COVER PAGE

Official Title	A Phase 3, Open-Label, Multicenter, Extension Study to Evaluate the Long-Term Safety and Efficacy of Pegcetacoplan in Subjects with Geographic Atrophy Secondary to Age-Related Macular Degeneration
NCT Number	NCT04770545
Document Date	18 July 2023

PEGCETACOPLAN (APL-2)

APL2-GA-305

PROTOCOL AMENDMENT 3

A PHASE 3, OPEN-LABEL, MULTICENTER, EXTENSION STUDY TO EVALUATE THE LONG-TERM SAFETY AND EFFICACY OF PEGCETACOPLAN IN SUBJECTS WITH GEOGRAPHIC ATROPHY SECONDARY TO AGE-RELATED MACULAR DEGENERATION

17 JULY 2023

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APPROVAL SIGNATURE

Sponsor's Approval

The protocol has been approved by Apellis Pharmaceuticals, Inc.

Responsible Medical Director

PPD

18-Jul-2023 | 16:30 EDT

Comp

Approval date

PPD MD, PhD

PPD Head of Development, Ophthalmology

Apellis Pharmaceuticals, Inc

PPD

INVESTIGATOR'S AGREEMENT

I have received and read the investigator's brochure for pegcetacoplan (APL-2). I have read the protocol for clinical study APL2-GA-305 and agree to conduct the study as outlined. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

_____

Printed Name of Investigator

_____

Signature of Investigator

_____

Date

PROTOCOL AMENDMENT SUMMARY OF CHANGES

Amendment 3: Summary of Changes From the Previous Version

Amendment Date: 17 July 2023

Updates to the protocol implemented in this amendment are provided in the table below.

Description of change	Section(s) affected by change	Rationale for Change
Nonsubstantial changes that did not impact the content of the document were made for clarity.	Entire document	For improved clarity of the protocol and adherence to style guide
Removed pretreatment adverse events	Synopsis	Not relevant to this study
Removed low luminance deficit in the study eye as a secondary objective and endpoint	Synopsis, Section 5.1.2, Section 5.2.2	Each individual component of LLD is assessed separately for change over time; the difference between does not provide additional meaningful information.
Added secondary endpoint: The rate of GA lesion growth in the study eye as assessed by FAF at month 12, month 24, and month 36	Synopsis, Section 5.2.2	To provide clarity that both the change and rate of growth in GA lesion size will be evaluated.
Removed monocular critical print size in the study eye as a secondary endpoint	Synopsis, Section 5.2.2	Critical print size is not a common legibility metric. In the APL2-303 and APL2-304 studies critical print size did not help with understanding reading performance. The clinical relevance of a difference in critical print size is not clear.
Added that the secondary objectives and endpoints of monocular and binocular maximum reading speed in the study eye are to be corrected for the number of words read incorrectly	Synopsis, Section 5.2.2	To provide clarity on how maximum reading speed will be calculated.
Removed binocular critical print size in the study eye as a secondary endpoint	Synopsis, Section 5.2.2	Critical print size is not a common legibility metric. In the APL2-303 and APL2-304 studies critical print size did not help with understanding reading performance. The clinical relevance of a difference in critical print size is not clear.
Added secondary endpoint: Change in additional microperimetry parameters (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) at month 12, month 24, and month 36.	Synopsis, Section 5.2.2	To clarify the additional assessments of macular functional response that are obtained from the mesopic microperimetry assessment.

Added NEI VFQ-39 scores to secondary endpoints	Synopsis, Section 5.2.2	To clarify that the additional optional items in the NEI-VFQ-25 instrument being collected allow for the calculation of the NEI VFQ-39 versions of the scale scores.
Specified safety endpoint of incidence of new active choroidal neovascularization (CNV) in the study eye would be as assessed by FA at month 12, month 24, and month 36	Synopsis, Section 5.2.3	To provide additional clarity on how safety endpoint of CNV will be assessed.
Added new safety objective: Incidence and severity of ocular and systemic adverse events (time frame: up to 36 months) of subjects being treated bilaterally with pegcetacoplan	Synopsis, Section 5.2.3	To specify the objective for subjects treated bilaterally.
Specified "in the study eye:" Subjects who permanently discontinue pegcetacoplan in the study eye for any reason will be terminated from the study.	Synopsis, Section 6.1, Section 9.1	To clarify that subjects would be terminated from the study based on pegcetacoplan discontinuation in the study eye (rather than fellow eye)
Added paragraph: "The fellow eyes with GA that meet certain criteria are allowed to receive treatment with pegcetacoplan when the treating physician and subject deem beneficial. The treatment regimen (monthly or EOM) should be decided by the investigator."	Synopsis, Section 6.1	To specify treatment for fellow eye.
Specified "in the study eye:" Subjects will receive monthly pegcetacoplan treatment in the study eye if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Subjects will receive EOM pegcetacoplan treatment in the study eye if they were in the EOM treatment group (pegcetacoplan or sham) in the antecedent study.	Synopsis, Section 6.1	To clarify that these sentences apply to the study eye.
Added: The following inclusion criterion applies to the fellow eye: 2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.	Synopsis, Section 7.1	To clarify which inclusion criteria apply to the fellow eye.
Added: The following exclusion criteria apply to the fellow eye:	Synopsis, Section 7.2	To clarify which exclusion criteria apply to the fellow eye.

1. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary. 2. Any contraindication to IVT injection including current ocular or periocular infection.		
Specified use of version 23.1 of the Medical Dictionary for Regulatory Activities (MedDRA)	Synopsis, Section 10.3.4	For clarity on which version of MedDRA was used.
Modified definition of safety set; added definitions for full analysis set and modified full analysis set	Synopsis, Section 11.2.1, Section 11.2.2, Section 11.2.3	To provide additional detail on the analysis population for efficacy and safety participants.
Specified that efficacy and safety analyses will be summarized by treatment group according to both the antecedent study and the APL2-GA-305 treatment and by visit.	Synopsis, Section 11.3	Clarified how results will be presented.
Updated efficacy analyses in the statistical methods section to include full analysis set and modified full analysis set; included antecedent study baseline	Synopsis, Section 11.3, Section 11.3.2	To provide further details on the planned efficacy analyses.
Changed statistical methods to specify ocular examination findings as well as imaging rather than physical examination findings	Synopsis, Section 11.4	To provide clarity that summaries of ocular examination findings as well as imaging will be conducted rather than summaries of physical examination findings.
Added summary of TEAEs for participants treated bilaterally.	Synopsis, Section 11.4	To specify safety analysis of participants being treated bilaterally.
Changed paragraph to indicate that Syfovre (pegcetacoplan injection) was approved by the FDA	Section 4.2.1	Updated to reflect FDA approval.
Changed Study APL2-103, Study APL2-303 (Derby) and APL2-304 (Oaks) to completed rather than ongoing.	Section 4.2.1	Updated to reflect completed status of studies.

Changed number of participants who have received pegcetacoplan in clinical studies of AMD; updated from 12 to 24 months.	Section 4.2.3	Updated to reflect current number of participants and length of dosing
Added text for benefit/risk assessment, intraocular infection, IOP increase, and exudative AMD from completed phase 2 and phase 3 studies. Additional references added.	Section 4.3; Section 13	Updated to align with investigator's brochure and NDA/MAA submission CTD module 2.5
Updated text for overall benefit/risk conclusion	Section 4.3.2	Updated to align with NDA/MAA submission CTD module 2.5
Removed footnotes (a,b) from IOP measurement in tables	Section 6.5 , Table 1, Table 4; Appendix F, Table 13, Table 16	Removed incorrect footnotes
Added "in the study eye" for new active choroidal neovascularization in footnotes for FAF and SD-OCT images	Section 6.5, Table 1, footnote k; Table 2, footnote h; Table 3, footnote h; Table 4, footnote k; Table 5, footnote h; Table 6, footnote h Section 8.5.1, Appendix F Table 13, footnote k; Table 14, footnote h; Table 15, footnote h; Table 16, footnote k; Table 17, footnote h; Table 18, footnote h	To improve clarity
Changed text regarding use of antiglaucomatous medications for IOP ≥30 mm Hg and recording of AEs in table footnotes	Section 6.5 , Table 1, footnote o; Table 2, footnote k; Table 3, footnote k; Table 4, footnote o; Table 5, footnote k; Table 6, footnote k Section 8.5.1, Appendix F, Table 13, footnote o; Table 14, footnote k; Table 15, footnote k; Table 16, footnote o; Table 17, footnote k; Table 18, footnote k	Updated to clarify when IOP issues should be recorded as AEs
Added line items for fellow eye IOP measurement, fundus autofluorescence, SD-OCT, and NIR; fellow eye pegcetacoplan administration, and fellow eye postinjection assessment	Section 6.5, Table 1, Table 2, Table 3, Table 4, Table 5, Table 6; Appendix F, Table 13, Table 14, Table 15, Table 16, Table 17, Table 18	To reflect new assessments for fellow eyes treated with pegcetacoplan
Added footnote: If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.	Section 6.5, Table 1, Table 2, Table 3, Table 4, Table 5, Table 6; Appendix F, Table 13, Table 14, Table 15, Table 16, Table 17, Table 18	To clarify order of injection if both study eye and fellow eye receive injection on the same day
Changed text to "through month 4"	Section 6.5, Table 4; Appendix F, Table 16; footnote n	Updated to correct month

Added sentence on women of childbearing potential	Section 7.1	Provided definition of women of childbearing potential
Moved section on acceptable methods of contraception from Section 10.3.6 to Section 7.3 and updated text	Section 7.3 , Section 10.3.6	To eliminate duplication and to provide clarification and updates on approved methods of contraception
Corrected text that introduces Table 7	Section 8.1	To reflect what is presented in the table.
Added “and procedures” to the section heading	Section 8.5	To indicate that this section covers both medications and procedures
Added text to specify recording of concomitant medications and procedures	Section 8.5	Updated to clarify how to record ongoing concomitant medications and procedures
Added section for treatment of the fellow eye with pegcetacoplan.	Section 8.5.1	Updated to specify allowable treatment of the fellow eye, as well as treatment and reporting requirements.
Added Sections 8.5.1.1 and 8.5.1.2 for inclusion and exclusion criteria for the fellow eye	Section 8.5.1	To clarify the criteria for inclusion and exclusion of the fellow eye.
Added text to specify how IOP increase in the study eye should be treated	Section 8.5.2	To clarify procedure for anti-VEGF therapy in the event of increased IOP.
Added text to specify recording of anti-VEGF treatments in the fellow eye	Section 8.5.2	Specified that any treatments or therapies administered to the fellow eye while on study should be recorded as concomitant medication/concomitant procedure, except for use of clinical pegcetacoplan, which will be recorded in the designated EDC form.
Added text to indicate that ocular imaging can be performed for safety monitoring during unscheduled visits.	Section 8.5.2	To clarify use of ocular imaging during unscheduled visits.
Deleted sentence: Any treatments or therapies administered to the fellow eye while on study should be recorded as a concomitant medication	Section 8.5.2	Removed incorrect statement; anti-VEGF treatment should be recorded on the specific anti-VEGF form.
Added sentence: During unscheduled visits, unscheduled ocular imaging can be performed for safety monitoring in the study eye or fellow eye.	Section 8.5.2	To specify when ocular imaging can be performed during unscheduled visits
Added section on management of optic ischaemic neuropathy.	Section 8.5.5	To clarify how participants who develop optic ischaemic neuropathy during the study should be assessed.

Added “for the study eye” for the last study visit (Month 36).	Section 8.7	To clarify the timing of the last study visit
Added text: An adverse event should always be reported as the most clinically relevant reason	Section 9.1	For clarification
Added text to clarify procedures for participants transitioning to commercially available pegcetacoplan.	Section 9.2	Clarified that participants transitioning to commercially available pegcetacoplan in the study eye will be asked to return for an early termination visit.
Deleted text referring to collection of medications and treatments for prior ocular surgeries and procedures.	Section 10.1.1.2	To provide clarification on what does/does not need to be collected.
Added: Refer to the eCRF Completion Guidelines (CCG) for detailed guidance.	Section 10.1.1.2	To indicate location of further guidance for recording ocular history.
Removed reference to definition of low-luminance deficit.	Section 10.1.1.3	To clarify this assessment has been excluded.
Specified that questionnaire data would be used to record vision-related quality of life changes	Section 10.1.2	Clarified that the participant-reported changes would specifically be related to vision.
Added text to describe the NEI VFQ-39 subscale	Section 10.1.2.1	For clarification
Changed text to indicate how ongoing medical history and resolved adverse event/procedures will be handled.	Section 10.2.2	Clarified that ongoing and resolved events from the parent study would be considered medical history if reported and deemed clinically relevant by the investigator.
Added text to specify how post-injection IOP increases should be recorded in the study eye and fellow eye.	Section 10.2.6	To clarify how to record “increase in IOP” and its treatment as AE and concomitant medication/concomitant procedure
Updated language to specify how abnormal laboratory test results should be recorded.	Section 10.2.7	To clarify how to record abnormal lab results as AE/SAE
Included “or medical history” in this sentence: Fluctuating or nonsignificant changes in laboratory values or medical history do not necessarily qualify for AE reporting.	Section 10.3.1.1	For clarification
Included additional information regarding BCVA loss and AEs. Added: BCVA loss should not be reported as an AE. Every attempt should be made to report the underlying cause of the change in BCVA as an AE. Any decrease in BCVA from prior visit between 15 and 30 letters with unknown cause	Section 10.3.1.1	To provide additional clarity on when BCVA loss should be classified as an AE.

should be reported as an AE using the term BCVA decrease. If BCVA loss is 30 or more letters from the prior visit, both the underlying cause/diagnosis, if known, and 'BCVA decreased' must be reported as SAEs.		
Added paragraphs to specify how natural disease progression, increase in IOP, and intraocular inflammation should be recorded as AEs or SAEs	Section 10.3.1.1	To provide clarity on recording of AEs and SAEs
Moved section on "Disease Progression" from Section 10.3.7 to Section 10.3.1.1	Section 10.3.1.1, Section 10.3.7	Included in definition section for clarity
Added section on Adverse Events of Special Interest	Section 10.3.3	Listed events of special interest and specified that they will be closely monitored and reported throughout the study.
Modified text about timing of reporting of AEs and SAEs	Section 10.3.4	To clarify that SAEs must be reported within 24 hours of an investigator becoming aware of the SAE.
Added reporting requirements for fellow eye	Section 10.3.4	To clarify how and where to record fellow eye AEs
Deleted paragraph: Any events that occur prior to dosing will be categorized as pretreatment events; events occurring after dosing will be recorded as TEAEs (start date of dosing and, therefore, categorization of the event will be dependent on randomization assignment).	Section 10.3.4	Randomization mentioned in this paragraph is not relevant to this study.
Modified title of section from "Reporting Adverse Events" to "Reporting Adverse Events to Health Authorities and Ethics Committees"	Section 10.3.5	For clarification
Updated language regarding pregnancy	Section 10.3.6	To comply with updated guidance consideration for inadvertent pregnancy in clinical trials
Removed requirement to follow and collect additional samples from participants with positive results for anti–pegcetacoplan peptide or anti-PEG antibodies in the last dosed sample after study discontinuation.	Section 10.6.1	Pegcetacoplan has a very low risk profile for immunogenicity when dosed IVT in GA based on two phase 3 studies (Studies APL2-GA-303 and APL2-GA-304) where no follow-up was performed. In these studies, the serum anti-peptide and anti-PEG ADA incidence was low and transient and not attributable to treatment (sham was similar to treated groups). Additionally, there was no observed correlation of serum ADAs and ocular or non-

		ocular AEs, including intraocular inflammation. Therefore, following up of serum ADAs for IVT pegcetacoplan has no clinical value.
Added estimand for the change from baseline in GA lesion size; added Table 12	Section 11.3.2	To provide clarity on what the estimand for the change from baseline in GA lesion size is.
Added the following: Descriptive summaries will be presented for treated fellow eye based on APL2-GA-305 baseline.	Section 11.3.2	To provide clarity.
Changed names of baseline for analysis	Section 11.4	To provide clarity.
Clarified how safety assessments of IOP, ocular examination, NL-BCVA, and ocular imaging will be summarized.	Section 11.4	To provide further clarity on the safety assessments that will be summarized.
Removed text “No formal interim analysis is planned.”	Section 11.6	Removed unnecessary text and specified that data may be analyzed at different times for specific reasons
Renumbered Tables 12 through 17 to Tables 13 through 18.	Appendix F	Added a table, which required these tables to be renumbered.
Added Appendix for country-specific protocol changes	Appendix G	To align the protocol across sites as specified by the EU-CTR.

1. SYNOPSIS

Name of Sponsor/Company:
Apellis Pharmaceuticals, Inc

Name of Investigational Product, Dosage, and Mode of Administration:
Pegcetacoplan, 15 mg/100 µL (monthly or every other month [EOM]), intravitreal (IVT) injections

Name of Active Ingredient:
Pegcetacoplan (APL-2)

Protocol Number: APL2-GA-305	**Phase: 3**

Title of Study:
A phase 3 open-label, multicenter, extension study to evaluate the long-term safety and efficacy of pegcetacoplan in participants with geographic atrophy secondary to age-related macular degeneration

Objectives:

Primary: To evaluate the long-term safety of IVT-injected pegcetacoplan

Secondary:

1. To assess changes in the total area of geographic atrophy (GA) lesion in the study eye measured by fundus autofluorescence (FAF).
2. To assess changes in visual function as measured by:
   a. Normal-luminance best-corrected visual acuity score (NL-BCVA) in the study eye
   b. Low-luminance best-corrected visual acuity score (LL-BCVA) in the study eye
   c. Reading speed in the study eye
3. To assess the macular functional response as assessed by mesopic microperimetry in the study eye (selected participants [those who had the assessment performed in the antecedent study] only).
4. To evaluate changes in participant-reported outcomes as measured by:
   a. National Eye Institute Visual Functioning Questionnaire 25 Item Version (NEI VFQ-25)
   b. Functional Reading Independence (FRI) Index

Endpoints:

Primary:

- Incidence and severity of ocular and systemic adverse events (time frame: up to 36 months)

Secondary:

Change from baseline in the following parameters:

- The total area of GA lesion(s) in the study eye (in mm^2) as assessed by FAF at month 12, month 24, and month 36
- The rate of change in GA lesion growth in the study eye as assessed by FAF at month 12, month 24, and month 36
- NL-BCVA score (study eye) as assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) chart at month 12, month 24, and month 36

- LL-BCVA score (study eye) as assessed by ETDRS chart at month 12, month 24, and month 36
- Monocular maximum reading speed (study eye), corrected for the number of words read incorrectly, as assessed by Minnesota Reading (MNRead) charts or Radner charts at month 12, month 24, and month 36
- Binocular maximum reading speed, corrected for the number of words read incorrectly, as assessed by MNRead charts or Radner charts at month 12, month 24, and month 36
- The number of scotomatous points (study eye) assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36
- Macular sensitivity (study eye) as assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36
- Change in additional microperimetry parameters in the study eye (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) at month 12, month 24, and month 36
- Mean Functional Reading Independence (FRI) Index score at month 12, month 24, and month 36
- National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25 and NEI VFQ-39 [at selected sites]) composite score, near activity subscale score, distance activity subscale score, and NEI VFQ-25 driving subscale score at month 12, month 24, and month 36

Safety:

- Presence of antibodies to the PEG and/or peptide moiety of pegcetacoplan (time frame: up to 36 months)
- Incidence of new active choroidal neovascularization in the study eye as assessed by FA at month 12, month 24, and month 36
- Incidence and severity of ocular and systemic adverse events (time frame: up to 36 months) of participants being treated bilaterally with pegcetacoplan

Overall Study Design:

This is a phase 3, multicenter, 36-month, open-label extension study to assess the safety and efficacy of long-term IVT injections of pegcetacoplan in participants with GA secondary to age-related macular degeneration (AMD).

