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
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STATISTICAL ANALYSIS PLAN

APL2-GA-305

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

PROTOCOL IDENTIFIER: GALE

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Study Sponsor:	Apellis Pharmaceuticals, Inc. 100 5th Ave Waltham, MA 02451
Author:	PPD
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REVISION HISTORY

Version	Issue Date	Summary of Changes
1.0	22Sep2023	Initial Version
2.0	26Sep2024	• Added APL2-GA-305 Bilateral Treatment Baseline for the analysis of month 24 and final datasets for analysis after subjects treated bilaterally. • Changed the covariate of ntecedent baseline base to APL2-GA-305 baseline base in the model for the analysis of the month 24 and final datasets for secondary efficacy endpoin based on APL2-GA-305 baseline to better adjust the covariates at APL2-GA-305 b seline. • Changed the 6-month knot in the rate of change analysis to 12 month knot for the secondary endpoint related to GA Le ion for the analysis of the month 24 and final datasets to better assess the long term results. • Added rate of change analysis for the analysis of the month 24 and final datasets for other secondary efficacy endpoints to summarize the longitudinal measures. Details about data of unacceptable quality which will be excluded from the analysis were inadvertently omitted from version 1.0 and are added here. • Added analysis for study eye compared with fellow eye for number of scotomatous points from antecedent study baseline for the analysis of the month 24 and final datasets to assess the difference between study eye and fellow eye for number of scotomatous point. • Removed rank preserving structural failure time model in the time to event analysis of NL-BCVA and Central 4 points due to difficult interpretation of the results. • Added time to conversion of central 16 points to scotoma analysis for the analysis of the month 24 and final datasets • Added summaries of TEAEs, AEs of special Interest, AEs related to retinal detachment after subjects being treated bilaterally with pegcetacoplan to assess the safety profile of bilateral treatment for the analysis of the month 24 and final datasets. • Other minor updates to provide clarity of analysis

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Version	Issue Date	Summary of Changes
3.0	05Sep2025	• Added information regarding subjects in Canada can continue receive treatment after Month 36 according to APL2-GA-305 protocol amendment 3.1 CAN. • Changed protocol deviations classification from major and minor to important and non-important based on protocol deviation management plan. • Added rate of change subgroup analysis of GA Lesion from antecedent study baseline to integrated Month 60 by antecedent study baseline characteristics to evaluate the consistency of the main rate of change analysis. • Added MMRM subgroup analysis compared with hypothetical sham of GA Lesion from antecedent study baseline to integrated Month 60 by antecedent study baseline ch racteristics to evaluate the consistency of the MMRM analysis compared with hypothetical sham. • Added rate of change subgroup analysis compared with hypothetical sham of GA Lesion from antecedent study baseline to integrated Month 60 by antecedent study baseline characteristics to evaluate the consistency of the rate of change analysis compared with hypothetical sham. • Removed subgroup analysis based on tertiles level of Low luminance deficit of the study eye at antecedent study baseline as this is no longer a baseline characteristic of interest to evaluate the consistency of the effect for all endpoints • Added MMRM analysis for the analysis of the final datasets for NEI VFQ-25 distance activity subscale score, NEI VFQ-25 Near Activity subscale score, NEI VFQ-25 composite score, NEI-VFQ-25 Driving subscale score endpoints based on APL2-GA-305 Baseline to Month 36 and Antecedent study baseline to Integrated Month 60 to assess the changes over time handling missing data with a missing at random strategy. • Removed microperimetry mean sensitivity and number of scotomatous points analyses based on paralesional zone area (>250µm, >375µm, and >500µm) due to limited relevance in characterizing the disease activity of GA. • Added combined preferred terms for adverse drug reactions in study eye to further assess the safety profile. • Other minor updates to provide clarity of analysis

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APPROVAL SIGNATURES

PPD

Electronically signed by: PPD
Reason: I am author of this document
Date: 05-Sep-2025 09:58:48 EDT

PPD, PhD
PPD, Biostatistics
Apellis Pharmaceuticals, Inc.

Date (dd-Mmm-yyyy)

PPD

Electronically signed by: PPD
PPD
Reason: I approve this document
Date: 05-Sep-2025 10:01:00 EDT

PPD, PhD
PPD, Biostatistics
Apellis Pharmaceuticals, Inc.

Date (dd-Mmm-yyyy)

PPD

Electronically signed by: PPD
PPD
Reason: I approve this document
Date: 05-Sep-2025 07:09:15 PDT

PPD, PhD
PPD, Clinical Science
Apellis Pharmaceuticals, Inc.

