. Employee of the PI or study centre with direct involvement in the proposed study or other studies under the direction of that PI or study centre, as well as family members of the employees or the PI.
Study Eye Exclusion:
13. Presence or history of an ocular condition that can adversely affect visual acuity or prevent improvement in visual acuity despite reduction macular oedema.
14. Macular oedema in the study eye considered to be due to a cause other than DMO.
15. Fovea macula in the study eye has substantial non-perfusion (ischemic) on Screening fluorescein angiography (FA), as determined by the CRC.
16. Substantial posterior capsule opacity in the study eye that, in the opinion of the PI, is likely to decrease visual acuity.
17. Presence of an epiretinal membrane or vitreo-retinal interface changes in the study eye which, in the opinion of the PI following input from the CRC, is the primary cause of macular oedema, or is severe enough to prevent improvement in visual acuity despite reduction in macular oedema.
18. Uncontrolled glaucoma with IOP > 21 mmHg.
19. Any history of vitrectomy in the study eye.
20. Aphakia, history of cataract surgery within 3 months before Screening, or any other previous intraocular surgery in the study eye.
21. Intraocular injections of VEGF antagonists in the study eye within 8 weeks prior to Day 1.
22. DMO treatment-naïve participants (no prior treatment for DMO in the study eye) are excluded from Cohort 1.
23. Intraocular steroids: Ozurdex® and triamcinolone acetonide (Kenalog) in the study eye within 24 weeks before Day 1. Any prior use of other forms of intraocular steroids in the study eye.
24. Any ocular condition (eg, foveal atrophy, pigment abnormalities, dense sub-foveal hard exudates, visually significant cataract, non-retinal condition, etc) such that, in the opinion of the PI following input from the CRC, visual acuity would not improve following resolution of DMO in the study eye.
25. A history of or active ocular condition in the study eye (other than DMO) that, in the opinion of the PI, might alter visual acuity during the study period (eg, uveitis or other inflammatory eye disease, neovascular glaucoma, etc.), or it is expected that the participant will require a procedure within the study period that may alter visual acuity in the study eye (eg, retinal photocoagulation treatment).
26. Active or history of retinal detachment in the study eye.
27. History of macular laser photocoagulation in the study eye.
28. Proliferative DR (excluding inactive / previous proliferative DR) or evidence of retinal neovascularisation in the study eye, as determined by the CRC.

Choroidal neovascularization

BENOBIO

A Phase 1, Open Label, Dose Escalation Study to Evaluate the Safety of BBC1501 Intravitreal Injection for Neovascular Age-Related Macular Degeneration

Primary objective: To evaluate the safety and tolerability of BBC1501 monotherapy when administered via intravitreal (IVT) injection in patients with nAMD

Trial details: Treatment is administered as a single intravitreal injection of BBC1501, which is a BET inhibitor.
Study duration will be up to 12 weeks. Patients who have neovascular AMD will initially be treated with the lowest dose and observed for Dose Limiting Toxicities (DLTs). After 3 patients are observed with no DLTs, the next patients to be enrolled will receive a higher dose.
The three doses are:

- 1.25µg
- 2.5µg
- 5µg

Inclusion:
1. Able to provide voluntary written informed consent on the approved ICF, understand the study requirements, and are willing to follow and complete all the study required procedures.
2. Male or female aged ≥ 50 years.
3. Participants who as per Investigator's judgment are non-responders (Section 5.4) to at least 2 prior anti-VEGF treatments (one of which was either aflibercept, ranibizumab or brolicizumab, Faricimab and bevacizumab) for nAMD in the study eye as confirmed by OCT. Response to available treatment is defined as a reduction of ≥ 30% of excess macular thickness or a reduction of ≥ 50 µm, relative to the last CST measurement prior to the IVT anti-VEGF.
4. Active CNV lesions, secondary to nAMD as confirmed with SD-OCT (or SS-OCT), FFA and fundus photography (FP) in the study eye.
5. BCVA between 73 and 21 letters, inclusive, in the study eye using ETDRS testing or BCVA between 20/60 and 20/400 letters, inclusive, in the study eye by Snellen chart.
6. Participant has CST of at least 300 µm if measured by Cirrus OCT or 325 µm if measured by Spectralis OCT, with presence of intraretinal and/or subretinal fluid.
7. Participants who have had a washout period of at least six weeks prior to first administration of the investigational medicinal product (IMP) for any IVT anti-VEGF medication and who, in the opinion of the PI, have disease sufficiently stable to enable this interval.