The study will enroll approximately 1200 participants across approximately 250 multinational sites who previously participated in a study evaluating pegcetacoplan for GA. Screening can happen on the same day as the last visit in the antecedent study or within 60 days of the last visit. Participants who meet all inclusion and none of the exclusion criteria will be included in this study. Participants will receive monthly pegcetacoplan treatment in the study eye if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Participants will receive EOM pegcetacoplan treatment in the study eye if they were in the EOM treatment group

(pegcetacoplan or sham) in the antecedent study. The study eye will be the same eye as the study eye of the antecedent study.

Participants who previously developed exudative AMD in the study eye in the antecedent study and are currently receiving anti–vascular endothelial growth factor (VEGF) therapy are eligible to participate in this extension study and will continue to receive pegcetacoplan. Participants who developed exudative AMD in the parent study or in this extension study will remain in the study and may also receive anti-VEGF in addition to pegcetacoplan based on the investigator assessment following standard of care.

Participants who permanently discontinue pegcetacoplan in the study eye will also be terminated from the study. Participants who discontinue the study should complete the early termination visit.

The fellow eyes with GA that meet certain criteria are allowed to receive treatment with pegcetacoplan when the treating physician and participant deem beneficial. The treatment regimen (monthly or EOM) should be decided by the investigator.

Study Treatment Groups:

Treatment Group	Abbreviation
Pegcetacoplan, 15 mg/100 µL, monthly for up to 36 months	PM
Pegcetacoplan, 15 mg/100 µL, EOM for up to 36 months	PEOM

Abbreviations: EOM = every other month; PEOM = pegcetacoplan every other month; PM = pegcetacoplan monthly.

Number of Participants (Planned):

Approximately 1200 participants across approximately 250 multinational sites who participated in a prior study in which they were administered pegcetacoplan for treatment of GA.

Diagnosis and Main Criteria for Inclusion: GA secondary to AMD

Main Criteria for Inclusion:

Ocular-specific inclusion criteria apply to the **study eye**.

1. Participated in APL2-103 (NCT03777332) or completed the treatment at month 24 of either APL2-303 (Derby, NCT03525613) or APL2-304 (Oaks, NCT03525600). Specifically, for the APL2-303 and APL2-304 studies, the following criterion also applies:
   a. Participants who did not permanently discontinue treatment but missed the month 24 visit are also eligible to participate in this extension study; however, to be eligible, these participants must be screened within 60 days from the last day of the expected month 24 visit window for the antecedent study.
2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.
3. Female participants must be:
   a. Women of nonchildbearing potential, or

b. Women of childbearing potential with a negative serum pregnancy test at screening and must agree to use protocol defined methods of contraception for the duration of the study and 90 days after their last dose of pegcetacoplan, and refrain from breastfeeding for the duration of the study.

4. Males with female partners of childbearing potential must agree to use protocol defined methods of contraception and agree to refrain from donating sperm for the duration of the study and for 90 days after their last dose of pegcetacoplan.
5. Willing and able to give informed consent and to comply with the study procedures and assessments.

Fellow Eye Inclusion Criteria

The following inclusion criterion applies to the fellow eye:

2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.

Main Criteria for Exclusion:

Ocular-specific exclusion criteria apply to the **study eye**.

1. Participants who permanently discontinued the study drug prior to month 24 in the APL2-303 or APL2-304 studies and remained only for safety assessments. Temporary pause of the study drug is not exclusionary.
2. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.
3. Any contraindication to IVT injection including current ocular or periocular infection.
4. Medical or psychiatric condition that, in the opinion of the investigator, is clinically significant and not suitable for study participation or make consistent follow-up over the 36-month treatment period unlikely.
5. Known hypersensitivity to fluorescein sodium for injection or hypersensitivity to pegcetacoplan or any of the excipients in pegcetacoplan solution.
6. Pregnancy, breastfeeding, or positive pregnancy test.

Fellow Eye Exclusion Criteria

The following exclusion criteria apply to the fellow eye:

2. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.
3. Any contraindication to IVT injection including current ocular or periocular infection.

Duration of Treatment: 36 months

Statistical Methods:

Unless otherwise stated, all efficacy and safety analyses will be summarized by treatment group according to both the antecedent study (APL2-103, APL2-303, and APL2-304) treatment and the APL2-GA-305 treatment and by visit. Continuous variables will be summarized using descriptive statistics (eg, mean, standard deviation, median, minimum, and maximum). For categorical variables, the frequency and percentage in each category will be displayed.

Populations for Analysis:

Safety Set:

The safety set will consist of all enrolled participants who receive at least one injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed according to the actual treatment received in the antecedent study and study APL2-GA-305.

Full Analysis Set:

The full analysis set will consist of all enrolled participants who receive at least one injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed

according to the treatment assigned when enrolled in the antecedent study and study APL2-GA-305.

Modified Full Analysis Set

The modified full analysis set will consist of all participants who are in the ITT set of APL2-303 and APL2-304 antecedent studies, haven't been enrolled in APL2-103, and receive at least one injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed according to the treatment assigned when enrolled in the antecedent study and study APL2-GA-305.

Safety:

Safety analyses will be conducted over the safety set. The change from baseline in safety parameters will be assessed. The baseline used for the safety parameters is defined as the last available nonmissing assessment prior to first study drug administration in the study eye in this study.

Adverse events will be coded using version 23.1 of the Medical Dictionary for Regulatory Activities (MedDRA). Treatment-emergent adverse events (TEAEs) will be summarized by System Organ Class, Preferred Term, and dose for number of participants and proportion reporting the event. Similar summaries will be produced for serious adverse events, AEs leading to termination, severe AEs, and AEs with at least a possible relationship to the investigational product. The intensity of AEs and the relationship to investigational product will be summarized for each System Organ Class and Preferred Term. Similar summaries of TEAEs after initiation of pegcetacoplan treatment in the fellow eye will also be presented for the subgroup of participants being treated bilaterally with pegcetacoplan.

Vital signs (systolic and diastolic blood pressure, pulse, body temperature, and respiratory rate), and ,findings of ocular examination and ocular imaging, will be summarized using appropriate descriptive statistics.

Efficacy:

Efficacy analyses will be performed using the full analysis set and modified full analysis set. There will be 2 baselines used in the efficacy analysis of this study: antecedent study baseline is defined as the baseline value in the antecedent studies, APL2-103, APL2-303 and APL2-304 participant had enrolled in; and APL2-GA-305 baseline is defined as the last available nonmissing assessment prior to first study drug administration in the study eye in study APL2-GA-305.

Absolute values and changes from antecedent study baseline will be summarized by antecedent treatment from the APL2-103, APL2-303, and APL2-304 studies and overall and by using descriptive statistics. The change from antecedent study baseline in the continuous efficacy endpoint (such as total area of GA lesion at each visit) will be summarized and assessed with a mixed effect model for repeated measure.

The change from APL2-GA-305 baseline in the continuous efficacy endpoint (such as total area of GA lesion at each visit) will be summarized and assessed with a mixed effect model for repeated measure that includes observed data from all treatment arms.

Planned Analysis:

The analysis of data from the first 12 months of the study will be performed when (1) all patients have completed study visits through month 12 or have discontinued from the study prior to month 12 and (2) all data from the first 12 months of the study are in

the database and have been reviewed. The analysis of data from the first 24 months of the study will be performed in a similar manner. The final study analysis based on data from the complete study will be performed when all patients have either completed the 3-year study period (ie, study visits through month 36) or have discontinued early from the study, all data from the study are in the database, and the database is locked.
Data Monitoring Committee: An external, independent data monitoring committee (DMC) will be formed with the purpose of reviewing all data across the conduct of the study on an ongoing basis. The DMC will follow a charter that will outline the frequency of meetings and the roles and responsibilities of all members. The DMC will meet at the beginning of the study and approximately every 12 months thereafter and will perform a review of all relevant events on an ongoing basis. An ad hoc meeting of the DMC may be convened by the sponsor or the DMC chairperson at any time between the regularly scheduled DMC meetings and data reviews if warranted by new safety information or for any other reason. The DMC will communicate its recommendations to the sponsor, who will notify the appropriate health authorities according to local regulatory requirements.

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3. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations and specialist terms are used in this study protocol.

Abbreviation/ specialist term	Definition
ADA	antidrug antibodies
AE	adverse event
AMD	age-related macular degeneration
BCVA	best-corrected visual acuity
C3	complement component 3
C3a	complement component 3, fragment a
C3d	complement component 3, fragment d
C5a	complement component 5, fragment a
CFB	complement factor B
CFH	complement factor H
CFI	complement factor I
CNV	choroidal neovascularization
COVID-19	coronavirus disease 2019
CRF	case report form
DMC	data monitoring committee
EDC	electronic data capture
EOM	every other month
ETDRS	early treatment diabetic retinopathy study
FAF	fundus autofluorescence
FFA	fundus fluorescein angiography
FRI (Index)	Functional Reading Independence Index
GA	geographic atrophy
GCP	Good Clinical Practice
HCG	human chorionic gonadotropin
IB	investigator's brochure
ICF	informed consent form
ICH	International Council for Harmonisation
IEC	independent ethics committee
IND	investigational new drug
IOP	intraocular pressure
IRB	institutional review board
IVT	intravitreal

Abbreviation/ specialist term	Definition
LL-BCVA	low-luminance best-corrected visual acuity
MAC	membrane attack complex
MedDRA	Medical Dictionary for Regulatory Activities
MNRead	Minnesota reading chart; Minnesota Low-Vision Reading Test
MOP	manual of procedures
NEI VFQ-25	National Eye Institute Visual Functioning Questionnaire 25-Item Version
NEI VFQ-39	National Eye Institute Visual Functioning Questionnaire 39-Item Version
NL-BCVA	normal-luminance best-corrected visual acuity
NOEL	no observed effect level
OCT	optical coherence tomography
OCT-A	optical coherence tomography angiography
PEG	polyethylene glycol
PEOM	pegcetacoplan injection every other month
PI	principal investigator
PM	pegcetacoplan injection monthly
RPE	retinal pigment epithelium
SAE	serious adverse event
SAP	statistical analysis plan
SC5b-9	soluble terminal complement complex (ie, soluble analog of MAC)
SD-OCT	spectral domain optical coherence tomography
SoA	schedule of activities
TEAE	treatment-emergent adverse event
VA	visual acuity
VEGF	vascular endothelial growth factor
WHO	World Health Organization
WOCBP	women of childbearing potential

4. INTRODUCTION

This study is being conducted as part of a series of studies for the clinical development of pegcetacoplan (also known as APL-2) for advanced age-related macular degeneration (AMD) (neovascular AMD and geographic atrophy [GA]). The study will be conducted in compliance with the protocol, Good Clinical Practice (GCP), and applicable regulatory requirements. The participant population will comprise adult male and female participants with GA secondary to AMD.

4.1. Study Rationale

The rationale for the use of a complement inhibitor in patients with AMD is based on evidence from both human and animal studies. Human biochemical, genetic, and clinical lines of evidence indicate that the complement system plays a role in the etiology of AMD. Complement component 3 (C3), the membrane attack complex (MAC), and complement factor H (CFH), are present in drusen and basal laminar deposits in eyes from patients with AMD (Crabb et al. 2002; Hageman et al. 2005; Lommatzsch et al. 2008; Mullins et al. 2000). Genetic variants of CFH (Hageman et al. 2005; Edwards et al. 2005; Haines et al. 2005; Klein et al. 2005; Maller et al. 2006), C3 (Seddon et al. 2013; Yates et al. 2007), complement factor I (CFI) (van de Ven et al. 2013), and other complement components (Fritsche et al. 2013; Gold et al. 2006; Horie-Inoue and Inoue 2014) have been associated with altered risks for the development of both the neovascular and atrophic forms of AMD. Patients with AMD also have signs of systemic complement activation, exhibiting higher serum levels of complement factor B (CFB), complement component 3, fragment a (C3a), complement component 5, fragment a (C5a), soluble terminal complement complex (SC5b-9), complement component 3, fragment d (C3d), and complement component B, fragment a (Ba) compared with age-matched controls (Hecker and Edwards 2010; Hecker et al. 2010; Machalinska et al. 2009; Scholl et al. 2008).

4.2. Background

4.2.1. Age-Related Macular Degeneration

Age-related macular degeneration is the leading cause of severe vision loss in people over the age of 65 in the US and other Western countries (Rein et al. 2009). In the US, about 1.75 million people have the advanced forms of AMD (Friedman et al. 2004). The early signs of AMD (drusen and pigmentary changes) are common in individuals over age 65 and precede the late-stage forms, which are visually devastating. The late-stage forms of AMD are classified into either macular neovascularization (neovascular, wet, or exudative AMD) or GA.

Geographic atrophy is responsible for approximately 20% of all cases of legal blindness in North America (Holz 2014) and is characterized by progressive loss of the retinal pigment epithelium (RPE) and concurrent atrophy of photoreceptors and choriocapillaris (Holz et al. 2014; Sunness et al. 1999a; Sunness et al. 1999b). Clinically, GA can result in irreversible visual function loss including reading, night vision, and dark adaptation. Once the atrophy progresses to the central fovea, severe vision loss and legal blindness can occur.

Genetic susceptibility has become increasingly recognized as a risk factor and important contributor to AMD. More than 19 genetic polymorphisms have been demonstrated to influence AMD risk, with as many as 5 of these encoded by genes that modulate the complement system.

Inflammatory processes, especially those mediated by complement are thought to play a key role in AMD (Sunness et al. 1999a). It is thought that these may contribute to loss of choriocapillaris, photoreceptors, and RPE cells.

GA is usually bilateral and relentlessly progressive. Syfovre (pegcetacoplan injection) was approved by FDA as the first treatment for GA in the US in February 2023.

The clinical development plan for pegcetacoplan includes 1 completed phase 1b (Study APL2-103) and 2 completed phase 3 clinical studies (Study APL2-303 [Derby] and APL2-304 [Oaks]) considered antecedent studies to this extension phase. An overview of available information regarding pegcetacoplan follows below. Further details can be found in the current pegcetacoplan investigator's brochure.

4.2.2. Pegcetacoplan

Pegcetacoplan is a PEGylated cyclic peptide inhibitor of complement C3. Pegcetacoplan is formed by 2 identical pentadecapeptides (combining a bioactive cyclic tridecapeptide C3-inhibiting moiety and a 2-amino acid linker) covalently coupled to each end of a linear 40 kilodalton (kDa) polyethylene glycol (PEG) chain. There are 2 peptide moieties per molecule of pegcetacoplan.

The peptide portion of the drug binds to complement C3 and is a broad inhibitor of the complement cascade, a biological process that is part of innate immunity and is involved in multiple inflammatory processes. The PEGylation of the molecule imparts slower clearance from the vitreous humor following administration.

4.2.3. Clinical Data

Clinical data from ongoing and completed studies with pegcetacoplan in participants with AMD indicates that pegcetacoplan is generally well tolerated and reduces the progression of GA when dosed for 24 months. In Study APL2-303 and Study APL2-304, 839 participants received at least one dose (15 mg/injection) of pegcetacoplan.

Additional details can be found in the current pegcetacoplan investigator's brochure.

4.3. Benefit/Risk Assessment

IVT pegcetacoplan, administered either monthly or every other month (EOM), demonstrated a clinically meaningful reduction in GA lesion growth at month 12 compared with sham in both phase 3 studies (Studies APL2-303 and APL2-304) as well as in the phase 2 study POT-CP121614. The treatment effect was sustained through month 24 in both studies APL2-303 and APL2-304. GA lesion growth was correlated with visual function decline and treatment effect in reducing lesion growth corresponds to a trend at 24 months toward visual function benefit measured by new scotomatous points in the junctional zone.

The safety monitoring practices employed by this protocol (complete ophthalmologic exam, intraocular pressure (IOP) monitoring, optical coherence tomography (OCT), fluorescein angiography, vital signs, hematology, serum chemistry, urinalysis, physical exam, vital signs, and adverse event [AE] questioning) are adequate to protect the participants' safety. There are also risks associated with the ophthalmic procedures required for participants in this study. However, these are all standard procedures that are widely performed in ophthalmology.

Risk of intraocular infection including endophthalmitis is deemed higher because of the IVT injection procedure, possibly because of exposure to the participant's own flora or a breach in aseptic technique. To minimize the risk of endophthalmitis in participants receiving pegcetacoplan through IVT administration, a standardized procedure that includes the use of topical povidone-iodine (Betadine) and sterile instruments must be used for the injection procedure. In the event of infection after IVT pegcetacoplan administration, local treatment guidelines for ocular infection should be followed.

After IVT injection, transient increase in IOP should be anticipated in the period immediately after injection. In addition, as with any other IVT injection, pegcetacoplan given IVT can lead to complications such as retinal detachment, retina hemorrhage, and traumatic cataract.
The administration of medications through the IVT route can lead to the development of intraocular inflammation. This inflammation is typically mild with transient signs of inflammation and visual symptoms.

In all participants, the combined month 24 results of APL2-303 and APL2-304 showed that the incidence of study eye exudative AMD in the pegcetacoplan monthly (PM) group (12.2%) was higher than in the pegcetacoplan every other month (PEOM) group (6.7%). The rate of study eye exudative AMD per 100 patient-years in the PM group (7.5) was higher than in the PEOM group (3.9). The incidence of exudative AMD AEs in the study eye was higher in participants with baseline fellow eye choroidal neovascularization (CNV) than in the subgroup of participants without baseline fellow eye CNV in the pegcetacoplan pooled (13.9% vs 8.3%) and sham pooled (9.2% vs 1.5%) groups. This observation was consistent with reports in published studies (Chew et al. 2014; Klein et al. 2008; Sunness et al. 1999c).

Most events were mild to moderate in severity, did not lead to treatment discontinuation, and had outcomes as expected after anti–vascular endothelial growth factor (VEGF) treatment (anti-VEGF treatment was concomitant with pegcetacoplan treatment). Exudative AMD is considered an important potential risk for IVT pegcetacoplan. Risk mitigation for exudative AMD is achieved by informing physicians of this risk through the product information. Patients receiving pegcetacoplan should be monitored for signs of exudative AMD. If IVT anti-VEGF is required for treatment of exudative AMD, it should be administered at least 30 minutes apart from pegcetacoplan.

Participants who developed exudative AMD continued treatment with pegcetacoplan and received anti-VEGF therapy per the label (regardless of the activity of CNV) in Studies APL2-303 and APL2-304. For Study APL2-GA-305, concomitant anti-VEGF therapy will be selected and administered at the investigator's discretion per the study protocol.

The amount of blood (see Section 10.2.8) planned for collection from each participant at any given visit and over the 36 months of the study is not anticipated to pose an undue risk in this participant population.

Apellis is not currently aware of any evidence associating pegcetacoplan use with specific risks or complications of COVID-19. Apellis recognizes the need to consider the public health risks of the COVID-19 pandemic within the context of conducting a clinical trial. Since these risks may change as the pandemic evolves, and may vary based on geographic location, Apellis will continue to evaluate the risk/benefit around study conduct on an ongoing and patient-by-patient basis.