Date (dd-Mmm-yyyy)

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ABBREVIATIONS

ADA	Antidrug antibodies
ADY	Analysis Study Day
AE	Adverse Event
AMD	Age-related Macular Degeneration
ATC	Anatomical Therapeutic Class
BCVA/NL-BCVA	(Normal luminance) Best Corrected Visual Acuity
COVID-19	Coronavirus disease 2019
CSR	Clinical Study Report
DCFP	Digital Color Fundus Photography
DLS	Double-layer sign
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EOM	Every Other Month
ETDRS	Early Treatment Diabetic Retinopathy Study
EOS	End of Study
FAF	Fundus Autofluoresce ce
FDA	Food and Drug Administration
FFA/FA	Fundus Fluo escein Angiography or Fluorescein Angiography
FRI	Functional Reading Independence
GA	Geographic Atrophy
IOP	Intra Ocular Pressure
ITT	Intent-to-Treat
IVT	Intravitreal
kg	K logram
LOV	Last Observed Value
LL-BCVA	Low Luminance Best Corrected Visual Acuity
LLD	Low Luminance Deficit
LS	Least Square
MAR	Missing at Random
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mITT	Modified Intention to Treat
mL	Milliliter

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mmHg	Millimeter of Mercury
MMRM	Mixed effect Model for Repeated Measure
MNRead	Minnesota Reading Chart
NEI VFQ-25	National Eye Institute Visual Functioning Questionnaire 25-item version
NEI VFQ-39	National Eye Institute Visual Functioning Questionnaire 39-item version
NIR	Near Infrared Reflectance
OCT	Optical Coherence Tomography
OCT-A	Optical Coherence Tomography Angiography
PEOM	Pegcetacoplan Every-Other-Month
PM	Pegcetacoplan Monthly
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
CCI	CCI
SD-OCT	Spectral Domain Optical Coherence Tomography
SEOM	Sham Every-Other-M nth
SM	Sham Monthly
SOC	System Organ Class
TEAE	Treatment Emergen Adverse Event
µL	Micro liter
VEGF	Vascular endothelial growth factor
WHO	World Health Organization
WPM	Words per Minute

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1. INTRODUCTION

The APL2-GA-305 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]). This statistical analysis plan (SAP) provides a technical and detailed elaboration of the statistical analyses of efficacy, and safety data, supplementing what is described in the study protocol, amendment 3, dated 17 July 2023. The purpose of this analysis plan is for reporting the results of the APL2-GA-305 study in a clinical summary report(s). In case of any conflict, the analyses specified in this analysis plan supersede the analysis plan described in he study protocol (protocol amendment 3, dated 17 July 2023). The analyses in this study SAP will cover the analysis of the data from the APL2-GA-305 study from 3 separate timepoints.

- Analysis of the Month 12 dataset
- Analysis of the Month 24 dataset
- Analysis of the Month 36 (final) dataset

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2. OBJECTIVES AND ENDPOINTS

2.1. Objectives

2.1.1. Primary Objective

The primary objective of this study is to evaluate the long-term safety of IVT injected pegcetacoplan.

2.1.2. Secondary Objectives

The secondary objectives are:

- To assess changes in the total area of GA lesion in the tudy eye measured by fundus autofluorescence (FAF)
- To assess changes in visual function as measured by:
  a. Normal-luminance best-corrected visual a uity score (NL-BCVA) in the study eye
  b. Low-luminance best-corrected visual acuity s ore (LL-BCVA) in the study eye
  c. Reading speed in the study eye
- To assess the macular functional response as assessed by mesopic microperimetry in the study eye (selected subjects [those who had the assessment performed in the antecedent study] only).
- To evaluate changes in subject-reported outcomes as measured by:
  a. National Eye Institut Visual Functioning Questionnaire 25 Item Version (NEI VFQ25)
  b. Functional Reading Independence (FRI) Index

2.1.3. Additional Safety Objectives

- To assess th presence of antibodies to the PEG and/or peptide moiety of pegcetacoplan
- To assess the ncidence of new active choroidal neovascularization in the study eye.

2.2. Endpoints

2.2.1. Primary Endpoint

The primary endpoint is the incidence and severity of ocular and systemic Adverse Events (AE)s through Month 36.