Exclusion:
Ocular:
1. Use of any of the following treatments or anticipated result of the following assessment to the study eye:
a. IVT or periocular corticosteroid, within 90 days prior to Visit 1 (Day 1) and throughout the study.
b. Glaucoma, evidenced by an IOP of > 21 mmHg or chronic hypotony (< 6 mmHg) in the study eye.
c. Evidence of any other ocular disease other than nAMD in the study eye that may confound the outcome of the study (e.g., active diabetic retinopathy, posterior uveitis, pseudo-vitelliform macular degeneration, or moderate/severe myopia).
d. Participants with advanced nAMD and no prognosis of BCVA as per Investigator's judgment (e.g. due to macular OCT signs of atrophy or photoreceptors disruption, or macular/foveal subretinal hemorrhage).
e. History of vitrectomy in the study eye.
2. Need for ocular surgery in the study eye during the course of the study.
3. YAG laser capsulotomy within 30 days prior to Visit 1 (Day 1) in the study eye.
4. Intraocular surgery, including lens removal or laser, within 90 days prior to Visit 1 (Day 1)

in the study eye.
5. Ocular or periocular infection in either eye.
6. Pupillary dilation inadequate for quality stereoscopic FP in the study eye.
7. Media opacity that would limit clinical visualization, intravenous FFA, or spectral domain optical coherence tomography (SD-OCT) evaluation in the study eye.
8. History of herpetic infection in the study eye or adnexa.
9. Presence of known active toxoplasmosis, inactive toxoplasmosis, or toxoplasmosis scar in either eye.
10. Presence of any form of ocular malignancy including choroidal melanoma in either eye.

Non-ocular:
11. Prior treatment with any agent targeting the endoglin pathway (including a fusion protein that binds bone morphogenic protein).
12. Prior treatment with BBC1501 injectable solution.
13. Use of any of the following treatments or anticipated use of any of the following treatments during the study:
a. Systemic treatment with anti-VEGF agents (e.g., bevacizumab, Ranibizumab, Aflibercept, Brolucizumab, sorafenib, dasatinib and nilotinib)
b. Agents targeting the endoglin pathway (e.g., Atezolizumab).
14. Allergy or hypersensitivity to IMP, fluorescein dye, or other study-related procedures/medications.
15. Any of the following laboratory abnormalities at screening:
a. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 2.5 × upper limit of normal (ULN);
b. Total bilirubin ≥ 1.5 mg/dL;
c. Peripheral white blood cell (WBC) count < 3000/μL;
d. Platelet count < 75000/μL;
e. Serum creatinine ≥ 1.5 × ULN or creatinine clearance ≤ 50 mL/min (calculated per institutional standard or using the Cockcroft-Gault formula if a local guideline is not available).
16. Active bleeding or pathologic condition that carries a high risk of bleeding (e.g., hereditary hemorrhagic telangiectasia).
17. History of hemorrhage, epistaxis, hemoptysis (> ½ teaspoon bright red blood), or treatment with anticoagulants within 90 days prior to Visit 1 (Day 1).
18. Myocardial infarction, stroke, or history of transient ischemic attacks within 180 days prior to Visit 1 (Day 1).
19. Major surgery within 90 days prior to Visit 1 (Day 1). Participants who have undergone major surgery > 90 days prior to Visit 1 (Day 1) may be excluded if the Investigator considers their recovery is insufficient to be suitable for the study. Major surgery is defined as any surgery involving a risk to the life of the participant, including any operation upon an organ within the cranium, chest, abdomen, or pelvic cavity.
20. Therapeutic radiation to the head or neck within 90 days prior to Visit 1 (Day 1).
21. Participation in other investigational drug or device clinical trials within 30 days prior to Visit 1 (Day 1) or planning to participate in other investigational drug or device clinical trials for the duration of the study. This includes both ocular and non-ocular clinical trials.
22. Uncontrolled blood pressure (defined as systolic > 180 mmHg and/or diastolic > 110 while participant is sitting). If a participant's initial reading exceeds these values, a second reading may be taken approximately 30 minutes later. If a participant's blood pressure needs to be controlled by antihypertensive medication, the participant can be eligible if
medication is taken continuously for at least 30 days prior to Visit 1 (Day 1).
23. Poorly uncontrolled type 2 diabetes (HbA1C > 8.5%).
24. Atrial fibrillation not controlled by the participant's primary care physician or cardiologist within 30 days prior to Visit 1 (Day 1) (e.g., heart rate < 100 bpm without significant symptoms).
25. Clinically significant concurrent illness or laboratory abnormality.
26. History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease condition that contraindicates the use of an investigational drug, might affect the interpretation of the results of the study, or renders the participant at high risk for treatment complications.
27. Any systemic infection within 30 days prior to Visit 1 (Day 1).
28. Females who are pregnant or lactating, and are not willing and able to use acceptable, highly effective double contraception from screening until 90 days after study completion, including the Follow-up period. Women of childbearing potential (WOCBP) must have a negative