IVT pegcetacoplan administered monthly or EOM was well tolerated and manageable in participants with GA secondary to AMD through 24 months of treatment. The benefits of pegcetacoplan outweigh the risks associated with IVT treatment.

4.3.1. COVID-19 Risk Mitigation Measures

In the event that an investigative site is closed or participant is unable/unwilling to attend study visit due to COVID-19 restrictions, and, if in the opinion of the investigator it is in the participant's best interest to continue in the study, the following mitigation measures may be implemented for the study and utilized if deemed necessary and authorized by the sponsor, including but not limited to:

- Collection of AEs or serious adverse events (SAEs) should be done over the phone and documented in the source documents and in the respective CRF page.
- Minimized schedule of assessment can be followed during COVID-19 restrictions (Appendix F), including the use of certified local laboratory.
- The electronic data capture (EDC) system will capture any missed assessments related to COVID-19.
- Where applicable, relevant study documentation will be updated and communicated to health authorities and/or institutional review board (IRBs)/independent ethics committee (IECs) as required.

4.3.2. Overall Benefit/Risk Conclusion

A significant unmet medical need exists for a treatment for patients with GA. In addition to the evidence provided from the clinical studies, the current understanding of the role of the complement system, including the central complement component C3 in the pathogenesis of GA, supports the biological plausibility of targeting C3 with pegcetacoplan.

In summary, the efficacy and safety data generated from the two well-controlled large phase 3 studies demonstrate a positive benefit-risk assessment of 15 mg/0.1 mL IVT PM and EOM in patients with GA secondary to AMD.

5. TRIAL OBJECTIVES AND ENDPOINTS

5.1. Objectives

5.1.1. Primary Objective

- To evaluate the long-term safety of IVT-injected pegcetacoplan

5.1.2. Secondary Objectives

1. To assess changes in the total area of GA lesion in the study eye measured by fundus autofluorescence (FAF)
2. To assess changes in visual function as measured by:
   a. Normal-luminance best-corrected visual acuity score (NL-BCVA) in the study eye
   b. Low-luminance best-corrected visual acuity score (LL-BCVA) in the study eye
   c. Reading speed in the study eye
3. To assess the macular functional response as assessed by mesopic microperimetry in the study eye (selected participants [those who had the assessment performed in the antecedent study] only).
4. To evaluate changes in participant-reported outcomes as measured by:
   a. National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25)
   b. Functional Reading Independence (FRI) Index

5.1.3. Additional Safety Objectives

1. To assess the presence of antibodies to the PEG and/or peptide moiety of pegcetacoplan
2. To assess the incidence of new active choroidal neovascularization (CNV) in the study eye

5.2. Endpoints

5.2.1. Primary Objective Endpoints

- Incidence and severity of ocular and systemic AEs (time frame: up to 36 months)

5.2.2. Secondary Objective Endpoints

Change from baseline in the following parameters:

- The total area of GA lesion(s) in the study eye (in mm^2) as assessed by FAF at month 12, month 24, and month 36
- The rate of GA lesion growth in the study eye as assessed by FAF at month 12, month 24, and month 36

- NL-BCVA score (study eye) as assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) chart at month 12, month 24, and month 36
- LL-BCVA score (study eye) as assessed by ETDRS chart at month 12, month 24, and month 36
- Monocular maximum reading speed (study eye) corrected for number of words read incorrectly as assessed by Minnesota Reading (MNRead) charts or Radner charts at month 12, month 24, and month 36
- Binocular maximum reading speed, corrected for number of words read incorrectly, as assessed by MNRead charts or Radner charts at month 12, month 24, and month 36
- The number of absolute scotomatous points (study eye) assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36
- Macular sensitivity (study eye) as assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36
- Change in additional microperimetry parameters in the study eye (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) at month 12, month 24, and month 36
- Mean FRI Index score at month 12, month 24, and month 36 (Appendix B)
- NEI VFQ25 and NEI VFQ-39 (at select sites) composite score, near activity subscale score, distance activity subscale score, and NEI VFQ-25 driving subscale score at month 12, month 24, and month 36

5.2.3. Safety Endpoints

- Presence of antibodies to the PEG and/or peptide moiety of pegcetacoplan (time frame: up to 36 months)
- Incidence of new active CNV in the study eye as assessed by FA at month 12, month 24, and month 36
- Incidence and severity of ocular and systemic adverse events (time frame: up to 36 months) of participants being treated bilaterally with pegcetacoplan

6. STUDY DESIGN

6.1. Overall Study Design

This is a phase 3, multicenter, 36-month, open-label extension study to assess the safety and efficacy of long-term IVT injections of pegcetacoplan in participants with GA secondary to AMD.

The study will enroll approximately 1200 participants across approximately 250 multinational sites that previously participated in a study evaluating pegcetacoplan for GA. Screening and baseline assessments can happen on the same day as the last visit in the antecedent study or within 60 days of the last visit. Participants who meet all inclusion and none of the exclusion criteria will be included in this study. Participants will receive monthly pegcetacoplan treatment in the study eye if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Participants will receive EOM pegcetacoplan treatment in the study eye if they were in the EOM treatment group (pegcetacoplan or sham) in the antecedent study. The study eye will be the same eye as the study eye of the antecedent study.

Participants who permanently discontinue pegcetacoplan in the study eye for any reason will be terminated from the study. Participants who discontinue the study should complete the early termination visit.

The fellow eyes with GA that meet certain criteria are allowed to receive treatment with pegcetacoplan when the treating physician and participant deem beneficial. The treatment regimen (monthly or EOM) should be decided by the investigator. See Section 8.5.1 for additional details.

Study Treatment Groups:

Treatment Group	Abbreviation
Pegcetacoplan, 15 mg/100 µL, monthly for up to 36 months	PM
Pegcetacoplan, 15 mg/100 µL, EOM for up to 36 months	PEOM

Abbreviations: EOM = every other month; PEOM = pegcetacoplan every other month; PM = pegcetacoplan monthly.

6.2. Scientific Rationale for Study Design

The purpose of this study is to continue evaluation of the long-term safety and efficacy of pegcetacoplan in the treatment of GA.

6.3. Dose Selection

All participants in this extension study will receive treatment with pegcetacoplan (15 mg/100 µL). Dosing will occur on the dosing regimen as in the antecedent study (ie, monthly or EOM, with no interruptions in dosing).

The dose (15 mg/injection) of pegcetacoplan that will be evaluated in this clinical study is the same that was evaluated in the antecedent studies and is expected to result in drug concentrations approximately 4.5-fold lower than the no observed effect level observed in cynomolgus monkeys.

6.4. Estimated Study Duration

This study is designed to last for 3 years. The end of the study is defined as the date of the last visit of the last participant in the study.

6.5. Schedule of Activities

The Schedule of Activities (SoA) for the monthly treatment group is shown in Table 1, Table 2, and Table 3. Table 4, Table 5, and Table 6 show the SoA for the EOM treatment group. Appendix F contains the SoA that can be followed during COVID-19 restrictions.

Table 1: Schedule of Activities—Monthly Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment												ET[q]
Visit #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Day	1	1	30	60	90	120	150	180	210	240	270	300	330	360	
Month	0	0	1	2	3	4	5	6	7	8	9	10	11	12	
Window (+ or – days)	N/A[a,b]		8	8	8	8	8	8	8	8	8	8	8	8	
Informed consent	x														
Demographic data	x														
Inclusion/exclusion criteria	x	x													
Blood draw—safety labs[a,b,c,s,t]		x												x	x
Urine sample collection[a,b,c]		x												x	x
Urine pregnancy test[a,b,c,d]		x	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a,b,c]		x						x						x	x
Vital signs[a,b,e]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination[a,b,f]		x												x	x
BCVA[a,b,g]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[a,b,g]		x						x						x	x
Slitlamp examination[a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy[a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement		x	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[a,b,g,h]		x						x						x	x
Mesopic microperimetry[i]		x						SE						x	x
NEI VFQ-25[a,b,j]		x												x	x
FRI Index[a,b,j]		x												x	x
SD-OCT[a,b,k,r]		x						x						x	x
FAF[a,b,k]		x						x						x	x
NIR[a,b,k]		x						x						x	x
DCFP[a,b,k]		x												x	x
FFA[a,b,k]		x												x	x
OCT-A[a,b,k]		x						x						x	x
Study eye pegcetacoplan administration[a,b,l,m]		x	x	x	x	x	x	x	x	x	x	x	x	x	
Follow-up call[n]		x	x	x	x										
Study eye postinjection assessment[a,b,o]		x	x	x	x	x	x	x	x	x	x	x	x	x	

Table 1: Schedule of Activities—Monthly Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment												ET[q]
Visit #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Day	1	1	30	60	90	120	150	180	210	240	270	300	330	360	
Month	0	0	1	2	3	4	5	6	7	8	9	10	11	12	
Window (+ or – days)	N/A[a,b]		8	8	8	8	8	8	8	8	8	8	8	8	
Concomitant medication/ concomitant ocular procedures[a,b,p]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events[a,b]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan															
Fellow eye IOP measurement		To be completed prior to fellow eye pegcetacoplan administration													
Fellow eye FAF, SD-OCT, and NIR[k]		To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule													
Fellow eye pegcetacoplan administration[u]		Regimen per PI's discretion													
Fellow eye postinjection assessment[o]		To be completed following fellow eye pegcetacoplan administration													

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LLBCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] The screening and baseline visits can occur on the same day as the last visit of the antecedent study or within 60 days of the last visit. Information collected at the last visit of the antecedent study, including safety laboratory tests and ocular imaging, can be used for the baseline visit. However, if data were not collected at the last visit of the antecedent study, then it is required to be collected at the baseline assessment. All assessments must be completed within a 3-day period. The study visit windows are calculated from the date of the baseline dose unless the dose was missed. If the dose was missed, the study visit window is calculated from the date study assessments were completed.

[b] Pegcetacoplan administration must occur within 3 days of completing screening and baseline assessments.

[c] Obtain prior to fluorescein angiography and before study drug administration.

[d] Beginning at Day 1, perform the urine pregnancy test only for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[e] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[f] Height and weight should be collected at baseline.

[g] Perform assessments prior to dilating the eyes.

[h] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select participants[those who had the assessment performed in the antecedent study]) will be performed postdilation.

[j] To be administered by the site staff prior to any other assessments performed on that day.

[k] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center..

[l] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[m] Pegcetacoplan will not be administered at the month 36 visit.

[n] Starting at Day 1, study participants will be contacted by study site staff within 4 ± 2 days after each study treatment visit (through month 3) to collect any information related to any safety concerns, decrease in vision, eye pain, unusual ocular events, or any new ocular symptoms in the study eye. If the physician determines that there are any safety concerns, a follow-up visit should be scheduled as soon as possible.

[o] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, handmotion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an antiVEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-antiVEGF IOP values must be measured and recorded on the eCRF.

[p] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[q] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[r] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline and treatment with anti-VEGF therapy must only be re-started if disease activity is detected by the investigator.

[s] At screening, serum pregnancy test should be performed for women of childbearing potential. If positive, participant is not eligible to continue in the study.

[t] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. Serum test is positive, study drug should not be administered and an early termination visit should be completed.

[u] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 2: Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ET[m]
Visit #	15	16	17	18	19	20	21	22	23	24	25	26	
Day	390	420	450	480	510	540	570	600	630	660	690	720	
Month	13	14	15	16	17	18	19	20	21	22	23	24	
Window (+ or – days)	8	8	8	8	8	8	8	8	8	8	8	8	
Blood draw—safety labs[a]												x	x
Urine sample collection[a]												x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]						x						x	x
Vital signs[c]	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination												x	x
BCVA[d]	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[d]						x						x	x
Slitlamp examination	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]						x						x	x
Mesopic microperimetry[f]						SE						x	x
NEI VFQ-25[g]												x	x
FRI Index[g]												x	x
SD-OCT[h,n]						x						x	x
FAF[h]						x						x	x
NIR[h]						x						x	x
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]						x						x	x
Study eye pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x	x	
Study eye postinjection assessment[k]	x	x	x	x	x	x	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 2: Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ET [m]
Visit #	15	16	17	18	19	20	21	22	23	24	25	26	
Day	390	420	450	480	510	540	570	600	630	660	690	720	
Month	13	14	15	16	17	18	19	20	21	22	23	24	
Window (+ or – days)	8	8	8	8	8	8	8	8	8	8	8	8	
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan													
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration[o]	Regimen per PI's discretion												
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration												

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 3: Schedule of Activities—Monthly Treatment Group (Year 3)

	Treatment												ET[m]
Visit #	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	
Day	**750**	**780**	**810**	**840**	**870**	**900**	**930**	**960**	**990**	**1020**	**1050**	**1080**	
Month	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	
Window (+ or – days)	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	
Blood draw—safety labs[a]												x	x
Urine sample collection[a]												x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]						x						x	x
Vital signs[c]	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination												x	x
BCVA[d]	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[d]						x						x	x
Slitlamp examination	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]						x						x	x
Mesopic microperimetry[f]						SE						x	x
NEI VFQ-25[g]												x	x
FRI Index[g]												x	x
SD-OCT[h,n]						x						x	x
FAF[h]						x						x	x
NIR[h]						x						x	x
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]						x						x	x
Study eye pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x		
Study eye postinjection assessment[k]	x	x	x	x	x	x	x	x	x	x	x		
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x	x	x	x	x	x	x
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan													

Table 3: Schedule of Activities—Monthly Treatment Group (Year 3)

	Treatment												ET[m]
Visit #	27	28	29	30	31	32	33	34	35	36	37	38	
Day	750	780	810	840	870	900	930	960	990	1020	1050	1080	
Month	25	26	27	28	29	30	31	32	33	34	35	36	
Window (+ or – days)	8	8	8	8	8	8	8	8	8	8	8	8	
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration[o]	Regimen per PI's discretion												
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration												

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or

anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 4: Schedule of Activities—Every-Other-Month Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment						ET[q]
Visit #	1	2	3	4	5	6	7	8	
Day	1	1	60	120	180	240	300	360	
Month	0	0	2	4	6	8	10	12	
Window (+ or – days)	N/A[a,b]		16	16	16	16	16	16	
Informed consent	x								
Demographic data	x								
Inclusion/exclusion criteria	x	x							
Blood draw—safety labs[a,b,c,s,t]		x						x	x
Urine sample collection[a,b,c]		x						x	x
Urine pregnancy test[a,b,c,d]		x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a,b,c]		x			x			x	x
Vital signs[a,b,e]		x	x	x	x	x	x	x	x
Physical examination[a,b,f]		x						x	x
BCVA[a,b,g]		x	x	x	x	x	x	x	x
LL-BCVA[a,b,g]		x			x			x	x
Slitlamp examination[a,b]		x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy[a,b]		x	x	x	x	x	x	x	x
Study eye IOP measurement		x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[a,b,g,h]		x			x			x	x
Mesopic microperimetry[i]		x			SE			x	x
NEI VFQ-25[a,b,j,]		x						x	x
FRI Index[a,b,j]		x						x	x
SD-OCT[a,b,k,r]		x			x			x	x
FAF[a,b,k]		x			x			x	x
NIR[a,b,k]		x			x			x	x
DCFP[a,b,k]		x						x	x
FFA[a,b,k]		x						x	x
OCT-A[a,b,k]		x			x			x	x
Study eye pegcetacoplan administration[a,b,l,m]		x	x	x	x	x	x	x	
Follow-up call[n]		x	x	x					
Study eye postinjection assessment[a,b,o]		x	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[a,b,p]		x	x	x	x	x	x	x	x

Table 4: Schedule of Activities—Every-Other-Month Treatment Group (Year 1)

	Screening[a,b]	Baseline[a, b]	Treatment						ET[q]
Visit #	1	2	3	4	5	6	7	8	
Day	1	1	60	120	180	240	300	360	
Month	0	0	2	4	6	8	10	12	
Window (+ or – days)	N/A[a,b]		16	16	16	16	16	16	
Adverse events[a,b]		x	x	x	x	x	x	x	X
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan									
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration								
Fellow eye FAF, SD-OCT, and NIR[k]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule								
Fellow eye pegcetacoplan administration[u]		Regimen per PI's discretion							
Fellow eye postinjection assessment[o]		To be completed following fellow eye pegcetacoplan administration							

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25-Item Version; NIR = near infrared reflectance; OCT-A = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] The screening and baseline visits can occur on the same day as the last visit of the antecedent study or within 60 days of the last visit. Information collected at the last visit of the antecedent study, including safety laboratory tests and ocular imaging, can be used for the baseline visit. However, if data were not collected at the last visit of the antecedent study, then it is required to be collected at the baseline assessment. All assessments must be completed within a 3-day period. The study visit windows are calculated from the date of the baseline dose, unless the dose was missed. If the dose was missed, the study visit window is calculated from the date study assessments were completed.

[b] Pegcetacoplan administration must occur within 3 days of completing screening and baseline assessments.

[c] Obtain prior to fluorescein angiography and before study drug administration.

[d] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[e] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[f] Height and weight should be collected at baseline.

[g] Perform assessments prior to dilating the eyes.

[h] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[j] To be administered by the site staff prior to any other assessments performed on that day.

[k] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA, and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and sent to the reading center for analysis.

[l] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[m] Pegcetacoplan will not be administered at the month 36 visit.

[n] Starting at Day 1, study participants will be contacted by study site staff within 4 ± 2 days after each study treatment visit (through month 4) to collect any information related to any safety concerns, decrease in vision, eye pain, unusual ocular events, or any new ocular symptoms in the study eye. If the physician determines that there are any safety concerns, a follow-up visit should be scheduled as soon as possible.

[o] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[p] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[q] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[r] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[s] At screening, serum pregnancy test should be performed for women of childbearing potential. If positive, participant is not eligible to continue in the study.

[t] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[u] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 5: Schedule of Activities—Every-Other-Month Treatment Group (Year 2)

	Treatment						ET[m]
Visit #	**9**	**10**	**11**	**12**	**13**	**14**	
Day	**420**	**480**	**540**	**600**	**660**	**720**	
Month	**14**	**16**	**18**	**20**	**22**	**24**	
Window (+ or – days)	**16**	**16**	**16**	**16**	**16**	**16**	
Blood draw—safety labs[a]						x	x
Urine sample collection[a]						x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]			x			x	x
Vital signs[c]	x	x	x	x	x	x	x
Physical examination						x	x
BCVA[d]	x	x	x	x	x	x	x
LL-BCVA[d]			x			x	x
Slitlamp examination	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]			x			x	x
Mesopic microperimetry[f]			SE			x	x
NEI VFQ-25[g]						x	x
FRI Index[g]						x	x
SD-OCT [h,n]			x			x	x
FAF[h]			x			x	x
NIR[h]			x			x	x
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]			x			x	x
Study eye pegcetacoplan administration[i,j]	x	x	x	x	x	x	
Study eye postinjection assessment[k]	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x

Table 5: Schedule of Activities—Every-Other-Month Treatment Group (Year 2)

	Treatment						ET[m]
Visit #	9	10	11	12	13	14	
Day	420	480	540	600	660	720	
Month	14	16	18	20	22	24	
Window (+ or – days)	16	16	16	16	16	16	
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[o]	Regimen per PI's discretion						
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant

fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 6: Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ET[m]
Visit #	**15**	**16**	**17**	**18**	**19**	**20**	
Day	**780**	**840**	**900**	**960**	**1020**	**1080**	
Month	**26**	**28**	**30**	**32**	**34**	**36**	
Window (+ or – days)	**16**	**16**	**16**	**16**	**16**	**16**	
Blood draw—safety labs[a]						x	x
Urine sample collection[a]						x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]			x			x	x
Vital signs[c]	x	x	x	x	x	x	x
Physical examination						x	x
BCVA[d]	x	x	x	x	x	x	x
LL-BCVA[d]			x			x	x
Slitlamp examination	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]			x			x	x
Mesopic microperimetry[f]			SE			x	x
NEI VFQ-25[g]						x	x
FRI Index[g]						x	x
SD-OCT[h,n]			x			x	x
FAF[h]			x			x	x
NIR[h]			x			x	x
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]			x			x	x
Study eye pegcetacoplan administration[i,j]	x	x	x	x	x		
Study eye postinjection assessment[k]	x	x	x	x	x		
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x

Table 6: Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ET[m]
Visit #	**15**	**16**	**17**	**18**	**19**	**20**	
Day	**780**	**840**	**900**	**960**	**1020**	**1080**	
Month	**26**	**28**	**30**	**32**	**34**	**36**	
Window (+ or – days)	**16**	**16**	**16**	**16**	**16**	**16**	
Adverse events	x	x	x	x	x	x	X
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[o]	Regimen per PI's discretion						
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator ; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

7. STUDY POPULATION

7.1. Participant Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Ocular-specific inclusion criteria apply to the **study eye**.