pregnancy test at screening and Day 1 and be willing to have additional pregnancy tests as required throughout the study. Women not of childbearing potential must be postmenopausal for > 12 months (postmenopausal status is to be confirmed through testing of follicle stimulating hormone (FSH) levels ≥ 40 IU/L at screening for amenorrhoeic female participants, see Section 10.2 for details).
29. Males who are not surgically sterile (> 10 weeks since vasectomy with no viable sperm), or are not willing to use an acceptable, highly effective contraceptive method (Section 10.2) from screening until study completion, including the Follow-up period if engaged in sexual relations with a WOCBP who is not surgically sterile (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy). Males must not donate sperm from the first dose of IMP until at least 4 weeks after IMP administration.
30. Use of marijuana, alcohol abuse or illegal medication within 30 days prior to Visit 1 (Day 1) and throughout the study.
31. Unable to comply with study procedures or follow-up visits.

Macular Telangiectasia Type II

MacTel NHOR

Natural history observation and registry Study Of macular telangiectasia type 2 - The mactel study

The primary objectives:
1. Characterize and document the clinical features and the structural and functional changes of MacTel Type 2 from the earliest to the vision-threatening stages;
2. Collect genetic samples of affected individuals and their family members to establish whether there is a genetic basis for the condition; and
3. Develop a scientific basis to initiate the conduct of clinical studies for MacTel therapies that are emerging for the treatment of other retinal vascular diseases. The results of these clinical studies, to be conducted under separate protocols, will be used to design randomized, controlled clinical trials with adequate power to evaluate potential treatments.

Inclusion

To be eligible to participate in this study, an individual must meet all of the following criteria:
1. Ability to review and understand the informed consent document and agree to the form's contents. (In cases with significant visual impairment, the informed consent may be read to the participant);
2. Stated willingness to comply with all study procedures;
3. Male or female, aged >18; and
4. Diagnosed with or suspected to be affected by MacTel Type 2; OR an immediate family member of a NHOR participant with MacTel; OR a healthy volunteer (control) or a volunteer (control) affected with a disorder thought to be related to MacTel Type 2.

Exclusion

An individual who meets any of the following criteria will be excluded from participation in this study:
1. Inability to provide informed consent or undergo required procedures; and
2. Confounding (excluding diabetic retinopathy) ocular disorder that impacts the ability of the Reading Center to analyze images.

Central macula oedema

KLARITY KIORA

A phase 2, open-label, multiple dose study of the safety, tolerability and efficacy of intravitreal KIO-104 in patients with macular edema (KLARITY-1)

Trial details: This is a multi-centre, open label study to assess the safety, tolerability, and efficacy of KIO-104 administered by IVT injection to the study eye1 of eligible participants with ME secondary to non-infectious uveitis, retinal vein occlusion, diabetic retinopathy or cataract surgery.

Inclusion

Participants must meet all the following criteria:
1. Be aged 18 to 85 years inclusive at the time of consent.
2. Provide informed consent prior to any study procedures, as stipulated by local laws, Ethics Committee (EC) and Regulatory Authority (RA) guidelines.
3. Be willing and able to follow all study instructions, attend all study visits, and complete all study assessments.
4. Have a clinical diagnosis of ME in the study eye7 secondary to noninfectious uveitis, retinal vein occlusion, diabetic retinopathy or cataract surgery.
5. If currently receiving systemic corticosteroid therapy or immunosuppressive therapy (or any combination thereof), be on a stable dose of therapy for at least 3 months prior to Screening and during the study.
6. Have a Central Subfield Thickness (CST) of ≥ 350 µm.
7. Have a Best Corrected Visual Acuity (BCVA) in the study eye of:
a. ≤ 20/32 (Feet); logMAR ≥ 0.2
b. ≥ 20/800 (Feet); log MAR ≤ 1.6
8. Have media clarity and pupillary dilation sufficient for adequate visualization and assessment of the study eye.
9. Be willing to avoid disallowed medications and treatments for the duration of the study.
10. Agree to follow appropriate contraception requirements from screening until 3 months after the last dose of the study drug.
a. Participants assigned female at birth who are of child-bearing potential (OCBP) must agree to a pregnancy test at Screening and prior to each dose of investigational medicinal product (IMP) and use an acceptable method of birth control including oral, transdermal, injectable, or implantable hormonal contraception, intrauterine device, abstinence from intercourse with partner assigned male at birth, or surgical sterilisation of
partner assigned male at birth.
b. Participants assigned female at birth are not OCBP if they have had a hysterectomy, bilateral oophorectomy, bilateral tubal ligation, or are post-menopausal by at least 12 months.
Post-menopausal status of amenorrheic female participants should be confirmed at Screening through testing of folliclestimulating hormone (FSH) as per analysing laboratory threshold.
c. Participants assigned male at birth with a partner OCBP must be surgically sterile for at least 3 months prior to starting study drug, or ensure their partner uses contraception as outlined above, and must use a male condom. Participants assigned male at birth must not donate sperm from Screening until 3 months after the last dose of IMP.
d. Participants who have practiced true abstinence for at least 1 year due to usual and preferred lifestyle choice are exempt from contraceptive requirements. If a participant who is abstinent becomes sexually active, they must agree to use appropriate contraception as described above.

Exclusion

Participants must not meet any of the following criteria:

1. Have media opacities (cornea, anterior or posterior synechia, cataract, vitreous haze and others) of either eye that preclude investigation and documentation of the posterior pole and intravenous fluorescein angiography, or optical coherence tomography evaluation in the study eye.
2. Receive local or systemic biologicals (i.e. tumour necrosis factor [TNF]-blockers, B-cell blockers, cytokines, cytokine-blockers, receptor antagonists) 90 days prior to Day 1 or planned during the study.
3. Receive treatment with cyclophosphamide or chlorambucil during the study.
4. Receive intravitreal injections (including but not limited to anti-vascular endothelial growth factors) 90 days prior to Day 1 or planned during the study.
5. Receive a posterior subtenon's or orbital floor injection of steroids 90 days prior to Day 1 or planned during the study.
6. Have any implantable corticosteroid-eluting device (Ozurdex, Iluvien, Retisert, triamcinolone intravitreal implant, fluocinolone intravitreal implant) in the study eye, with the following exceptions:
a. If the device had been removed more than 90 days prior to Day 1 of the study.
b. If Ozurdex® had been implanted at least 6 months before Day 1 of the study.
c. If Iluvien® or Retisert® had been implanted at least 3 years before Day 1 of the study.
d. Use of topical steroids are permissible provided the participant is receiving a stable dose for at least 3 months prior to Screening and during the study.
7. Have ocular surgery (including cataract extraction, vitreoretinal or scleral buckling surgery) in the study eye, within 90 days prior to Day 1, or planned during the study.
8. Have a capsulotomy in the study eye, within 30 days prior to Day 1, and during the study.
9. Have Intraocular pressure (IOP) ≥ 25 mmHg in the study eye (glaucoma patients maintained on no more than one topical medication with IOP < 25 mmHg are allowed to participate).
10. Have ocular hypotony (IOP < 6 mmHg).
11. Have aphakia or anterior chamber lens in the study eye
12. Have visible scleral thinning, scleral ectasia or keratoconus in the study eye.
13. Have presence of any ocular malignancy in either eye.
14. Have evidence of any other clinically significant ocular disease that might interfere with the study assessments.
15. Have ocular or periocular (either eye) or systemic infection and/or a temperature greater than 38.0°C, or the use of systemic or topical ocular antibiotics within 14 days of Day 1.
16. Have a psychiatric condition that, in the investigator's opinion, precludes compliance with the protocol; past or present psychoses; past or present bipolar disorder; disorder requiring lithium; or within five years prior to screening, a history of suicide plan.
17. Have any clinically significant abnormality at screening determined by medical and ophthalmic history, vital signs, clinical biochemistry, hematology, urinalysis, or a 12-lead electrocardiogram (ECG), as assessed by the investigator, which might interfere with the study assessments or the ability of the participant to complete the study.
18. Have any other medical condition or significant co-morbidities, or any finding during screening, which in the view of the investigator is likely to interfere with the study or put the participant at risk, confound study data, or interfere significantly with study participation.
19. Have participated in any other investigational drug or device clinical trial within 90 days prior to Day 1 or planning to participate in other investigational drug or device clinical trials during the study and within 90 days following Day 1. This includes both ocular and non-ocular clinical trials.
20. Receive any anticoagulant or thrombocyte aggregation inhibiting agent (marcumar, warfarin, heparin, enoxaparin, apixaban, rivaroxaban, pentosanpolysulfate, dabigatran, aspirin and others) within 14 days prior to Day 1 or planned during the study.
21. Have a known allergy or hypersensitivity to the study medication, any component of the delivery vehicle, any corticosteroids, any diagnostic agents used during the study (e.g., fluorescein, dilation drops), or any other standard of care medications likely to be used during the study (e.g., antibiotic drops, povidone, rescue medications).
22. Be pregnant or breast-feeding, or plan to become pregnant during the study.