1. Participated in APL2-103 (NCT03777332) or completed the treatment at month 24 of either APL2-303 (Derby, NCT03525613) or APL2-304 (Oaks, NCT03525600). Specifically, for the APL2-303 and APL2-304 studies, the following criterion also applies:
    a. Participants who did not permanently discontinue treatment but missed the month 24 visit are also eligible to participate in this extension study; however, to be eligible, these participants must be screened within 60 days from the last day of the expected month 24 visit window for the antecedent study.
2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.
3. Female participants must be:
    a. Women of nonchildbearing potential, or
    b. Women of childbearing potential (WOCBP), defined as any women who have experienced menarche and who are not permanently sterile or postmenopausal, must have a negative serum pregnancy test at screening and must agree to use protocol defined methods of contraception for the duration of the study and 90 days after their last dose of pegcetacoplan, and refrain from breastfeeding for the duration of the study.
4. Males with female partners of childbearing potential must agree to use protocol defined methods of contraception and agree to refrain from donating sperm for the duration of the study and for 90 days after their last dose of pegcetacoplan.
5. Willing and able to give informed consent as described in Section 12.2 and to comply with the study procedures and assessments.

Inclusion criterion #2 applies to the fellow eye.

7.2. Participant Exclusion Criteria

Ocular-specific exclusion criteria apply to the study eye.

1. Participants who permanently discontinued the study drug prior to month 24 in the APL2-304 or APL2-304 studies and only for safety assessments. Temporary pause of the study drug is not exclusionary.
2. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.

3. Any contraindication to IVT injection including current ocular or periocular infection.
4. Medical or psychiatric condition that, in the opinion of the investigator, is clinically significant and not suitable for study participation or make consistent follow-up over the 36-month treatment period unlikely.
5. Known hypersensitivity to fluorescein sodium for injection or hypersensitivity to pegcetacoplan or any of the excipients in pegcetacoplan solution.
6. Pregnancy, breastfeeding, or positive pregnancy test.

Exclusion criteria 2 and 3 apply to the fellow eye.

7.3. Acceptable Methods of Contraception

Women of childbearing potential (WOCBP) and male participants with female partners of childbearing potential will be instructed to practice an acceptable method of birth control throughout the duration of the study and for 90 days following the end of study drug administration.

A woman is considered to be of childbearing potential following menarche and until becoming postmenopausal, unless she is permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.

Approved methods of contraception include:

- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
    - oral, intravaginal, or transdermal
- Progestogen-only hormonal contraception associated with inhibition of ovulation:
    - oral, injectable, or implantable
- Intrauterine device
- Intrauterine hormone-releasing system
- Bilateral tubal occlusion
- Vasectomized partner (*provided that partner is the sole sexual partner of the WOCBP trial participant and that the vasectomized partner has received medical assessment of the surgical success*)
- Sexual abstinence (*defined as refraining from heterosexual intercourse during the entire period of risk associated with study treatments*)
- Male condom with or without spermicide (for male study participants with female partners of childbearing potential only)

Not all methods of contraception may be available in all of the countries in which this study is being conducted.

Note: Sexual abstinence is only accepted when it is the preferred and usual lifestyle of the participant.

Participants must agree to use an approved method of contraception during the study and for 90 days after their last dose of investigational product.

7.4. Lifestyle Considerations

No restrictions are required.

7.5. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but who do not meet inclusion/exclusion criteria. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAE.

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened within 60 days from the last visit in the antecedent study.

8. TREATMENT OF PARTICIPANTS

8.1. Study Interventions

Each participant will be assigned a unique screening number after providing written informed consent. Participants who complete the study screening assessments and meet all the eligibility criteria will be scheduled to enter the study.

Participants will receive monthly pegcetacoplan treatment if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Participants who were in the EOM treatment group (pegcetacoplan or sham) in the antecedent study will receive pegcetacoplan EOM in this extension study. The study eye will be the same eye as the study eye of the antecedent study. Table 7 presents information about the investigational product.

Table 7: Investigational Product

Intervention name	Pegcetacoplan
Type	Drug
Dose formulation	Sterile, isotonic solution of pegcetacoplan in acetate-buffer, pH 5.0, containing trehalose
Unit dose strength(s)	15 mg/0.1 mL (150 mg/mL)
Route of administration	IVT injection
Dosage level(s)	0.1 mL IVT injection monthly or EOM
Use	Experimental
Sourcing	Provided centrally by the sponsor
Packaging and labeling	Pegcetacoplan will be provided in stoppered glass vials. Each vial will be labeled in accordance with country requirements, as described in Section 8.1.1.
Former name(s) or alias(es)	APL-2

Abbreviations: EOM = every other month; IVT = intravitreal.

8.1.1. Packaging and Labeling of Study Interventions

Pegcetacoplan IVT injection 15 mg/0.1 mL will be provided as a 150 mg/ mL sterile solution of pegcetacoplan in stoppered glass vials. Changes to sponsor-supplied packaging prior to dosing may not occur without full agreement, in advance, by Apellis Pharmaceuticals, Inc.

Labels containing study information and pack identification are applied to the investigational product(s) container.

All investigational product is labeled with a minimum of the following: protocol number, dosage form (including product name and quantity in pack), route of administration, directions for use, storage conditions, batch number and/or packaging reference, the statements “For clinical trial use only” and/or “CAUTION: New Drug—Limited by Federal (or US) Law to Investigational Use,” and name and address of the sponsor.

Space is allocated on the label so that the site representative can record a unique participant identifier and visit number of the participant.

Additional labels may, on a case-by-case basis, be applied to the investigational product in order to satisfy national, local, or institutional requirements, but must not do any of the following: contradict the clinical study label, obscure the clinical study label, or identify the study participant by name.

Additional labels may not be added without the prior full agreement of Apellis Pharmaceuticals, Inc.

8.1.2. Study Drug Administration

Pegcetacoplan is administered as an IVT injection and must be performed by trained personnel. Detailed instructions on drug preparation, preinjection procedures, administration of pegcetacoplan, and postinjection procedures will be provided in the applicable study plans.

Clinic staff involved in the injection tray assembly, anesthetic preparation, and study drug preparation and administration will follow appropriate aseptic techniques to minimize the risk of potential AEs associated with IVT injections.

Administration of pegcetacoplan is only allowed if preinjection IOP is ≤21 mm Hg. If necessary, antiglaucomatous medication can be given to lower the IOP. To minimize transient IOP elevation after IVT injection of pegcetacoplan, decompression of the eye **must** be performed before all pegcetacoplan injections. This is done by applying moderate pressure to the globe with cotton swabs for 30 to 60 seconds during anesthetic preparation. In addition to the procedures outlined in the protocol and applicable study plans, adherence to specific institutional policies associated with IVT injections will be observed.

8.2. Preparation, Handling, Storage, and Accountability

Pegcetacoplan IVT injection 15 mg/0.1 mL will be provided as a 150 mg/ mL sterile solution pegcetacoplan in stoppered glass vials. Pegcetacoplan is an isotonic solution in acetate-buffer, pH 5.0, containing trehalose. The drug product is packaged in 2R clear Type I glass vials with 13 mm FluroTec-coated chlorobutyl grey stoppers and sealed with 13-mm aluminum/polypropylene flip-off type seals.

Vials should be stored as per the instructions until ready for use. Each vial should only be used once. Vials should not be shaken and should be protected from sunlight.

The investigational product should be stored refrigerated at 2 to 8 °C. Temperature monitoring is required at the investigator site (or documented storage location) to ensure that the investigational product is maintained within an established temperature range.

The investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study intervention received and any discrepancies are reported and resolved before use of the study intervention.

Only participants enrolled in the study may receive study intervention and only authorized site staff may supply or administer study intervention. All investigational product must be stored in a secure, environmentally controlled, and monitored area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff. Study drug that has

been dispensed to a participant and returned unused must not be re-dispensed to a different participant.

The investigator, institution, or the head of the medical institution (where applicable) is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records). Where allowed, the investigator may choose to delegate drug accountability responsibilities to a pharmacist or other appropriate individual.

All unused and used study drug vials should be retained at the center until they are inventoried by the study monitor. All used, unused, or expired study drug vials will be returned to Apellis Pharmaceuticals, Inc, or its designee for destruction and destruction will be documented, or if authorized, disposed of at the study center per the center's standard operating procedures and documented.

Further guidance and information for the final disposition of unused study interventions are provided in the pharmacy manual.

8.3. Measures to Minimize Bias: Randomization and Masking

8.3.1. Randomization

Pegcetacoplan treatment assignments (monthly or EOM) are based on treatment assignment in the antecedent studies.

8.3.2. Masking

No masking of treatment is required, as this is an open-label study.

8.4. Treatment Compliance

The date and time of each dose administered will be recorded in the source documents and in the case report form (CRF). The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site staff other than the person administering the study intervention.

8.5. Concomitant Medications and Procedures

Medications administered and procedures performed from the time of informed consent through the end of the study must be recorded as concomitant, along with:

- Reason for use
- Dates of administration including start and end dates
- Dosage information including dose and frequency

The medical monitor should be contacted if there are any questions regarding concomitant or prior therapy.

Any ongoing concomitant medications a participant is receiving at the start of the study or that are given for any reason during the study (except for routine medications given for ocular

procedures required by the protocol, such as topical anesthetic) must be recorded in the source documents and CRF including start and stop date and time, dose, route, and indication.

In addition, all intraocular procedures from the antecedent study must also be recorded as medical history in the source documents and CRF including start and stop dates.

Any concomitant procedures performed during the study should be recorded in the source documents and eCRF, with the exception of procedures for routine dental or medical care, including screening tests (eg, blood work, colonoscopy, mammogram). Abnormal findings detected at the screening tests should be recorded if deemed clinically significant per PI's discretion.

Any paramedical or alternative therapies (eg, surgical anesthetics, acupuncture, herbal supplements) given for any reason during the study should also be recorded in the source documents and appropriate eCRF.

Metoclopramide or other agents to prevent nausea induced by fluorescein injection may be administered at the discretion of the principal investigator (PI) and do not need to be recorded on the eCRF.

8.5.1. Treatment of the Fellow Eye with Pegcetacoplan

Fellow eyes with GA that meet the inclusion and exclusion criteria as detailed below are allowed to receive treatment with pegcetacoplan when the treating physician and participant deem beneficial. The treatment regimen (monthly or every-other month) should be decided by the investigator.

The fellow eye treatment should follow the same guidelines used for the study eye regarding the study drug administration (refer to Section 8.1.2). In case a participant receives pegcetacoplan treatment in his/her fellow eye at a study visit, the study eye will be the first to receive the treatment. Pegcetacoplan treatment in the fellow eye must be recorded in the specific EDC form. Adverse events reporting requirements will remain applicable to the fellow eye. When the fellow eye receives treatment with clinical drug, preinjection IOP must be ≤21 mm Hg and post injection safety assessment used for the study eye must also be performed for the fellow eye (refer to Section 10.2.6 Postinjection Safety Assessment).

Prior to administering pegcetacoplan to the fellow eye for the first time, FAF, SD-OCT, and NIR images must be obtained and sent to the reading center. The initial administration of pegcetacoplan to the fellow eye may be administered within 3 days after the ocular assessments (FAF, SD-OCT, and NIR) are completed. If they fall outside this 3-day window all ocular assessments for the fellow eye must be recaptured and sent to the reading center.

8.5.1.1. Fellow Eye Inclusion Criteria

To be eligible for treatment, the fellow eye needs to meet inclusion criterion #2:

2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.

8.5.1.2. Fellow Eye Exclusion Criteria

The following exclusion criteria apply to the fellow eye:

2. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.
3. Any contraindication to IVT injection including current ocular or periocular infection.

8.5.2. Treatment of New Exudation Related to Active Choroidal Neovascularization in the Study Eye and/or Fellow Eye

Participants who developed exudation related to CNV in the study eye in the antecedent study or during this extension study are eligible to enroll or continue in this study and will receive pegcetacoplan and anti-VEGF therapy. If the investigator suspects new exudation in the study eye, OCT, optical coherence tomography angiography, and fluorescein angiography should be captured prior to anti-VEGF therapy at the same visit.

Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator. After the first treatment with anti-VEGF therapy is provided, these participants can then be treated following local standard of care. For participants who developed exudation at or after month 20 of the antecedent studies, during this study anti-VEGF treatment should be provided following local standard of care.

If anti-VEGF therapy is administered on the same day as a pegcetacoplan injection, the anti-VEGF therapy shall be administered first and the pegcetacoplan injection shall occur at least 30 minutes after the anti-VEGF injection and only if the IOP is ≤21 mm Hg. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP to the appropriate range to allow for the pegcetacoplan injection or after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure.

Treatment with anti-VEGF is allowed in the fellow eye. The treatments for the fellow eye can be administered according to the site's standard protocol for CNV treatment.

During unscheduled visits, unscheduled ocular imaging can be performed for safety monitoring in the study eye or fellow eye.

8.5.3. Prohibited Therapies

The PI should make a determination regarding participant continuation of therapies used to treat concomitant medical conditions.

8.5.4. Endophthalmitis Treatment

Endophthalmitis cases must be reported to Apellis Safety as SAEs. The decision to treat a participant for endophthalmitis or suspected endophthalmitis will be guided by the clinical judgment of the investigator and in accordance with local guidelines (as applicable). A culture sample should be performed prior to making a decision on treatment. The treatment method (pars

plana vitrectomy vs IVT injection of antibiotics) and choice of antimicrobial agents are also at the discretion of the physician and should follow current standard practice patterns. The decision to use IVT steroids (eg, dexamethasone) for the treatment of endophthalmitis is also at the discretion of the physician. Any treatment done for endophthalmitis should be recorded in the concomitant medication or concomitant procedure form.

8.5.5. Management of Optic Ischaemic Neuropathy

Participants who develop optic ischaemic neuropathy during the study must be assessed by fluorescein angiography (FA) and color fundus photographs and referred to neuroophthalmologists for further work-ups. A decision to treat a participant for optic ischaemic neuropathy will be guided by the clinical judgement of the investigator and a neurophthalmologist in accordance with local guidance (as applicable).

8.6. Dose Modification

Not applicable.

8.7. Intervention After the End of the Study

The last study visit (month 36) for the study eye will occur 30 days after the last pegcetacoplan injection for the pegcetacoplan monthly group or 60 days for the pegcetacoplan every-other-month group and will collect safety and efficacy information.

9. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

9.1. Discontinuation of Study Intervention

In certain instances, it may be necessary for the participant to permanently discontinue (definitive discontinuation) pegcetacoplan. The date of and reason for treatment discontinuation must be determined by the investigator and recorded in the participant's medical record and on the appropriate electronic case report form (eCRF). If it is determined that there was more than one reason for the discontinuation, each reason should be documented in the source document and the most clinically relevant reason, as determined by the investigator, should be entered on the eCRF. An adverse event should always be reported as the most clinically relevant reason.

Any participant who discontinues treatment early, or is withdrawn from the study early, due to a serious treatment-emergent adverse event (TEAE) will be followed until the serious TEAE resolves (returns to normal or baseline values) or stabilizes, or until it is judged by the investigator to no longer be clinically significant.

If pegcetacoplan is permanently discontinued in the study eye, the participant will also be terminated from the study. Participants who discontinue the study should be encouraged to complete the early termination visit. See the SoA for data to be collected at the time of discontinuation of study intervention and follow-up and for any further evaluations that need to be completed.

9.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at his/her own request or may be withdrawn at any time at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons.

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted at least 30 days after the last pegcetacoplan injection, as shown in the SoA. The participant will be permanently discontinued both from the study intervention and from the study at that time. If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent. If the participant withdraws from the study, he/she may request destruction of any samples taken and not tested, and the investigator must document this in the site study records.

Any participant who chooses to withdraw from the study and transition to commercially available pegcetacoplan in the study eye once it is available to them will be asked to return to the clinical study site for an early termination visit before starting treatment with commercially available pegcetacoplan. Study participation for these participants will be concluded following completion of the early termination visit. Early termination visit assessments will be performed as described in the SoA (Section 6.5).

9.3. Lost to Follow-up

A participant will be considered lost to follow-up if he/she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether the participant wishes to and/or should continue in the study.
- Before the participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record.

Should the participant continue to be unreachable, he/she will be considered to have withdrawn from the study. Closure of specific sites or of the study as a whole are described in Section 12.8.

10. STUDY ASSESSMENTS AND PROCEDURES

Evaluations will be performed during the study as outlined in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6). Refer to the manual of procedures (MOP) for detailed descriptions of study-related procedures.

Written informed consent for participation must be obtained before performing any study-specific assessments. Informed consent for all participants should be maintained within the participant source documentation.

All participants will return every month or EOM to the clinical site for assessments and pegcetacoplan injections according to their treatment regimen assignment in the antecedent study through month 36. In addition, participants will be contacted via phone by study staff 4 (±2) days after each of the first 3 study treatments to collect safety information. The study eye will be the same eye as the study eye of the antecedent study. Screening for this study can happen at the last visit of the antecedent study.

The end of the trial for each participant is defined as when the participant completes their last visit. Participants who discontinue study treatment should return to the clinic for study assessments as per the outlined visit schedule.

Immediate safety concerns should be discussed with the sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management and obtained before signing of the informed consent form (ICF) may be utilized for screening or baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the SoA.

10.1. Efficacy Assessments

10.1.1. Clinical Assessments

10.1.1.1. Ophthalmologic Evaluation

Note: All ophthalmic procedures (including imaging) are to be performed on both eyes, except where specified.

Prior to the administration of fluorescein, blood and urine should be collected for safety laboratory tests (including blood for human chorionic gonadotropin/follicle-stimulating hormone/luteinizing hormone, if applicable) and vital signs along with a physical examination including weight and height should be performed.

The complete ophthalmic exam will consist of the following:

- External examination of the eye and adnexa.
- Routine screening for eyelids/pupil responsiveness (including ptosis, abnormal pupil shape, unequal pupils, abnormal reaction to light, and afferent pupillary defect).
- Slitlamp examination (cornea, anterior chamber, iris, lens, aqueous reaction) (cells and flare). Please see Appendix D for grading scales.
- Dilated fundus exam including evaluation of retina and vitreous (ie, posterior segment abnormalities, retinal hemorrhage/detachment, and vitreal hemorrhage density and vitreous cells). Vitreal hemorrhage density and vitreous cells grading scales are outlined in Appendix E.
- IOP measurement—A measurement of intraocular pressure will be conducted using either Tono-Pen or Goldmann applanation tonometer as outlined in the MOP. This should be performed prior to dilating the eyes, and the same method should be used for all measurements in the same participant throughout the study.

10.1.1.2. Ocular History

Ocular history within the previous 7 years should be collected and recorded for all participants. The history should include any significant previous ocular surgeries and procedures. Ocular history will be carried over from each participant's antecedent study as allowed per applicable regulations. Refer to the eCRF Completion Guidelines (CCG) for detailed guidance.

10.1.1.3. Best-Corrected Visual Acuity and Low-Luminance Best-Corrected Visual Acuity

Best-corrected visual acuity (BCVA) and LL-BCVA will be measured using the ETDRS method by certified study staff per the SoA. All examiners will require certification prior to performing these assessments as part of the study.

Best-corrected visual acuity testing should precede any examination requiring administration of eye drops to dilate the eye or any examination requiring contact with the eye.

The LL-BCVA acuity will be measured by placing a neutral density trial lens causing a reduction of 2.0 log units in luminance. The same requirements apply to measurement of low-luminance visual acuity as described above for BCVA.

A visual acuity specifications procedure manual and training materials will be provided to all sites.

10.1.1.4. Minnesota Low-Vision Reading Test or Radner Reading Charts (in Select Countries)

The Minnesota Low-Vision Reading Test (MNRead) or Radner Reading Charts (Appendix C) should be administered first monocularly for each eye and then binocularly. The Manual of Operations should be referenced for a list of versions that should be administered based on country. These tests should be administered prior to dilating the eyes.

10.1.1.5. Ocular Imaging and Microperimetry

The following ocular images will be obtained and sent to the reading center as outlined in the visit schedule. A reading center manual along with training materials will be provided to all sites which will provide information on standardized procedures for the collection, storage, and transmission of all images. Prior to any images being taken at the site, site personnel must be properly trained and certified and test images and systems and software must be certified and validated by the reading center. Only trained and certified site staff delegated the responsibility of image collection should perform this task. Ocular images obtained as part of this study are:

- Digital color fundus photographs
- Fluorescein angiography
- Spectral domain optical coherence tomography imaging
- Fundus autofluorescence (Heidelberg Spectralis Instrument)
- Near infrared reflectance
- Mesopic microperimetry: select participants only (those who had the assessment performed in the antecedent study)
- Optical coherence tomography angiography: select participants (those who had the assessment performed in the antecedent study) only

If a participant misses a visit during which ocular images should have been taken, the images should be collected at the next scheduled study visit.

10.1.2. Patient-Reported Outcomes

Data will be collected via interview-administered questionnaires to assess patient-reported outcomes during scheduled visits as outlined in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6). The questionnaires should be performed prior to any other assessments being performed that day.

Questionnaire data will be used to assess participant-reported efficacy of pegcetacoplan and changes in vision-related quality of life over time. Questionnaires will be translated into the appropriate language for each country or region.

10.1.2.1. The NEI VFQ 25-Item Version

The NEI VFQ is an interviewer-administered questionnaire designed to assess patient-reported visual function (Appendix A). It is a 25-item questionnaire with a composite score and covers 12 domains of functional health status and well-being (general health, general vision, ocular pain, near activities (select countries), distance activities (select countries), social functioning, mental health, role difficulties, dependency, driving, color vision, and peripheral vision). Scoring yields 12 subscales based on the 12 domains covered in the questionnaire. These scales are scored from 0 to 100 with higher scores indicating better visual function. The recall period is not specified; however, it is important that the participant uses the same recall period each time the questionnaire is administered throughout their participation in the study.

There are 13 additional items (labeled A1-A13) included in the Appendix of the NEI-VFQ-25. These items should be included/administered if they are provided in the language in which the survey is administered. They fall into the same generic health domains as the 25 base items, so no new categories are introduced. These 13 additional items allow for the calculation of NEI-VFQ-39 scores.

10.1.2.2. The FRI Index

The FRI Index will be administered by site staff and is an individualized assessment of functional reading independence (Appendix B). The questionnaire has 7 items with one total index score. Higher levels on the scale represent higher functional reading independence. The recall period is 7 days.

10.2. Safety Assessments

10.2.1. Safety Parameters

10.2.2. Demographic/Medical History

Demographic information and medical history will be carried over from each participant's antecedent study as allowed per applicable regulations. Ongoing medical history and resolved adverse event/procedures that occurred in the parent studies if reported and deemed clinically significant by the investigator, will be considered as medical history. In addition, resolved medical history that ended within 2 years of the start of the antecedent study will also be captured under medical history. Antecedent study number and dosing regimen will also be captured.

Illnesses first occurring or detected during the study and/or worsening of a concomitant illness during the study are to be documented as AEs on the eCRF in accordance with Section 10.3.3.

10.2.3. Vital Signs

Vital signs (body temperature, respiration rate, heart rate, and systolic and diastolic blood pressure measurements) will be evaluated at the visits indicated in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6). On injection visits, vital signs will be measured prior to dosing. Vital signs should be taken with the participant in a seated position after resting for 5 minutes, except when they are supine or semireclined because of study procedures and/or AEs, or if deemed necessary by the investigator. Blood pressure measurements are to be taken in the same arm for the duration of the study. Vital signs will be measured before venipuncture.

Vital signs measurements will be repeated if clinically significant or if machine/equipment errors occur. Out-of-range blood pressure, respiratory rate, or heart rate measurements will be repeated at the investigator's discretion. Any confirmed, clinically significant vital signs measurements must be recorded as AEs.

10.2.4. Weight and Height

Body weight and height will be recorded at the baseline visit. Both body weight and height will be assessed without shoes on.

10.2.5. Physical Examination

All physical examinations, performed by the investigator or designee, will include, at a minimum, assessment of the following: general, head, ears, eyes, nose, throat, dentition, thyroid (endocrine), heart, chest, lungs, abdomen, skin, extremities, back/neck, musculoskeletal, and lymph nodes. Additional symptom-driven physical examinations may be performed at any time, as deemed necessary by the investigator.

10.2.6. Postinjection Safety Assessment

The study and/or fellow eye will be assessed after the IVT injection of pegcetacoplan to ensure that the injection procedure and/or the study medication have not endangered the health of the eye. The initial postinjection assessments should be done within 5 minutes postinjection and include a gross assessment of vision (light perception, hand motion). If the participant passes the gross vision test, he/she can be released from the clinic. If the participant does not pass the gross vision test, IOP must be measured at that time. Additional IOP measurement must be taken approximately every 30 minutes thereafter until IOP is ≤30 mm Hg and the participant is able to be released from the clinic.

Any participant who develops a significant and sustained raise in IOP (>30 mm Hg) after the study/fellow eye injection, should be monitored according to the investigator's clinical judgment and may undergo additional procedures and measurements of IOP beyond those specified in the protocol as well as IOP-lowering procedures. If post-injection IOP is >30 mm Hg antiglaucomatous medication/procedure may be used to control the IOP per the physician's discretion. The post-injection IOP increase that required treatment should be recorded as an AE and the corresponding medication/procedure should be recorded as concomitant medication/concomitant procedure. The participant should remain at the study site until the IOP is under control per the physician's clinical judgment. IOP increase that does not require any treatment to return to normal levels after the IVT injection does not need to be reported as an AE/SAE.

10.2.7. Laboratory Assessments

Laboratory assessment samples (Table 8) are to be obtained at designated visits as detailed in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6). All samples (including urine) should be collected prior to treatment and fundus fluorescein angiography (if applicable). Procedures for the collection and processing of blood and urine are provided in the laboratory manual.

Blood and urine samples will be analyzed at one or more central (or certified local) laboratory facilities, as defined in the laboratory manual. Urine samples will be analyzed by dipstick and a microscopic analysis. All laboratory reports must be reviewed, signed, and dated by the investigator. A legible copy of all reports must be filed with the participant's medical record (source document) for that visit. Any abnormal laboratory test result requiring an intervention, leading to discontinuation of the IP injection, or to discontinuation of the study should be reported as an AE/SAE. For abnormal laboratory tests with a known underlying cause/diagnosis, only the underlying cause/diagnosis should be reported as AE/SAE. Clinically significant abnormal values occurring during the study will be followed up until repeat test results return to normal, stabilize, or are no longer clinically significant.

Instructions for collection, handling, processing, storage, and shipping of samples will be provided in a separate laboratory reference manual prior to study initiation.

Table 8: Laboratory Assessments

Hematology	Chemistry	Urinalysis	Other
• Hemoglobin • Hematocrit • Red blood cell (RBC) count • White blood cell (WBC) count with differential • Platelet count	• Blood urea nitrogen (BUN) • Creatinine • Bilirubin (total, direct and indirect) • Albumin • Alkaline phosphatase (ALP) • Aspartate aminotransferase (AST) • Alanine aminotransferase (ALT) • Creatine kinase • Glucose • Electrolytes (sodium, potassium, chloride, bicarbonate)	• pH • Specific gravity • Protein • Glucose • Ketones • Bilirubin • Blood • Nitrite • Urobilinogen • Leukocyte esterase	• Anti–pegcetacoplan peptide Ab and anti-PEG Ab • Human chorionic gonadotropin (HCG)[a] • Follicle-stimulating hormone (FSH)[b] • Luteinizing hormone (LH)[b]

Abbreviation: Ab = antibody.
[a] Serum pregnancy test (ie, human chorionic gonadotropin test) will be performed for women of childbearing potential at screening only.
[b] Follicle-stimulating hormone and luteinizing hormone test will be performed for postmenopausal females at screening only.

10.2.7.1. Pregnancy Screen

For WOCBP, a serum pregnancy test will be performed at screening, and a urine pregnancy test will be performed at every visit, including baseline visit. Participants with a positive result will be excluded or discontinued from the study. A urine pregnancy test will also be performed at times indicated in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6) for WOCBP. Male participants will be counseled to avoid donating semen during the time between the first screening and the final exit visit and for 90 days after their last dose of study drug.

10.2.8. Blood Volume for Study Assessments

Total study blood volume is presented in Table 9.

Table 9: Total Study Blood Volume

Assay	Number of time points	Approximate volume per time point[a] (mL)	Approximate sample volume over course of study (mL), all groups
Anti–pegcetacoplan peptide Ab and anti-PEG Ab	8	2	16
Hematology[a]	5	4	20
Chemistry[b] (incl. HCG/LH)	6	5	30
FSH/LH (postmenopausal women only)	1	5	5
Total blood volume			**71[c]**

Abbreviations: Ab = antibody; FSH = follicle-stimulating hormone; HCG = human chorionic gonadotropin; incl. = including; LH = luteinizing hormone.
[a] Volume will vary slightly between regions and analyzing laboratory tests based on the standard methodology.
[b] In some regions, may be included in the chemistry sample based on local methodology.
[c] Represents the standard collection volume planned over the duration of the study; actual volume may vary by group and across sites.

10.3. Adverse and Serious Adverse Events

10.3.1. Definition of Adverse Events

10.3.1.1. Adverse Events

An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not it is considered study drug-related. An AE can, therefore, be any unfavorable and unintended sign, including a clinically significant abnormal laboratory finding, symptom, or disease temporally associated with the use of an investigational product, whether considered related to the investigational product.

Adverse events can be spontaneously reported by the participant and/or in response to a question from the study personnel or revealed by observation and will be recorded during the study at the investigational site. All identified AEs/SAEs must be recorded and described on the AE page of the eCRF.

Fluctuating or nonsignificant changes in laboratory values or medical history do not necessarily qualify for AE reporting. If these changes are assessed as clinically significant and/or lead to discontinuation of administration of investigational product, these should be reported as an AE. If these changes are linked to a diagnosis, only the diagnosis should be reported as an AE.

BCVA loss of less than 15 letters compared to the previous visit without an identified underlying cause should not be reported as an AE. Every attempt should be made to report the underlying cause of the change in BCVA as an AE. Any decrease in BCVA from prior visit between 15 and

30 letters with unknown cause should be reported as an AE using the term BCVA decrease. If BCVA loss is 30 or more letters from the prior visit, both the underlying cause/diagnosis, if known, and 'BCVA decreased' must be reported as SAEs.

BCVA loss due to natural progression of GA should not be reported as an AE, regardless of the magnitude of the change.

If any treatment is necessary to lower IOP post IVT injection, 'IOP increased' should be recorded as an AE and the medication/AC tap should be recorded as a concomitant medication/concomitant procedure.

Endophthalmitis must always be reported as a SAE. Intraocular inflammation (IOI) events that require treatment and/or result in the interruption of the study treatment **must be** reported as AEs.

Slit lamp/indirect ophthalmoscopic findings of AC cells/flare or vitreal cells that do not require treatment and do not result in the interruption of the study treatment **do not** need to be reported as an AE.

Normal progression or worsening of the medical condition under study (eg, vision loss due to the progression of GA in either eye), by itself, does not necessarily constitute an AE unless the change can be reasonably attributed to an action of pegcetacoplan and not only to its lack of efficacy. Disease progression that requires an intervention (eg, administration of IVT anti-VEGF agents for neovascular AMD) should be recorded as an AE in the eCRF.

10.3.1.2. Serious Adverse Events

An SAE is any AE or suspected adverse reaction that, in the view of either the investigator or sponsor, results in any of the following outcomes: death; life-threatening; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; a congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening*, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical/surgical intervention to prevent one of the outcomes listed in the above definition.

Examples of important medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home: blood dyscrasias or convulsions that do not result in inpatient hospitalization; or the development of drug dependency or drug abuse.

**Life-threatening* is defined as an AE or suspected adverse reaction, which, in the view of either the investigator or sponsor, places the participant at immediate risk of death as it occurred. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.

Unexpected AEs

An AE is considered "unexpected" if it is not listed in the Reference Safety Information section of the investigator brochure (IB) in effect at that time of event onset.

10.3.2. Evaluation of Adverse Events

The investigator or their medically qualified designee will review each event and assess its relationship to pegcetacoplan or the injection procedure (not related, unlikely related, possibly related, or definitely related). The date and time of onset, time relationship to study drug dosing, duration, severity (mild, moderate, or severe), and outcome (recovered/resolved, recovered/resolved with sequelae, recovering/resolving, not recovered/not resolved, fatal, or unknown) of each event will be noted.

Table 10 should be considered when evaluating the relationship of AEs/SAEs to study treatment or injection procedure.

Table 10: Definitions of Adverse Event Relatedness

Classification	Definition
Definitely related	Strong evidence of a causal relationship; the influence of other factors is unlikely
Possibly related	Some evidence of a causal relationship, but other factors may have caused or contributed to the event (eg, another illness or concomitant treatment)
Unlikely related	A causal relationship is not a reasonable possibility, but it cannot be completely ruled out with the available evidence.
Not related	No evidence of a causal relationship

Table 11 presents the definitions that should be considered when evaluating the severity of AEs and SAEs.

Table 11: Severity of Events

Severity	Definition/description
Mild	Event results in mild or transient discomfort, not requiring intervention or treatment; does not limit or interfere with daily activities (eg, insomnia, mild headache).
Moderate	Event is sufficiently discomforting, so as to limit or interfere with daily activities; may require interventional treatment (eg, febrile illness requiring oral medication).
Severe	Event results in significant symptoms that prevents normal daily activities; may require hospitalization or invasive intervention (eg, anemia resulting in blood transfusion).

10.3.3. Adverse Events of Special Interest

The following events of special interest will be closely monitored and reported throughout the study:

- Exudative AMD
- Increased intraocular pressure

- Intraocular inflammation
- Endophthalmitis
- Optic ischemic neuropathy

An AE of special interest can be serious or nonserious but must be reported to the sponsor/Apellis Safety in the same manner as an SAE, as described in Section 10.3.4.

10.3.4. Recording Adverse Events

Adverse events and SAEs will be collected from the signing of the consent form until the last visit or early termination visit, 30 days after the last dose of pegcetacoplan for the PM treatment group and 60 days after the last dose of pegcetacoplan for the pegcetacoplan every-other-month treatment group. If an investigator becomes aware of an SAE that is suspected of being related to study treatment, regardless of the time since the participant completed the clinical trial, the SAE must be reported within 24 hours of awareness to the sponsor.

For each (S)AE, the investigator will evaluate and report the onset date (and time if applicable), resolution date (and time if applicable), intensity, causality, action taken, serious outcome, and whether or not it caused the participant to discontinue the study.

If possible, the outcome of any (S)AE that caused permanent discontinuation or was present at the end of the study should be reported, particularly if the (S)AE was considered by the investigator to be related to the investigational product. Participants experiencing (S)AEs that cause interruption or discontinuation of investigational product, or those experiencing (S)AEs that are ongoing at the last visit or early termination visit should receive follow-up as appropriate.

All SAEs must be reported to the sponsor/Apellis Safety via eCRF within 24 hours of becoming aware of the event, whether or not the event is deemed treatment related. If the EDC system is not operational, the site must complete the paper SAE form and email to Safety@Apellis.com within 24 hours of becoming aware of the event. The reported information submitted as a paper SAE must be entered into the EDC system once it becomes operational.

Adverse events will be coded in accordance with the Medical Dictionary for Regulatory Activities (MedDRA version 23.1). If known, the diagnosis of the underlying illness or disorder should be recorded, rather than its individual symptoms.

Adverse events reporting requirements will remain applicable to the fellow eye when the fellow eye is treated with clinical pegcetacoplan. Post injection IOP in the fellow eye will need to be recorded in the EDC designated form when the fellow eye is treated with clinical pegcetacoplan.

10.3.5. Reporting Adverse Events to Health Authorities and Ethics Committees

The sponsor has the responsibility to inform concerned health authorities, ethics committees, and investigators about suspected unexpected serious adverse reactions in line with GCP guidance and applicable regulatory requirements.

If required, specific SAEs should be reported to the concerned ethic committees in compliance with local requirements.

10.3.6. Pregnancy

Although pregnancy is not an AE, all pregnancies and suspected pregnancies (including a positive pregnancy test regardless of age or disease state) occurring with a female participant or the female partner of a male participant, are recommended to be followed to conclusion to determine their outcome.

The pregnancy, suspected pregnancy, or positive pregnancy test must also be reported to Apellis Safety within 24 hours of the investigator's awareness using the paper Pregnancy Report Form, This form must be signed and dated by the investigator and submitted via email to Safety@Apellis.com.

Follow-up regarding the course of a pregnancy is subject to the participant's consent and must be discussed with the participant and/or partner. If consent is provided, the investigator should follow the pregnancy until completion of the pregnancy and must report the outcome of the pregnancy (eg, delivery, termination, etc.) within 24 hours of awareness via email to Safety@Apellis.com.

An abnormal outcome is defined as any pregnancy that results in the birth of a child with persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomalies, or birth defects. In the event of an abnormal outcome, an SAE Report Form will be required to be submitted to Safety@Apellis.com within 24 hours of awareness.

Refer to Section 7.3 for acceptable methods of contraception.

10.3.7. Drug Abuse, Misuse, Overdose, and Medication Error

Occurrences of events of drug abuse, drug misuse, drug overdose, and medication error must be reported to Apellis Safety.

Abuse of a medicinal product: Persistent or sporadic, intentional excessive use of medicinal products, which is accompanied by harmful physical or psychological effects.