Intermediate dry AMD

ISIGHT-2 ILUMEN

Microcurrent stimulation therapy for intermediate to advanced nonexudative age-related macular degeneration (i-SIGHT2): a multicentre, randomised, sham controlled, double-masked, clinical device trial.

Trial details:
Evaluate the safety and effectiveness of i-Lumen AMD's proprietary transpalpebral microcurrent stimulation (MCS) therapy for participants with intermediate to advanced nonexudative (dry) age-related macular degeneration (AMD)

Participants will be randomised in a 2:1 allocation of active vs. sham treatment arms. The randomisation will be stratified based on absence or presence of macula-involving geographic atrophy (GA) in the primary study eye (if unilateral, this is the designated primary study eye; if bilateral, if one eye has macula-involving GA, this is the designated primary study eye, or if both or neither have GA, then the eye with the worst distance BCVA at Baseline is the designated primary study eye).

Inclusion:
Participants must meet all of the following criteria:
1. Age ≥60 years.
2. If applicable, a participant taking medications or supplements to slow the progression of AMD and/or GA at time of Screening and is on a stable regimen (≥ 4 weeks) must agree to remain on the same regimen through completion of study participation, unless changes are medically necessary.
3. Able to understand and provide informed consent themselves.
Additionally, the participants' study eye(s) must meet all of the following criteria:
4. Presence of at least one large druse >125 microns in diameter due to AMD, as assessed by CF and OCT.
7. Distance BCVA ETDRS letter score between 35 to 70 letters (inclusive) (Snellen equivalent 6/12 to 6/60 [20/40 to 20/200]) as measured by Clinical Trial Suite (CTS; M&S Technologies).
5. Difference in distance Baseline BCVA ETDRS letter score and distance Screening BCVA ETDRS letter score ≤ ±7 letters

Exclusion:
Participants must not meet any of the following criteria to be enrolled in the study:
1. Any implanted electrical device(s) including deep brain stimulator, hearing or visual implants (i.e., cochlear implant, auditory brainstem implant, retinal prostheses), and/or cardiac defibrillator/pacemaker.
2. Implanted metallic device within 5 cm of the Treatment electrode (study eye(s) and/or the grounding electrode (base of the hairline on the back of the neck).
3. History of arterial and/or venous occlusion in the eye, head and/or neck.
4. Uncontrolled diabetes, defined as glycated haemoglobin (HbA1c) >10% (13.3 mmol/L).
5. Current tobacco or tobacco-related product use or history within the past 5 years of heavy smoking (defined as, on average, more than half a pack of cigarettes per day).
6. Known severe allergy to fluorescein dye.
7. Current or previous use of medications known to be toxic to the retina (e.g., hydroxychloroquine thioridazine, desferrioxamine, pentosan polysulfate sodium, etc.).
8. Medical diagnosis of severe dry eye defined as requiring either artificial tears more than six (6) times a day or prescription drops (i.e., Restasis, Xiidra, or Cequa).
9. History of seizure disorders, chronic migraines and/or cluster headaches.
10. Exposure to an investigational medical device or participation in any other clinical trial or research study within 30 days prior to consent and through the duration of study participation.