Misuse: Intentional and inappropriate use of a medicinal product not in accordance with the prescribed or authorized dose, route of administration, and/or the indication(s) or not within the legal status of its supply.

Overdose: Administration of a quantity of study drug given per administration or per day, which is above the assigned dose.

Medication Error: An error made in prescribing, dispensing, administration, and/or use of the study drug. Medication errors are reportable to the sponsor as defined below:

- The dispensing, administration, and/or use of the unassigned study drug.
- The administration and/or use of an expired study drug.

All AEs or SAEs associated with drug abuse, drug misuse, drug overdose, or medication error must be reported as appropriate.

10.4. Pharmacokinetics

Pharmacokinetic parameters are not evaluated in this study.

10.5. Pharmacodynamics

Pharmacodynamic parameters are not evaluated in this study.

10.6. Immunogenicity Assessments

10.6.1. Anti–Pegcetacoplan Peptide and Anti-PEG Antibody Assessments

Samples for the assessment of antidrug antibodies (ADA) will be collected as outlined in the SoA (Table 1, Table 2, Table 3, Table 4, Table 5, Table 6).

The sampling schedule was established to capture the ADA signal at baseline of this study, along with any potential early onset and the dynamic profile (transient or persistent) of antibody formation while minimizing study drug level in the sample.

11. STATISTICS

A formal statistical analysis plan (SAP) will be developed and finalized prior to locking the database. The study will be analyzed by the sponsor or its agent. The full details of data presentations and analyses will be provided in the SAP. Additional statistical analyses other than those described in this section may be performed if deemed appropriate and included in the SAP. Any deviations from the final SAP or from what is outlined in the protocol will be discussed in the final study report.

The analysis of data from the first 12 months of the study will be performed when (1) all patients have completed study visits through month 12 or have discontinued from the study prior to month 12 and (2) all data from the first 12 months of the study are in the database and have been reviewed. The analysis of data from the first 24 months of the study will be performed in a similar manner.

The final study analysis based on data from the complete study will be performed when all patients have either completed the 3-year study period (ie, study visits through month 36) or have discontinued early from the study, all data from the study are in the database and have been reviewed, and the database is locked.

The SAP will provide the statistical methods and definitions for the analysis of the efficacy and safety data, as well as describe the approaches to be taken for summarizing other study information such as participant disposition, demographics and baseline characteristics, investigational product exposure, and prior and concomitant medications. The SAP will also include a description of how missing, unused, and spurious data will be addressed.

To preserve the integrity of the statistical analysis and study conclusions, the SAP will be finalized prior to database lock. All statistical analyses will be performed using SAS (SAS Institute, Cary, NC 27513).

11.1. Determination of Sample Size

This study comprises GA participants who previously participated in and completed the treatment period in a prior study evaluating pegcetacoplan for treatment of GA. The study will recruit up to 1200 participants across approximately 250 multinational sites.

11.2. Populations for Analysis

11.2.1. Safety Set

The safety set will consist of all enrolled participants who receive at least 1 injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed according to the actual treatment received in the antecedent study and study APL2-GA-305.

11.2.2. Full Analysis Set

The full analysis set will consist of all enrolled participants who receive at least 1 injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed according to the treatment assigned when enrolled in the antecedent study and study APL2-GA-305.

11.2.3. Modified Full Analysis Set

The modified full analysis set will consist of all participants who are in the ITT set of APL2-303 and APL2-304 antecedent studies, haven't been enrolled in APL2-103, and receive at least 1 injection of pegcetacoplan in study APL2-GA-305. Participants will be analyzed according to the treatment assigned when enrolled in the antecedent study and study APL2-GA-305.

11.2.4. Data Review for Analysis Set

After all data have been verified, coded, and entered into the database, a review will be performed. The purpose of this review will be to define the analysis populations. The review will also check the quality of the data, identifying outliers, and make decisions on how to deal with any data issues (eg, missing values, withdrawals, protocol deviations). After the preanalysis review, resolution of all issues, and documentation of all decisions, the database will be locked.

11.3. Efficacy Analysis

Efficacy analyses will be performed using the full analysis set and modified full analysis set.

Unless otherwise stated, all efficacy analyses will be summarized by both the treatment assigned when enrolled in the antecedent study and the APL2-GA-305 treatment and by visit.

There will be 2 baselines used in the efficacy analysis of this study: antecedent study baseline is defined as the baseline value in the antecedent studies, APL2-103, APL2-303 and APL2-304, participant had enrolled in; and APL2-GA-305 baseline is defined as the last available nonmissing assessment prior to first study drug administration in the study eye in study APL2-GA-305.

11.3.1. Analysis of Primary Efficacy Endpoint

Not applicable.

11.3.2. Analysis of Secondary Efficacy Endpoints

Continuous variables will be summarized using descriptive statistics (eg, mean, standard deviation, median, minimum, and maximum, etc). For categorical variables, the frequency and percentage in each category will be displayed.

Efficacy analyses based on APL2-GA-305 baseline will be performed in the full analysis set. The change from APL2-GA-305 baseline in the continuous efficacy endpoint (such as total area of GA lesion at each visit) will be summarized and assessed with a mixed effect model for repeated measure analysis that includes observed data from all treatment arms. The estimand for the first secondary efficacy endpoint is presented in Table 12. A description of all estimands will be presented in the statistical analysis plan.

Table 12: Estimand for the Change from Baseline in the Total Area of GA lesion in the Study Eye Measured by FAF

Attributes	Definition
Population	GA participants defined through inclusion and exclusion criteria in full analysis set.
Treatment conditions	The treatment regimens of interest in this study are the combined antecedent study treatment and APL2-GA-305 treatment groups
Endpoint	Change in total area of GA lesions in the study eye from APL2-GA-305 study baseline measured by FAF to month 36.
Strategy for addressing intercurrent events	Treatment discontinuation in the APL2-GA-305 study will be handled with a treatment policy strategy
Population-level summary	Least square mean change of GA lesion from APL2-GA-305 study baseline to month 36 within each treatment group according to mixed effect model for repeated measure analysis.

Efficacy analyses based on antecedent study baseline will be performed in the modified full analysis set unless otherwise noted. The change from the antecedent study baseline in the continuous efficacy endpoint (such as total area of GA lesion at each visit) will be summarized and assessed with a mixed effect model for repeated measure analysis.

Descriptive summaries will be presented for treated fellow eye based on APL2-GA-305 baseline.

11.4. Safety Analysis

All safety analyses will be summarized for the safety set.

Adverse events will be coded using MedDRA. All AEs, including TEAEs, will be summarized by System Organ Class, Preferred Term, treatment group for number of participants, and proportion reporting the event. A similar summary will be produced for SAEs, AEs leading to discontinuation, severe AEs, and AEs related to the investigational product. The intensity of AEs and the relationship to investigational product will be summarized for each System Organ Class and Preferred Term by treatment group. Similar summaries for TEAEs after initiation of pegcetacoplan treatment in the fellow eye will also be presented for the subgroup of participants being treated bilaterally with pegcetacoplan.

Withdrawals due to AEs will be summarized for each body system and Preferred Term by treatment group. Patient deaths and primary cause of death will be summarized by treatment group.

Treatment-emergent AEs are defined as those AEs that develop or worsen after the first dose of study medication until study exit or the early termination follow-up visit.

Separate summaries will be prepared for systemic (nonocular) and ocular AEs, with events in the study eye and untreated fellow eye summarized separately.

For participants being treated bilaterally with pegcetacoplan, separate summaries will be presented for systemic (nonocular) and ocular AEs for study eye and treated fellow eye.

AE summaries will be presented across all participants. All AEs will be listed by participant, along with information regarding onset, duration, relationship, and severity to investigational product, action taken with investigational product, treatment of event, and outcome.

Unless otherwise specified, APL2-GA-305 baseline is defined as the last available non-missing assessment prior to first study drug administration in the study eye in study APL2-GA-305.

Laboratory assessments and anti-pegcetacoplan/anti-PEG antibodies will be summarized by treatment group using appropriate descriptive statistics.

Changes from APL2-GA-305 baseline in clinical laboratory tests will be summarized, using descriptive statistics, by visit and nominal time after dosing. Out-of-range values will be flagged in data listings.

Changes from APL2-GA-305 baseline in vital signs will be summarized, using descriptive statistics, by treatment, visit, and nominal time after dosing.

Change from APL2-GA-305 baseline in IOP and incidence of IOP above specified thresholds [(ie, >21 mmHg at pre-injection (first measurement of the day); >30 mmHg post injection] will be summarized by treatment and visit.

Shift from APL2-GA-305 baseline in ocular examination assessments including slit lamp examination and indirect ophthalmoscopy will be summarized by treatment and visit.

Incidence of participants who lost letters based on NL-BCVA categories (≥15, ≥15-<30, ≥30 ETDRS letters) will be summarized by treatment and visit.

Change from APL2-GA-305 baseline in ocular imaging assessments will be summarized by treatment and visit.

11.5. Other Analyses

Concomitant medications, concomitant ocular procedures, and study medication exposure will be summarized by the treatment group.

World Health Organization (WHO) and MedDRA coding dictionaries will be used for the concomitant medications and concomitant procedures, respectively.

11.6. Interim Analysis

The data from this study may be analyzed at different times for specific reasons (eg, providing data to a regulatory agency).

11.7. Data Monitoring Committee

An external, independent data monitoring committee (DMC) will be formed with the purpose of reviewing all data across the conduct of the study on an ongoing basis. The DMC will follow a charter that will outline the frequency of meetings and the roles and responsibilities of all members. The DMC will meet at the beginning of the study and approximately every 12 months thereafter and will perform a review of all relevant events on an ongoing basis. An ad hoc meeting of the DMC may be convened by the sponsor or the DMC chairperson at any time between the regularly scheduled DMC meetings and data reviews if warranted by new safety information or for any other reason. The DMC will communicate its recommendations to the

sponsor, who will notify the appropriate health authorities according to local regulatory requirements.

12. REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

12.1. Regulatory and Ethical Considerations

- This study will be conducted in accordance with the protocol and with the following:
  - Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
  - Applicable ICH GCP Guidelines
  - Applicable laws and regulations
- The protocol, protocol amendments, ICF, IB, and other relevant documents (eg, advertisements) must be submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study is initiated. The investigator must provide a copy of the IRB/IEC approval to Apellis Pharmaceuticals, Inc, before enrollment of any patient/participant into the study.
- Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.
- The investigator will be responsible for the following:
  - Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC
  - Notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures
  - Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH guidelines, the IRB/IEC, European regulation 536/2014 for clinical studies (if applicable), and all other applicable local regulations

12.2. Informed Consent Process

- The investigator or his/her representative will explain the nature of the study to the participant or his/her legally authorized representative, including full and adequate oral and written information about the nature, purpose, and possible risks and benefits of the study, and answer all questions regarding the study. Participants should have the opportunity to consider the information provided before providing their consent.
- Participants must be informed that their participation is voluntary and that they are free to discontinue from the study at any time. Participants or their legally authorized representative will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance

Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

- The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.
- Participants must be re-consented to the most current version of the ICF(s) during their participation in the study should there be updated and approved versions available.
- A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative.

A participant who is rescreened is not required to sign another ICF if the rescreening occurs within 60 days from the previous ICF signature date.

12.3. Data Protection

- Participants will be assigned a unique identifier by the sponsor. Any participant records or datasets that are transferred to the sponsor will contain the identifier only; participant names or any information which would make the participant identifiable will not be transferred.
- The participant must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection laws. The level of disclosure must also be explained to the participant, who will be required to give consent for their data to be used as described in the informed consent.
- The participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

12.4. Dissemination of Clinical Study Data

This study will be listed with ClinicalTrials.gov.

12.5. Site Qualification and Study Monitoring

Before an investigational site can enter a participant into the study, a representative of Apellis Pharmaceuticals, Inc, (or designee) will assess the investigational study site to:

- Determine the adequacy of the facilities
- Discuss with the investigator(s) and other personnel their responsibilities with regard to protocol adherence, and the responsibilities of Apellis Pharmaceuticals, Inc, or its representatives. This will be documented in a clinical study agreement between Apellis Pharmaceuticals, Inc, and the investigator.

During the study, a monitor from Apellis Pharmaceuticals, Inc, or representative will have regular contacts with the investigational site, for the following:

- Provide information and support to the investigator(s)
- Confirm that facilities remain acceptable
- Confirm that the investigational team is adhering to the protocol, that data are being accurately recorded in the case report forms, and that investigational product accountability checks are being performed
- Perform source data verification as described in Section 12.6.
- Record and report any protocol deviations not previously sent to Apellis Pharmaceuticals, Inc
- Confirm that all AEs and SAEs have been properly documented on CRFs and confirm that any SAEs have been forwarded to Apellis Pharmaceuticals, Inc, and those SAEs that met criteria for reporting have been forwarded to the IRB

The investigator must allow the monitor to inspect the drug storage area, study drug stocks, drug accountability records, participant charts and study source documents, and other records relative to study conduct.

The monitor will be available between visits if the investigator(s) or other staff needs information or advice.

12.6. Data Quality Assurance

- All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.
- The investigator must maintain accurate documentation (source data; see Section 12.7) that supports the information entered in the CRF.
- The investigator must permit study-related monitoring, audits, IRB/IEC review, and regulatory agency inspections and provide direct access to source data documents. The investigator should contact Apellis Pharmaceuticals, Inc, immediately if contacted by a regulatory agency about an inspection.
- Monitoring details describing strategy (eg, risk-based initiatives in operations and quality such as Risk Management and Mitigation Strategies and Analytical Risk-Based Monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, remote, or on-site monitoring) are provided in the clinical monitoring plan or equivalent document.
- The sponsor or designee is responsible for the data management of this study including quality checking of the data.
- The sponsor assumes accountability for actions delegated to other individuals (eg, contract research organizations).

- Study monitors will perform ongoing source data verification to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.
- Records and documents, including signed ICFs, pertaining to the conduct of this study must be retained by the investigator for a period of 2 years after the last marketing application approval, or if not approved, for 2 years following the discontinuance of the test article for investigation, unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor.

12.7. Source Documents

- Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator's site.
- Data reported on the CRF or entered in the eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

12.8. Study and Site Start and Closure

The study start date will be the date in which the clinical study will be open for screening of participants.

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/IEC or local health authorities, the sponsor's procedures, or GCP guidelines
- Inadequate recruitment of participants by the investigator
- Discontinuation of further study intervention development

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s)

used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

12.9. Publication Policy

- The results of this study may be published or presented at scientific meetings. If this is foreseen, the investigator agrees to submit all manuscripts or abstracts to the sponsor before submission, to allow the sponsor to protect proprietary information and to provide comments.
- The sponsor will comply with the requirements for publication of study results. In accordance with standard editorial and ethical practice, the sponsor will generally support publication of multicenter studies only in their entirety and not as individual site data. In this case, a coordinating investigator will be designated by mutual agreement.
- Authorship will be determined by mutual agreement and in line with International Committee of Medical Journal Editors authorship requirements.

Both the use of data and the publication policy will be detailed within the clinical study agreement. Intellectual property rights (and related matters), generated by the investigator and others performing the clinical study, will be subject to the terms of a clinical study agreement that will be agreed between the institution and Apellis Pharmaceuticals, Inc, or its designee. With respect to such rights, the Apellis Pharmaceuticals, Inc, or its designee will solely own all rights and interests in any materials, data, and intellectual property rights developed by investigators and others performing the clinical study described in this protocol, subject to the terms of any such agreement. In order to facilitate such ownership, investigators will be required to assign all such inventions, either to their institution or directly to Apellis Pharmaceuticals, Inc, or its designee, as will be set forth in the clinical study agreement.

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14. APPENDICES

APPENDIX A: NATIONAL EYE INSTITUTE VISUAL FUNCTIONING QUESTIONNAIRE 25-ITEM VERSION

PB/IA

National Eye Institute
Visual Functioning Questionnaire - 25
(VFQ-25)

version 2000

(INTERVIEWER ADMINISTERED FORMAT)

January 2000

RAND hereby grants permission to use the "National Eye Institute Visual Functioning Questionnaire 25 (VFQ-25) July 1996, in accordance with the following conditions which shall be assumed by all to have been agreed to as a consequence of accepting and using this document:

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7/29/96

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Instructions:

I'm going to read you some statements about problems which involve your vision or feelings that you have about your vision condition. After each question I will read you a list of possible answers. Please choose the response that best describes your situation.

Please answer all the questions as if you were wearing your glasses or contact lenses (if any).

Please take as much time as you need to answer each question. All your answers are confidential. In order for this survey to improve our knowledge about vision problems and how they affect your quality of life, your answers must be as accurate as possible. Remember, if you wear glasses or contact lenses for a particular activity, please answer all of the following questions as though you were wearing them.

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Visual Functioning Questionnaire - 25

PART 1 - GENERAL HEALTH AND VISION

1. In general, would you say your overall health is*:

(Circle One)

READ CATEGORIES:

Excellent	1
Very Good	2
Good	3
Fair	4
Poor	5

2. At the present time, would you say your eyesight using both eyes (with glasses or contact lenses, if you wear them) is excellent, good, fair, poor, or very poor or are you completely blind?

(Circle One)

READ CATEGORIES:

Excellent	1
Good	2
Fair	3
Poor	4
Very Poor	5
Completely Blind	6

* Skip Question 1 when the VFQ-25 is administered at the same time as the SF-36 or RAND 36-Item Health Survey 1.0

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3. How much of the time do you worry about your eyesight?

(Circle One)

READ CATEGORIES:

None of the time	1
A little of the time	2
Some of the time	3
Most of the time	4
All of the time?	5

4. How much pain or discomfort have you had in and around your eyes (for example, burning, itching, or aching)? Would you say it is:

(Circle One)

READ CATEGORIES:

None	1
Mild	2
Moderate	3
Severe, or	4
Very severe?	5

PART 2 - DIFFICULTY WITH ACTIVITIES

The next questions are about how much difficulty, if any, you have doing certain activities wearing your glasses or contact lenses if you use them for that activity.

5. How much difficulty do you have reading ordinary print in newspapers? Would you say you have:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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6. How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

7. Because of your eyesight, how much difficulty do you have finding something on a crowded shelf?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

8. How much difficulty do you have reading street signs or the names of stores?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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9. Because of your eyesight, how much difficulty do you have going down steps, stairs, or curbs in dim light or at night?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

10. Because of your eyesight, how much difficulty do you have noticing objects off to the side while you are walking along?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

11. Because of your eyesight, how much difficulty do you have seeing how people react to things you say?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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12. Because of your eyesight, how much difficulty do you have picking out and matching your own clothes?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

13. Because of your eyesight, how much difficulty do you have visiting with people in their homes, at parties, or in restaurants ?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

14. Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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15. Now, I'd like to ask about driving a car. Are you currently driving, at least once in a while?

(Circle One)

Yes ..... 1 *Skip To Q 15c*

No 2

15a. IF NO, ASK: Have you never driven a car or have you given up driving?

(Circle One)

Never drove ..... 1 *Skip To Part 3, Q 17*

Gave up..... 2

15b. IF GAVE UP DRIVING: Was that mainly because of your eyesight, mainly for some other reason, or because of both your eyesight and other reasons?

(Circle One)

Mainly eyesight ..... 1 *Skip To Part 3, Q 17*

Mainly other reasons ..... 2 *Skip To Part 3, Q 17*

Both eyesight and other reasons ... 3 *Skip To Part 3, Q 17*

15c. IF CURRENTLY DRIVING: How much difficulty do you have driving during the daytime in familiar places? Would you say you have:

(Circle One)

No difficulty at all..... 1

A little difficulty 2

Moderate difficulty 3

Extreme difficulty..... 4

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16. How much difficulty do you have driving at night? Would you say you have: (READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Have you stopped doing this because of your eyesight	5
Have you stopped doing this for other reasons or are you not interested in doing this	6

16a. How much difficulty do you have driving in difficult conditions, such as in bad weather, during rush hour, on the freeway, or in city traffic? Would you say you have:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Have you stopped doing this because of your eyesight	5
Have you stopped doing this for other reasons or are you not interested in doing this	6

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PART 3: RESPONSES TO VISION PROBLEMS

The next questions are about how things you do may be affected by your vision. For each one, I'd like you to tell me if this is true for you all, most, some, a little, or none of the time.

READ CATEGORIES:	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	(Circle One On Each Line)				
17. Do you accomplish less than you would like because of your vision?	1	2	3	4	5
18. Are you limited in how long you can work or do other activities because of your vision?	1	2	3	4	5
19. How much does pain or discomfort in or around your eyes, for example, burning, itching, or aching, keep you from doing what you'd like to be doing? Would you say:	1	2	3	4	5

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For each of the following statements, please tell me if it is definitely true, mostly true, mostly false, or definitely false for you or you are not sure.

(Circle One On Each Line)

	Definitely True	Mostly True	Not Sure	Mostly False	Definitely False
20. I stay home most of the time because of my eyesight.....	1	2	3	4	5
21. I feel frustrated a lot of the time because of my eyesight.....	1	2	3	4	5
22. I have much less control over what I do, because of my eyesight.	1	2	3	4	5
23. Because of my eyesight, I have to rely too much on what other people tell me..	1	2	3	4	5
24. I need a lot of help from others because of my eyesight.....	1	2	3	4	5
25. I worry about doing things that will embarrass myself or others, because of my eyesight.....	1	2	3	4	5

That's the end of the interview. Thank you very much for your time and your help.

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Appendix of Optional Additional Questions

SUBSCALE: GENERAL HEALTH

A1. How would you rate your overall health, on a scale where zero is as bad as death and 10 is best possible health?

(Circle One)

0	1	2	3	4	5	6	7	8	9	10
Worst										Best

SUBSCALE: GENERAL VISION

A2. How would you rate your eyesight now (with glasses or contact lens on, if you wear them), on a scale of from 0 to 10, where zero means the worst possible eyesight, as bad or worse than being blind, and 10 means the best possible eyesight?

(Circle One)

0	1	2	3	4	5	6	7	8	9	10
Worst										Best

SUBSCALE: NEAR VISION

A3. Wearing glasses, how much difficulty do you have reading the small print in a telephone book, on a medicine bottle, or on legal forms? Would you say:
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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A4. Because of your eyesight, how much difficulty do you have figuring out whether bills you receive are accurate?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

A5. Because of your eyesight, how much difficulty do you have doing things like shaving, styling your hair, or putting on makeup?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

SUBSCALE: DISTANCE VISION

A6. Because of your eyesight, how much difficulty do you have recognizing people you know from across a room?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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A7. Because of your eyesight, how much difficulty do you have taking part in active sports or other outdoor activities that you enjoy (like golf, bowling, jogging, or walking)?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

A8. Because of your eyesight, how much difficulty do you have seeing and enjoying programs on TV?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

SUBSCALE: SOCIAL FUNCTION

A9. Because of your eyesight, how much difficulty do you have entertaining friends and family in your home?
(READ CATEGORIES AS NEEDED)

(Circle One)

No difficulty at all	1
A little difficulty	2
Moderate difficulty	3
Extreme difficulty	4
Stopped doing this because of your eyesight	5
Stopped doing this for other reasons or not interested in doing this	6

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SUBSCALE: DRIVING

A10. [This items, "driving in difficult conditions", has been included as item 16a as part of the base set of 25 vision-targeted items.]

SUBSCALE: ROLE LIMITATIONS

A11. The next questions are about things you may do because of your vision. For each item, I'd like you to tell me if this is true for you all, most, some, a little, or none of the time.
(READ CATEGORIES AS NEEDED)

(Circle One On Each Line)

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Do you have more help from others because of your vision?	1	2	3	4	5
b. Are you limited in the kinds of things you can do because of your vision?	1	2	3	4	5

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SUBSCALES: WELL-BEING/DISTRESS (#A12) and DEPENDENCY (#A13)

The next questions are about how you deal with your vision. For each statement, please tell me if it is definitely true, mostly true, mostly false, or definitely false for you or you don't know.

(Circle One On Each Line)

	Definitely True	Mostly True	Not Sure	Mostly False	Definitely False
A12. I am often irritable because of my eyesight.....	1	2	3	4	5
A13. I don't go out of my home alone, because of my eyesight.....	1	2	3	4	5

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APPENDIX B: FUNCTIONAL READING INDEPENDENCE INDEX

Kimel M, Yu R, Leidy N. The Functional Reading Independence (FRI) Index—User Manual (Version 1.2). Evidera; 2015.

APPENDIX C: MINNESOTA LOW-VISION READING TEST (MNREAD) AND RADNER READING CARDS

The MOP should be referenced for a detailed table of countries and languages to determine which test will be administered. Equipment and testing procedures will also be described in detail in the MOP for both tests.

Minnesota Low-Vision Reading Test:

The Minnesota Low-Vision Reading Test (MNRead) Acuity Charts are continuous-text reading-acuity cards used for measuring the reading acuity and speed of normal and low-vision patients. These charts were developed at the Minnesota Laboratory for Low-Vision Research, University of Minnesota, Minneapolis, Minnesota, USA.

The MNRead Acuity Charts will be used to measure:

-
- Maximum reading speed: the patient's reading speed when reading is not limited by print size

Radner Reading Cards:

The Radner Reading Cards consist of sentence optotypes, which are optimized reading test items, standardized by construction and statistical selection. These cards allow for accurate and comparable measurements of reading acuity and reading speed.

APPENDIX D: GRADING SCALE FOR ASSESSMENT OF ANTERIOR CHAMBER FLARE OR CELLS

AQUEOUS REACTION—FLARE

Grade	Description
0	No protein is visible in the anterior chamber when viewed by an experienced observer using slitlamp biomicroscopy; a small, bright, focal slit-beam of white light; and high magnification.
Trace	Trace amount of protein detectable in the anterior chamber. This protein is visible only with careful scrutiny by an experienced observer using slitlamp biomicroscopy; a small, bright, focal slit-beam of white light; and high magnification.
1+	Mild amount of protein detectable in the anterior chamber. This protein is immediately apparent to an experienced observer using slitlamp biomicroscopy and high magnification, but such protein is detected only with careful observation with the naked eye and a small, bright, focal slit-beam of white light. Note presence of any fibrin.
2-3+	Moderate amount of protein detectable in the anterior chamber. These grades are similar to 1+ but the opacity would be readily visible to the naked eye of an observer using any source of a focused beam of white light. This is a continuum of moderate opacification, with 2+ being less apparent than 3+. Note presence of any fibrin.
4+	A large (severe) amount of protein is detectable in the anterior chamber. Similar to 3+, but the density of the protein approaches that of the lens. Additionally, frank fibrin deposition is frequently seen in acute circumstances. It needs to be noted that because fibrin may persist for a period of time after partial or complete restoration of the blood-aqueous barrier, it is possible to have resorbing fibrin present with lower numeric assignations for flare (eg, 1+ flare with fibrin).

AQUEOUS REACTION—CELLS

Grade	Description
0	No cells are seen in any optical section when a large slitlamp beam is swept across the anterior chamber.
Trace	Rare (1-3) cells are observed when the slitlamp beam is swept across the anterior chamber. When the instrument is held stationary, not every optical section contains circulating cells.
1+	3-10 cells/optical section are seen when the slitlamp beam is swept across the anterior chamber. When the instrument is held stationary, every optical section contains circulating cells. Note stage of hypopyon, if applicable.
2+	10-25 cells are seen when the slitlamp beam is swept across the anterior chamber. When the instrument is held stationary, every optical section contains circulating cells. Note stage of hypopyon, if applicable.
3+	25-50 cells are seen when the slitlamp beam is swept across the anterior chamber. When the instrument is held stationary, every optical section contains circulating cells. Keratic precipitates or cellular deposits on the anterior lens capsule may be present. Note stage of hypopyon, if applicable.
4+	More than 50 cells are seen when the slitlamp beam is swept across the anterior chamber. When the instrument is held stationary, every optical section contains circulating cells or hypopyon is noted. As for the fibrin deposition, hypopyon may persist for a period of time after exudation of cells into the anterior chamber has diminished or ceased entirely, making it possible for have 1+ circulating cells in the anterior chamber with a resolving hypopyon.

APPENDIX E: GRADING SCALE FOR ASSESSMENT OF VITREOUS CELLS

Grade	Description	Cells in retro-illuminated field
0	Clear	0
Trace	Few opacities	1-20
1	Scattered opacities	21-50
2	Moderate opacities	51-100
3	Many opacities	101-250
4	Dense opacities	≥251

APPENDIX F: PROTOCOL CHANGES TO BE FOLLOWED DURING COVID-19 RESTRICTIONS

OVERVIEW

In response to the COVID-19 crisis, to ensure the safety of study participants and investigative sites as well as proper conduct of the study, TEMPORARY changes to the protocol have been implemented. These changes should be followed only during COVID-19 restrictions and include extended investigational product (IP) administration windows, rescreening instructions, and a revised schedule of assessments.

Where feasible, sites could continue to follow the full schedule of assessments (based on their treatment group assignment).

EXTENDED IP ADMINISTRATION WINDOWS

In order to allow more flexibility to sites and participants, and to potentially mitigate missed IP administration, an extended IP administration window can be followed. The extended window can ONLY be used in situations related to COVID-19 restrictions and after medical monitor approval. Footnote "r" of each COVID-19 assessment tables below reflects these extended IP options.

Per protocol, the study window is as follows:

- Monthly treatment group: +/– 8 days
- EOM treatment group: +/– 16 days

During COVID-19 restrictions, the IP administration window can be extended to the following:

- Monthly treatment group: –8 days to +15 days. Note, interval for consecutive injections must be at least 14 days
- EOM treatment group: –16 days to +30 days for the first study year and –16 days to +30 days for the second study year

MINIMUM SCHEDULE OF ACTIVITIES

Where feasible, sites could continue to follow the full Schedule of Activities (based on their treatment group assignment). The minimum assessment tables, only to be followed during this COVID-19 effort and if determined necessary to use based on the investigator's clinical judgment, are provided below to reduce the time required for each study visit. Participants in the EOM treatment group do not need to be seen for the non-IP administration visits. Assessments not performed (even those that have been removed in the minimum assessment table) should be documented.

Participants who are not able to come into the clinic for a study visit due to COVID-19–related restrictions, should be contacted via the phone for the collection of adverse events (including serious adverse events) and concomitant medications. **All serious adverse events are still required to be reported to Apellis within 24 hours of site awareness, even if reported via phone call**. All communications via phone call should also be documented in the source documentation and in the respective CRF page. In addition, these participants should be

instructed to self-monitor their vision at home and report any changes in vision or their overall health via phone call. The site must inform the sponsor of any participants lost to follow-up.

It is critical that local, country, and regional governance regarding COVID-19 is followed along with your best clinical judgment when managing this situation. All visits or assessments missed as a result of COVID-19 will be captured in the case report forms.

The schedules of assessments for the monthly and every-other-month treatment groups are shown below for years 1, 2, and 3.

Table 13: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment												ET[q]
Visit #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Day	1	1	30	60	90	120	150	180	210	240	270	300	330	360	
Month	0	0	1	2	3	4	5	6	7	8	9	10	11	12	
Window (+ or – days)	N/A[a,b]		8	8	8	8	8	8	8	8	8	8	8	8	
Informed consent	x														
Demographic data	x														
Inclusion/exclusion criteria	x	x													
Blood draw—safety labs[a,b,c,t,u]		x												x	x
Urine sample collection[a,b,c]		x												x	x
Urine pregnancy test[a,b,c,d]		x	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a,b,c]		x												x	x
Vital signs[a,b,e]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination[a,b,f]		x												x	x
BCVA[a,b,g]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[a,b,g]		x						x						x	x
Slitlamp examination[a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy[a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement		x	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[a,b,g,h]		x												x	x
Mesopic microperimetry[i]		x												x	x
NEI VFQ-25[a,b,j]		x												x	x
FRI Index[a,b,j]		x												x	x
SD-OCT[a,b,k,s]		x						x						x	x
FAF[a,b,k]		x						x						x	x
NIR[a,b,k]		x						x						x	x
DCFP[a,b,k]		x												x	x
FFA[a,b,k]		x												x	x
OCT-A[a,b,k]		x						x						x	x

Table 13: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment												ET[q]
Visit #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Day	1	1	30	60	90	120	150	180	210	240	270	300	330	360	
Month	0	0	1	2	3	4	5	6	7	8	9	10	11	12	
Window (+ or – days)	N/A[a,b]		8	8	8	8	8	8	8	8	8	8	8	8	
Study eye pegcetacoplan administration[a,b,l,m,r]		x	x	x	x	x	x	x	x	x	x	x	x	x	
Follow-up call[n]		x	x	x	x										
Study eye postinjection assessment[a,b,o]		x	x	x	x	x	x	x	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[a,b,p]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events[a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan															
Fellow eye IOP measurement		To be completed prior to fellow eye pegcetacoplan administration													
Fellow eye FAF, SD-OCT, and NIR[k]		To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule													
Fellow eye pegcetacoplan administration[v]		Regimen per PI's discretion													
Fellow eye postinjection assessment[o]		To be completed following fellow eye pegcetacoplan administration													

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] The screening and baseline visits can occur on the same day as the last visit of the antecedent study or within 60 days of the last visit. Information collected at the last visit of the antecedent study, including safety laboratory tests and ocular imaging, can be used for the baseline visit. However, if data were not collected at the last visit of the antecedent study, then it is required to be collected at the baseline assessment. All assessments must be completed within a 3-day period. The study visit windows are calculated from the date of the baseline dose, unless the dose was missed. If the dose was missed, the study visit window is calculated from the date study assessments were completed.

[b] Pegcetacoplan administration must occur within 3 days of completing screening and baseline assessments.

[c] Obtain prior to fluorescein angiography and before study drug administration.

[d] Beginning at Day 1, perform the urine pregnancy test only for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.
[e] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.
[f] Height and weight should be collected at baseline.
[g] Perform assessments prior to dilating the eyes.
[h] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.
[i] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.
[j] To be administered by the site staff prior to any other assessments performed on that day.
[k] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.
[l] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.
[m] Pegcetacoplan will not be administered at the month 36 visit.
[n] Starting at Day 1, study participants will be contacted by study site staff within 4 ± 2 days after each study treatment visit (through month 3) to collect any information related to any safety concerns, decrease in vision, eye pain, unusual ocular events, or any new ocular symptoms in the study eye. If the physician determines that there are any safety concerns, a follow-up visit should be scheduled as soon as possible.
[o] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.
[p] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.
[q] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.
[r] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 8 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.
[s] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.
[t] At screening, serum pregnancy test should be performed for women of childbearing potential. If positive, participant is not eligible to continue in the study.

[u] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.
[v] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 14: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ET[m]
Visit #	15	16	17	18	19	20	21	22	23	24	25	26	
Day	390	420	450	480	510	540	570	600	630	660	690	720	
Month	13	14	15	16	17	18	19	20	21	22	23	24	
Window (–8 to +15 days)	-8 to +15 days												
Blood draw—safety labs[a]												x	x
Urine sample collection[a]												x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]												x	x
Vital signs[c]	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination												x	x
BCVA[d]	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[d]						x						x	x
Slitlamp examination	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]												x	x
Mesopic microperimetry[f]												x	x
NEI VFQ-25[g]												x	x
FRI[g]												x	x
SD-OCT[h,o]						x						x	x
FAF[h]						x						x	x
NIR[h]						x						x	x
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]												x	x
Study eye pegcetacoplan administration[i,j,n]	x	x	x	x	x	x	x	x	x	x	x	x	
Study eye postinjection assessment[k]	x	x	x	x	x	x	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 14: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ET[m]
Visit #	15	16	17	18	19	20	21	22	23	24	25	26	
Day	390	420	450	480	510	540	570	600	630	660	690	720	
Month	13	14	15	16	17	18	19	20	21	22	23	24	
Window (–8 to +15 days)	-8 to +15 days												
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan													
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration[i,j,n,p]	Regimen per PI's discretion												
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration												

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP to the appropriate range to allow for the pegcetacoplan injection or after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 8 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.

[o] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[p] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 15: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 3)

	Treatment												ET[m]
Visit #	27	28	29	30	31	32	33	34	35	36	37	38	
Day	750	780	810	840	870	900	930	960	990	1020	1050	1080	
Month	25	26	27	28	29	30	31	32	33	34	35	36	
Window (–8 to +15 days)	-8 to +15 days												
Blood draw—safety labs[a]												x	x
Urine sample collection[a]												x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]												x	x
Vital signs[c]	x	x	x	x	x	x	x	x	x	x	x	x	x
Physical examination												x	x
BCVA[d]	x	x	x	x	x	x	x	x	x	x	x	x	x
LL-BCVA[d]						x						x	x
Slitlamp examination	x	x	x	x	x	x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]												x	x
Mesopic microperimetry[f]												x	x
NEI VFQ-25[g]												x	x
FRI[g]												x	x
SD-OCT[h,o]						x						x	x
FAF[h]						x						x	x
NIR[h]						x						x	x
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]												x	x
Study eye pegcetacoplan administration[i,j,n]	x	x	x	x	x	x	x	x	x	x	x		
Study eye postinjection assessment[k]	x	x	x	x	x	x	x	x	x	x	x		
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 15: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 3)

	Treatment												ET[m]
Visit #	27	28	29	30	31	32	33	34	35	36	37	38	
Day	750	780	810	840	870	900	930	960	990	1020	1050	1080	
Month	25	26	27	28	29	30	31	32	33	34	35	36	
Window (–8 to +15 days)	-8 to +15 days												
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan													
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration[i, j,n,p]	Regimen per PI's discretion												
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration												

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test only for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and also submitted to the reading center.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 8 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.