11. Any physical condition that, in the investigator's opinion, would prevent adequate study compliance or pose increased risk.
Participants must meet none of the following criteria in either eye:
12. History and/or evidence of diabetic retinopathy in either eye as assessed by CF, fundus FA, and OCT, to be confirmed by the Central Reading Centre.
13. Other conditions which pre-dispose to chorioretinal atrophy such as inherited retinal dystrophy (i.e., Stargardt's disease, Best's disease, pattern dystrophy, central areolar choroidal dystrophy, etc.).
Additionally, the participants' study eye(s) must not meet any of the following criteria:
14. History and/or evidence of exudative AMD in the study eye as assessed by CF, FA, and OCT, to be confirmed by Central Reading Centre.
15. GA involving the foveal centre, as assessed by the Central Reading Centre using AF.
16. GA lesion area >17.5 mm2
, as assessed by the Central Reading Centre using AF.
17. Confluent and non-confluent GA that surrounds the foveal centre by an aggregate of more than 270 degrees, as assessed by the Central Reading Centre.
18. History of intravitreal injections for GA (e.g., Syfovre or Izervay).
19. Other causes of macular scarring or potential for choroidal neovascularization (e.g., ocular histoplasmosis syndrome), as assessed by either the site investigator or Central Reading Centre.
20. Evidence of vitreoretinal traction or significant epiretinal membrane affecting the central fovea (umbo) as noted on OCT by the Central Reading Centre.
21. Treatment with PBM therapy or short pulse laser within 12 months prior to screening.
22. Glaucoma requiring ≥3 medications and/or drops per day, or history of trabeculectomy.
23. History of any kind of intraocular surgery, excluding cataract surgery performed ≥3 months from Screening.
24. History of yttrium aluminium garnet (YAG) laser posterior capsulotomy <1 month from Screening.
25. Any form of corneal degeneration or dystrophy that reduces VA.
26. High myopia or former high myopia (spherical equivalent greater than 6 dioptres).
27. Visually significant cataracts and/or visually significant posterior capsular opacification that may interfere with VA or imaging, and/or anticipated to require surgery or YAG laser procedure prior to the 12 Month timepoint.
28. History of amblyopia.
29. Eyelid pathology, including allergy, dermatitis, and diseases of the eyelid which would prevent proper application of the transpalpebral electrodes (e.g. ptosis).

Autosomal Dominant Optic Atrophy

MYRTLE

A Phase 1b Open-Label, Randomized, Single Dose and Repeat Dose Study to Evaluate the Single and Repeat Dose Safety and Tolerability of Intravitreally Administered PYC-001 in Participants with Confirmed OPA1 Mutation-Associated Autosomal Dominant Optic Atrophy

Trial details:
The primary objective of both single dose and repeat dose cohorts is to evaluate the safety and tolerability of a single and multiple doses of intravitreally administered PYC-001 in participants with confirmed OPA1 mutation associated with ADOA
Further, to determine optimal dose and dosing regimen for PYC-001.
Adult participants will be distributed:
Single Dose Cohort:

- Single 60 µg dose

Repeat Dose Cohorts:

- Repeat dose:
- Cohort 1: 10 µg (low dose)
- Cohort 2: 30 µg (medium dose)
- Cohort 3: 60 µg (high dose)

And Two dosing regimens:
Group A: Once every 8 weeks
Group B: Once every 12 weeks

Inclusion:

1. Must give written informed consent before any study-related activity is carried out and must be able to understand the full nature and purpose of the study, including possible risks and adverse effects;
2. Adult males and females, aged 18 years and above at screening;
3. Body mass index ≥18.0 and ≤32.0 kg/m2, with a body weight ≤100 kg at screening;
4. Have a recent (within five years) genetic diagnosis of *OPA1* mutation-associated (haploinsufficiency) ADOA and/or confirmed diagnosis during screening, as determined by the PI. In case of complex mutation profile, eligibility will be determined in consultation with the Sponsor. Rollover participants are exempt from this criterion as their genetic diagnosis was confirmed in PYC-001-101;
5. Treatment naïve participants with best-corrected visual acuity (BCVA) of between ≤20/40 (≤70 Early Treatment of Diabetic Retinopathy Study [ETDRS] letters) and ≥20/200 (≥35 ETDRS letters). If both eyes meet this eligibility criteria, the eye with better fixation as determined by the PI in consultation with the Sponsor will be selected as the study eye and the other eye will be designated as the fellow eye. In the event that both eyes are eligible and have adequate fixation to reliably perform all study assessments, the worse eye as determined by the physician will be taken as the study eye. PYC-001-101 participants are exempt from this criterion and will have the same study eye and fellow eye as determined in PYC-001-101;
6. Treatment Naïve participants (participants from PYC-001-101 are exempt from this criterion) with mild to moderate visual field loss and retinal nerve fiber layer (RNFL) loss in the study eye only as determined by the Spectralis Glaucoma Module Premium Edition (GMPE) RNFL & visual field structure function data (map), defined as:
a. Mild disease = RNFL abnormalities (outside normal range) in no more than one of six sectors;
b. Moderate disease = RNFL abnormalities (outside normal range) in no more than three of six sectors;
c. Severe disease = RNFL abnormalities (outside normal range) in four of six sectors;
d. Advanced disease = RNFL abnormalities (outside normal range) in six of six sectors;
7. Medically healthy (in the opinion of the PI), as determined by pre-study medical history, and without clinically significant abnormalities including (assessments may be repeated at the discretion of the PI if an out-of-range value is determined to be erroneous):
a. Physical examination without any clinically relevant findings;

b. Systolic blood pressure (BP) in the range of 90 to 160 mmHg and diastolic BP in the range of 50 to 95 mmHg after five minutes in sitting or supine or semi-supine position;
c. Heart rate (HR) in the range of 45 to 110 bpm after five minutes rest in sitting or supine or semi-supine position;
d. Body temperature (tympanic), between 35.5 35.5°C and 37.7°C;
e. No clinically significant findings in clinical chemistry, hematology, coagulation and urinalysis tests at screening (see Section 5.4 for specific ranges).
8. Female participants must be of non-childbearing potential, ie, surgically sterilized (hysterectomy, bilateral salpingectomy, bilateral oophorectomy at least six weeks before the screening visit) or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause and a follicle stimulating hormone [FSH] level consistent with postmenopausal status, per local laboratory guidelines). Females receiving hormone replacement therapy (HRT) may be considered for inclusion if the need for HRT is for no other medical reason than to treat symptoms associated with menopause. If female participants are of childbearing potential, they must:
a. Have a negative pregnancy test at the screening visit and on study Day -1;
b. Agree not to attempt to become pregnant or donate ova from signing of the consent form until at least 130 days after final IVT dose administration of PYC-001;
c. Agree to use adequate contraception (defined as use of a condom by the male partner combined with use of a highly effective method of contraception (defined in Appendix 13.1) from one month prior to screening until at least 130 days after final IVT dose administration of PYC-001 , if not exclusively in a same-sex relationship or abstinent as a committed lifestyle.
9. Male participants must:
a. Agree not to donate sperm from signing the consent form until at least 190 days after final IVT dose administration of PYC-001;
b. If engaging in sexual intercourse with a female partner who could become pregnant, agree to use adequate contraception (defined as use of a condom combined with use of a highly effective method of contraception (defined in Appendix 13.1) from signing the consent form until at least 190 days after final IVT dose administration of PYC-001;
c. If engaging in sexual intercourse with a female partner who is not of childbearing potential or a same-sex partner, agree to use a condom from signing the consent form until at least 190 days after final IVT dose administration of PYC-001 and;
10. Willing and able to comply with all study assessments and adhere to the protocol schedule and restrictions.