[o] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[p] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 16: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment						ET[q]
Visit #	1	2	3	4	5	6	7	8	
Day	1	1	60	120	180	240	300	360	
Month	0	0	2	4	6	8	10	12	
Window (–16 to +30 days)	N/A[a,b]		-16 to +30 days						
Informed consent	x								
Demographic data	x								
Inclusion/exclusion criteria	x	x							
Blood draw—safety labs[a,b,c,t,u]		x						x	x
Urine sample collection[a,b,c]		x						x	x
Urine pregnancy test[a,b,c,d]		x	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a,b,c]		x						x	x
Vital signs[a,b,e]		x	x	x	x	x	x	x	x
Physical examination[a,b,f]		x						x	x
BCVA[a,b,g]		x	x	x	x	x	x	x	x
LL-BCVA[a,b,g]		x			x			x	x
Slitlamp examination[a,b]		x	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy[a,b]		x	x	x	x	x	x	x	x
Study eye IOP measurement		x	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[a,b,g,h]		x						x	x
Mesopic microperimetry[i]		x						x	x
NEI VFQ-25[a,b,j]		x						x	x
FRI[a,b,j]		x						x	x
SD-OCT[a,b,k,s]		x			x			x	x
FAF[a,b,k]		x			x			x	x
NIR[a,b,k]		x			x			x	x
DCFP[a,b,k]		x						x	x
FFA[a,b,k]		x						x	x
OCT-A[a,b,k]		x						x	x
Study eye pegcetacoplan administration[a,b,l,m,r]		x	x	x	x	x	x	x	
Follow-up call[n]		x	x	x					
Study eye postinjection assessment[a,b,o]		x	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[a,b,p]		x	x	x	x	x	x	x	x

Table 16: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 1)

	Screening[a,b]	Baseline[a,b]	Treatment						ET[q]
Visit #	1	2	3	4	5	6	7	8	
Day	1	1	60	120	180	240	300	360	
Month	0	0	2	4	6	8	10	12	
Window (–16 to +30 days)	N/A[a,b]		-16 to +30 days						
Adverse events[a,b]		x	x	x	x	x	x	x	X
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan									
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration								
Fellow eye FAF, SD-OCT, and NIR[k]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule								
Fellow eye pegcetacoplan administration[a,b,l,m,r,v]		Regimen per PI's discretion							
Fellow eye postinjection assessment[0]		To be completed following fellow eye pegcetacoplan administration							

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] The screening and baseline visits can occur on the same day as the last visit of the antecedent study or within 60 days of the last visit. Information collected at the last visit of the antecedent study, including safety laboratory tests and ocular imaging, can be used for the baseline visit. However, if data were not collected at the last visit of the antecedent study, then it is required to be collected at the baseline assessment. All assessments must be completed within a 3-day period. The study visit windows are calculated from the date of the baseline dose, unless the dose was missed. If the dose was missed, the study visit window is calculated from the date study assessments were completed.

[b] Pegcetacoplan administration must occur within 3 days of completing screening and baseline assessments.

[c] Obtain prior to fluorescein angiography and before study drug administration.

[d] Beginning at Day 1, perform the urine pregnancy test for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[e] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[f] Height and weight should be collected at baseline.

[g] Perform assessments prior to dilating the eyes.

[h] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[j] To be administered by the site staff prior to any other assessments performed on that day.

[k] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior

to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA, and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and sent to the reading center for analysis.

[l] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[m] Pegcetacoplan will not be administered at the month 36 visit.

[n] Starting at Day 1, study participants will be contacted by study site staff within 4 ± 2 days after each study treatment visit (through month 4) to collect any information related to any safety concerns, decrease in vision, eye pain, unusual ocular events, or any new ocular symptoms in the study eye. If the physician determines that there are any safety concerns, a follow-up visit should be scheduled as soon as possible.

[p] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[o] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, handmotion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, the tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an antiVEGF injection during the same visit as the study treatment, the treatment with anti-VEGF must be performed first. The pre- and post-antiVEGF IOP values must be measured and recorded on the eCRF.

[q] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[r] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 16 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.

[s] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[t] At screening, serum pregnancy test should be performed for women of childbearing potential. If positive, participant is not eligible to continue in the study.

[u] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[v] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 17: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 2)

	Treatment						ET[m]
Visit #	**9**	**10**	**11**	**12**	**13**	**14**	
Day	**420**	**480**	**540**	**600**	**660**	**720**	
Month	**14**	**16**	**18**	**20**	**22**	**24**	
Window (–16 to +30 days)	**–16 to +30 days**						
Blood draw—safety labs[a]						x	x
Urine sample collection[a]						x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and antipegcetacoplanG Ab assays[a]						x	x
Vital signs[c]	x	x	x	x	x	x	x
Physical examination						x	x
BCVA[d]	x	x	x	x	x	x	x
LL-BCVA[d]			x			x	x
Slitlamp examination	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]						x	x
Mesopic microperimetry[f]						x	x
NEI VFQ-25[g]						x	x
FRI[g]						x	x
SD-OCT[h,o]			x			x	x
FAF[h]			x			x	x
NIR[h]			x			x	x
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]						x	x

Table 17: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 2)

	Treatment						ET[m]
Visit #	**9**	**10**	**11**	**12**	**13**	**14**	
Day	**420**	**480**	**540**	**600**	**660**	**720**	
Month	**14**	**16**	**18**	**20**	**22**	**24**	
Window (–16 to +30 days)	**–16 to +30 days**						
Study eye pegcetacoplan administration[i,j,n]	x	x	x	x	x	x	
Study eye postinjection assessment[k]	x	x	x	x	x	x	
Concomitant medication/ concomitant ocular procedures[l]	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[i,j,n, p]	Regimen per PI's discretion						
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA, and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and sent to the reading center for analysis.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, the tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP to the appropriate range to allow for the pegcetacoplan injection or after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as the study treatment, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 16 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.

[o] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[p] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

Table 18: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ET[m]
Visit #	15	16	17	18	19	20	
Day	780	840	900	960	1020	1080	
Month	26	28	30	32	34	36	
Window (–16 to +30 days)	–16 to +30 days						
Blood draw—safety labs[a]						x	x
Urine sample collection[a]						x	x
Urine pregnancy test[a,b]	x	x	x	x	x	x	
Anti–pegcetacoplan peptide Ab and anti-PEG Ab assays[a]						x	x
Vital signs[c]	x	x	x	x	x	x	x
Physical examination						x	x
BCVA[d]	x	x	x	x	x	x	x
LL-BCVA[d]			x			x	x
Slitlamp examination	x	x	x	x	x	x	x
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
Study eye IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (select countries)[d,e]						x	x
Mesopic microperimetry[f]						x	x
NEI VFQ-25[g]						x	x
FRI[g]						x	x
SD-OCT[h,o]			x			x	x
FAF[h]			x			x	x
NIR[h]			x			x	x
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]						x	x
Study eye pegcetacoplan administration[i,j,n]	x	x	x	x	x		
Study eye postinjection assessment[k]	x	x	x	x	x		

Table 18: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ET[m]
Visit #	**15**	**16**	**17**	**18**	**19**	**20**	
Day	**780**	**840**	**900**	**960**	**1020**	**1080**	
Month	**26**	**28**	**30**	**32**	**34**	**36**	
Window (–16 to +30 days)	**–16 to +30 days**						
Concomitant medication/ Concomitant ocular procedures[l]	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x
Schedule of Activities for Participants Receiving Fellow Eye Treatment with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on the day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[i,j,n,p]	Regimen per PI's discretion						
Fellow eye postinjection assessment[k]	To be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = best-corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-corrected visual acuity; MNRead = Minnesota Low-Vision Reading Test; N/A = not applicable; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire 25-Item Version; NIR = near infrared reflectance; OCTA = optical coherence tomography angiography; PI = principal investigator; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

[a] Obtain prior to fluorescein angiography and before study drug administration.

[b] Beginning at Day 1, perform the urine pregnancy test for WOCBP at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early termination visit should be completed.

[c] Blood pressure, respiratory rate, heart rate, and temperature. On dosing days, vital signs should be taken predose.

[d] Perform assessments prior to dilating the eyes.

[e] In select countries, the MNRead Acuity Charts or Radner Reading Charts should be done during the study visit, prior to dilating the eyes. It should be performed monocularly first, then binocularly.

[f] Microperimetry assessments (select participants [those who had the assessment performed in the antecedent study]) will be performed postdilation.

[g] To be administered by the site staff prior to any other assessments performed on that day.

[h] FAF and SD-OCT images, near infrared reflectance, fluorescein angiograms, and fundus photographs, as specified in the above schedule, will be sent to the reading center for evaluation (consult the reading center manual for specifics on image capture, processing, and transmission). Images should be captured prior to dosing on dosing days. If a participant misses a study visit or images cannot be obtained at a specific visit, study staff should make every effort to obtain images at the next scheduled visit. If new active choroidal neovascularization in the study eye is suspected, SD-OCT, FFA, and OCT-A (select participants [those who had the assessment performed in the antecedent study]) images should be collected and sent to the reading center for analysis.

[i] Administration of pegcetacoplan can be done on a separate day from the assessment visit if both days fall within the visit window. If this occurs on the Day 1 (Visit 2), then the administration of pegcetacoplan should be done within 3 days of Day 1 and after approval from the medical monitor. When pegcetacoplan administration is on a day other than a study visit, then the only assessment that must be done is preinjection IOP.

[j] Pegcetacoplan will not be administered at the month 36 visit.

[k] Postinjection assessments should be performed within 5 minutes after dosing by the physician or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If a participant passes gross vision test, the participant may leave the site. If a participant fails gross vision test, the tonometry should be performed. IOP should be ≤30 mm Hg in order for the participant to leave the site. Antiglaucomatous medication or anterior chamber (AC) tap can be used to lower the IOP after the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment is necessary to lower the IOP, the increase in the IOP should be recorded as an AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the participant passes gross vision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an anti-VEGF injection during the same visit as the study treatment, the treatment with anti-VEGF must be performed first. The pre- and post-anti-VEGF IOP values must be measured and recorded on the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) used by the participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.

[n] During the COVID-19 pandemic, the following flexibility is allowed for pegcetacoplan administration: +/– 16 days after medical monitor approval. Note, interval for consecutive injections must be at least 14 days.

[o] Participants who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator.

[p] If pegcetacoplan is being injected bilaterally on the same day, the study eye should be administered first.

APPENDIX G: COUNTRY-SPECIFIC PROTOCOL CHANGES

Country-specific changes to this protocol are listed below.

GERMANY

Section 9.1—Discontinuation of Study Intervention

Added text:

The investigator may discontinue treatment of the participant at any time for safety reasons.

Explanation:

It was clarified that the investigator may discontinue treatment of the participant at any time for safety reasons.

Section 9.4—Discontinuation or Suspension of the Study or Parts of the Study:

Added text:

The sponsor may discontinue or suspend the study or parts of the study at any time for reasons that include but are not limited to

- emergent information about the investigational product that leads to a change in the benefit-risk profile
- safety reasons
- administrative reasons

If the study or parts of the study are prematurely discontinued or suspended, the sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s) used in the study of the reason for discontinuation or suspension as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

Explanation:

A new section, Section 9.4, was added; it describes the reasons that the study or parts of the study may be discontinued or suspended by the sponsor. Language previously included in Section 12.8 that was related to study discontinuation was moved to Section 9.4.

Section 10.3.3—Recording Adverse Events:

Changed text:

All SAEs must be reported to the sponsor/Apellis Safety via eCRF ~~within 24 hours of becoming aware of the event~~immediately, whether or not the event is deemed treatment related. If the EDC system is not operational, the site must complete the paper SAE form and email to Safety@Apellis.com immediately ~~and also within 24 hours of becoming aware of the event~~. The reported information submitted as a paper SAE must be entered into the EDC system once it becomes operational.

Explanation:

The serious adverse event reporting timeline was changed from "within 24 hours of becoming aware of the event" or "within 24 hours of site awareness" to "immediately."

Section 12.2—Informed Consent Process:

Changed text:

- The investigator or his/her representative will explain the nature of the study to the participant ~~or his/her legally authorized representative~~, including full and adequate oral and written information about the nature, purpose, and possible risks and benefits of the study, and answer all questions regarding the study. Participants should have the opportunity to consider the information provided before providing their consent.
- Participants must be informed that their participation is voluntary and that they are free to discontinue from the study at any time. Participants ~~or their legally authorized representative~~ will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

Explanation:

Language was removed that permitted a participant's legally authorized representative to provide informed consent on behalf of the participant.

Section 12.8—Study and Site Start and Closure:

Changed text:

~~If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.~~

Explanation:

This text was moved to Section 9.4.

Appendix F—Protocol Changes To Be Followed During COVID-19 Restrictions

Changed text:

All serious adverse events are still required to be reported to Apellis ~~within 24 hours of site awareness~~immediately, even if reported via phone call.

Explanation:

The serious adverse event reporting timeline was changed from "within 24 hours of becoming aware of the event" or "within 24 hours of site awareness" to "immediately."

FRANCE

Synopsis and Section 7.2—Participant Exclusion Criteria

Added text:

Persons deprived of their liberty by a judicial or administrative decision, persons under psychiatric care, persons admitted to a sanitary or social institution for purposes other than research, and major persons subject to a legal protection measure.

Explanation:

Added exclusion criterion.

APPENDIX H: AMENDMENT HISTORY

AMENDMENT 1: SUMMARY OF CHANGES FROM THE PREVIOUS VERSION **Updates to the protocol implemented in this amendment are provided in the table below. Additions to the protocol are marked in underline; deletions are marked by ~~strikethrough~~.**		
Protocol versions		
Summary of change(s) since last version of approved protocol		
Amendment 1	**Amendment date** **16 October 2020**	**Global**
Description of change		**Section(s) affected by change**
Nonsubstantial editorial and technical changes that did not impact content of the document have been made for grammar, clarity, and document usability.		Entire document
Clarified the screening window for eligible subjects who missed the month 24 visit in the antecedent study.		Synopsis, Section 7.1
Added "and baseline assessments" to clarify timing of assessments.		Section 6.1
Updated tables and footnotes to clarify timing of assessments.		Table 1, Table 4, Table 12, Table 15
Deleted the sentence "Rescreened participants should be assigned the same participant number as for the initial screening."		Section 7.4

Amendment 2: Summary of Changes From the Previous Version

Amendment Date: 04 December 2020

Updates to the protocol implemented in this amendment are provided in the table below.

Description of change	**Section(s) affected by change**
Nonsubstantial changes that did not impact content of the document have been made for clarity.	Entire document
Protocol Amendment Summary of Changes: Moved Amendment 1 Summary of Changes to Appendix G Amendment History	Protocol Amendment Summary of Changes, Appendix G
Main Criteria for Exclusion clarified: Subjects who permanently discontinued the study drug prior to month 24 in the APL2-303 or APL2-304 studies and remained ~~in the antecedent study~~ only for safety assessments. Temporary pause of the study drug is not exclusionary.	Section1, Section 7.2

Clarified that baseline 1 for efficacy analysis includes baseline value from APL2-103 study.	Section 1, Section 11.3, Section 11.3.2
Updated Schedule of Activities to be consistent with Section 10.2.7, adding two additional footnotes to Blood draw—safety labs: [s/t] At screening, serum pregnancy test should be performed for women of childbearing potential. If positive, subject is not eligible to continue in the study. [t/u] Beginning at Day 1, perform the urine pregnancy test for women of childbearing potential at each treatment visit. If positive, perform a serum pregnancy test. If serum test is positive, study drug should not be administered and an early term visit should be completed.	Table 1, Table 4, Table 12, Table 15
Updated assessments needed when subject is assessed for anti–vascular endothelial growth factor (VEGF) therapy: Added Schedule of Activities footnote to SD-OCT: [r/n/s/o] Subjects who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator. Section 8.5.1: Subjects who developed exudation related to CNV in the study eye in the antecedent study or during this ~~extension~~ study are eligible to enroll or continue in this extension study and will receive pegcetacoplan and anti-VEGF therapy. If the investigator suspects new exudation in the study eye, OCT, optical coherence tomography angiography, and fluorescein angiography should be captured prior to anti-VEGF therapy at the same visit. Subjects who developed exudation related to CNV prior to month 20 of the antecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is detected by the investigator. After the first treatment with anti-VEGF therapy is provided, these subjects can then be treated following local standard of care. For subjects who developed exudation at or after month 20 of the antecedent studies, during this study anti-VEGF treatment should be provided following local standard of care. ~~If the investigator suspects new exudation in the study eye, OCT, optical coherence tomography angiography, and fluorescein angiography should be captured at the same visit. Treatment for exudation is sole responsibility of the investigator and should follow local standard of care~~.”	Footnote r: Table 1, Table 4 Footnote n: Table 2, Table 3, Table 5, and Table 6 Footnote s: Table 12, Table 15 Footnote o: Table 13, Table 14, Table 16, Table 17 Section 8.5.1
Clarified microperimetry and OCT-A assessments: Microperimetry assessments (select ~~sites~~ subjects [those who had the assessment performed in the antecedent study]) … … and OCT-A (select ~~sites~~ subjects [those who had the assessment performed in the antecedent study]) …	Table 1 (footnotes i and k), Table 2 (footnotes f and h) Table 3 (footnotes f and h) Table 4 (footnotes i and k) Table 5 (footnotes f and h) Table 6 (footnotes f and h) Section 5.1.2 Section 10.1.1.5 Table 12 (footnotes i and k)

	Table 13 (footnotes f and h) Table 14 (footnotes f and h) Table 15 (footnotes i and k) Table 16 (footnotes f and h) Table 17 (footnotes f and h)
Clarification of study randomization: Pegcetacoplan treatment assignments (monthly or EOM) are based on ~~randomization~~ treatment assignment in the antecedent studies.	Section 8.3.1
Clarified endophthalmitis event consideration: Endophthalmitis cases must be reported to Apellis Safety as SAEs. ~~All confirmed or suspected cases of endophthalmitis are considered an adverse event. of special interest (AESI) (see Section 10.3.1.3).~~	Section 8.5.3
Corrections made in Section 9.1: Any subject who discontinues treatment early or is withdrawn from the study early due to a serious treatment-emergent adverse event (TEAE)~~, whether serious or nonserious,~~ will be followed until the serious TEAE resolves (returns to normal or baseline values) or stabilizes, or until it is judged by the investigator to no longer be clinically significant.	Section 9.1
Addition of clarification: Antecedent study number and dosing regimen will also be captured.	Section 10.2.2
Corrections made in Section 10.2.7: A legible copy of all reports must be filed with ~~both~~ the subject's ~~eCRF and~~ medical record (source document) for that visit.	Section 10.2.7
Updated Section 10.2.7.1 to be consistent with Table 8: For WOCBP, a serum pregnancy test will be performed at screening, and a urine pregnancy test will be performed at every visit, ~~pegcetacoplan is administered,~~ including baseline visit.	Section 10.2.7.1

<table>
<tr><td>Updated total study blood volume to be consistent with the SoA:
<table>
<tr><th>Assay</th><th>Number of time points</th><th>Approximate volume per time point[a] (mL)</th><th>Approximate sample volume over course of study (mL), all groups</th></tr>
<tr><td>Anti–pegcetacoplan peptide Ab and anti-PEG Ab</td><td><s>9</s>8</td><td>2</td><td><s>18</s>16</td></tr>
<tr><td>Hematology[a]</td><td><s>8</s>5</td><td>4</td><td><s>32</s>20</td></tr>
<tr><td>Chemistry[b] (incl. HCG/LH)</td><td><s>8</s>6</td><td>5</td><td><s>40</s>30</td></tr>
<tr><td>FSH/LH (postmenopausal women only)</td><td>-1</td><td>5</td><td>-5</td></tr>
<tr><td>Total blood volume</td><td></td><td></td><td><s>168</s>71[c]</td></tr>
</table></td><td>Table 9</td></tr>
<tr><td>Clarified endophthalmitis event consideration:
<s>Endophthalmitis is classified as an AESI. An AESI can be serious or nonserious but must be reported to the sponsor/Apellis Safety via eCRF in the same manner as an SAE, within 24 hours of the investigator's awareness of the event. Section 8.5.3 presents treatment recommendations for suspected or confirmed events of endophthalmitis.</s></td><td>Removed Section 10.3.1.3</td></tr>
<tr><td>Updated adverse event recording:
All SAEs that are suspected of being related to study treatment must be reported immediately to the sponsor if the investigator becomes aware of them, regardless of the time since the completion of the clinical trial.</td><td>Section 10.3.3</td></tr>
</table>