Exclusion Criteria:

Participants will be excluded from the study if there is evidence of any of the following (to be assessed at the Screening visit and on study Day -1, unless otherwise specified):
1. Participant has a known allergy to PYC-001 or any of its excipients;
2. Demonstrated clinically significant co-morbidities, which, in the opinion of the PI, would interfere with the participant's ability to participate in the study and/or confound study outcomes;
3. Females who are breastfeeding or planning to breastfeed;
4. Based on recent (within five years of screening [for rollover PYC-001-101 participants, within five years of entry into PYC-001-101]) genetic testing, the participant has mutations in genes that cause ADOA, other than OPA1 (for example in case of dominant negative ADOA and ADOA Plus) or has other pathological variants that result in an ADOA-like optic atrophic phenotype or other pathologic genetic findings indicating presence of additional confounding ocular diseases based on comprehensive genetic screening. Eligibility will be determined by the PI in consultation with the Sponsor as needed;
5. Have received any prior cell or gene therapy for a retinal condition, excluding participation in study PYC-001-101;
6. Within three months prior to study Day -1, have undergone any vitreoretinal surgery (scleral buckle, pars plana vitrectomy, retrieval of a dropped nucleus or intraocular lens, radial optic neurotomy, sheathotomy, cyclodestructive procedures or multiple filtration surgeries [two or more]) or any other ocular surgery in the study eye. This criterion does not apply for rollover participants from PYC-001-101;
7. Within three months prior to study Day -1, have placement of an Ozurdex® implant. This criterion does not apply for rollover participants from PYC-001-101;
8. Within three years prior to study Day -1, have placement of Retisert® of Iluvien® implants. This criterion does not apply for rollover participants from PYC-001-101;

9. Have ocular media opacity or poor pupillary dilation prohibiting quality ophthalmic evaluation or photography, as assessed by the PI in the study eye ;
10. Macular edema (intraretinal, sub-retinal or other fluid) in the study eye requiring treatment.
11. History of recurrent uveitis (idiopathic or immune-related) or active ocular inflammation;
12. Have used within 30 days of the Screening visit or is using any investigational drug or over-the-counter drug such as Idebenone or Vitamin B6 or a device which in the opinion of the PI or Sponsor could affect the optic nerve and/or influence functional vision or visual function during the study period. A decision will be made on a case-by-case basis by the PI in consultation with the Sponsor. Participation in observational studies is allowable based on PI discretion and consultation with the Sponsor's Medical Representative. Participation in PYC-001-101 is allowed;
13. Over-the-counter drugs like CoQ10 and other Nutraceutical usage will require a washout by five half-lives prior to baseline visit. Participants may need to stop taking the drug for the duration of the study based on Physician discretion and in consultation with the Medical Monitor;
14. Have a recent history (<6 months) of or current excessive recreational drug or alcohol use, in the opinion of the PI. Excessive alcohol use is defined as regular consumption of >10 standard drinks per week or >4 standard drinks per day, where one standard drink is defined as 10 grams of pure alcohol*;*
15. Positive alcohol breath test as assessed at screening, and on study Day -1 and study Day 1;
16. Positive urine drugs of abuse as assessed at screening and on study Day -1 and study Day 1;
17. Any retinal pathology other than ADOA or any other condition or prior therapy that in the opinion of the PI would make the volunteer unsuitable for this study, including inability to cooperate fully with the requirements of the study protocol or likelihood of noncompliance with any study requirements;
18. Presence of illness or pathology that, per investigator, include symptoms and/or the associated treatments that can alter visual function. For example, cancers or pathology of the central nervous system, including multiple sclerosis;
19. Positive test for human immunodeficiency virus, hepatitis B or C virus;
20. Clinically significant findings in clinical chemistry, hematology, coagulation and urinalysis tests at screening, defined as:
o Alanine transaminase (ALT) or aspartate aminotransferase (AST) >2 × upper limit of normal (ULN) or bilirubin >1.5 × ULN (unless patient has Gilbert's syndrome);
o Estimated glomerular filtration rate <60 mL/min/1.73 m2;
o HbA1c level ≥7.0%;
o International normalized ratio ≥1.2;
o hemoglobin <10 g/dL, platelets <100,000/μL, and white blood cells within the normal range;
o Clinically significant abnormalities in the urine analysis.