2.2.2. Secondary Endpoints

- The total area of GA lesion(s) in the study eye (in mm^2) as assessed by FAF
  – Change from the APL2-GA-305 study baseline in the total area of GA lesion(s) in the study eye (in mm^2) through Month 12, Month 24, and Month 36, as assessed by FAF

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  - Change from antecedent study baseline in the total area of GA lesion(s) in the study eye (in mm^2) through Integrated Month 36, Integrated Month 48, and Integrated Month 60, as assessed by FAF

- The rate of change in GA lesion growth in the study eye as assessed by FAF
  - The rate of change from the APL2-GA-305 study baseline in the total area of GA lesion(s) growth in the study eye (in mm^2) through Month 12, Month 24, and Month 36, as assessed by FAF
  - The rate of change from antecedent study baseline in the total area of GA lesion(s) growth in the study eye (in mm^2) through Integrated Month 36, Integrated Month 48, and Integrated Month 60, as asse sed by FAF
- NL-BCVA score (study eye) as assessed by Early Treatment Diabetic Retinopathy Study (ETDRS) chart
  - Change from the APL2-GA-305 study baseline in NL-BCVA score (study eye) as assessed by ETDRS chart through Month 12 Month 24, and Month 36
  - Change from antecedent study baseline in NL-BCVA score (study eye) as assessed by ETDRS chart through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- LL-BCVA score (study eye) as as essed by ETDRS chart
  - Change from the APL2-GA-305 study baseline in LL-BCVA score (study eye) as assessed by ETDRS chart th ough Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in LL-BCVA score (study eye) as assessed by ETDRS hart through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- Monocular maximum re ding speed (study eye), corrected for the number of words read incorrectly, as assessed by Minnesota Reading (MNRead) charts or Radner charts
  - Change from the APL2-GA-305 study baseline in monocular maximum corrected reading speed (study eye) as assessed by MNRead charts or Radner through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in monocular maximum corrected reading speed (study eye) as assessed by MNRead charts or Radner through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- Binocular maximum reading speed, corrected for the number of words read incorrectly, as assessed by MNRead charts or Radner charts
  - Change from the APL2-GA-305 study baseline in binocular maximum corrected reading speed (study eye) as assessed by MNRead charts or Radner through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in binocular maximum corrected reading speed (study eye) as assessed by MNRead charts or Radner through Integrated Month 36, Integrated Month 48, and Integrated Month 60

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- The number of scotomatous points (study eye) assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only)
  - Change from the APL2-GA-305 study baseline in the number of scotomatous points (study eye) assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only) through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in the number of scotomatous points (study eye) assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only) through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- Macular sensitivity (study eye) as assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only)
  - Change from the APL2-GA-305 study baseline in mean threshold sensitivity (study eye) as assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only) through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in mean threshold sensitivity (study eye) as assessed by mesopic microperimetry (selected subjects [those who had the assessment performed in the antecedent study] only) through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- 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)
  - Change from the APL2-GA-305 study baseline in additional microperimetry parameters (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) (selected subjects [those who had the assessment performed in the antecedent study] only) through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in additional microperimetry parameters (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) (selected subjects [those who had the assessment performed in the antecedent study] only) through Integrated Month 36, Integrated Month 48, and Integrated Month 60
- Mean FRI Index score
  - Change from the APL2-GA-305 study baseline in mean FRI index score (subject-level assessment) through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in mean FRI index score (subject-level assessment) through Integrated Month 36, Integrated Month 48, and Integrated Month 60

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- 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, and distance activity subscale score, and NEI VFQ-25 driving subscale score
  - Change from the APL2-GA-305 study baseline in NEI VFQ-25 and NEI VFQ-39 (at selected sites) (subject-level assessment) composite score, near activity subscale score, distance activity subscale score, and NEI VFQ-25 driving subscale score through Month 12, Month 24, and Month 36
  - Change from antecedent study baseline in NEI VFQ-25 and NEI VFQ-39 (at selected sites) (subject-level assessment) composite score, near activity subscale score, distance activity subscale score, and NEI VFQ-25 driving subscale score through Integrated Month 36, Integrated Month 48, and Integrated Month 60

2.2.3. Safety Endpoints

- Incidence of new active exudative age-related ma ular degeneration (AMD) in the study eye through Month 12, Month 24, and Month 36.
- Incidence of new onset of subclinical xudative AMD in the study eye OCT-A through Month 12, Month 24, and Month 36.
- Incidence and severity of ocular nd systemic adverse events through Month 36 of subjects being treated bilaterally with pegcetacoplan.
- Summary of Anti-VEGF therapy with new onset exudative AMD in the study eye from APL2-GA-305 study b seline through Month 12, Month 24, and Month 36
- Change from APL2-GA-3 5 study baseline in Intra Ocular Pressure (IOP) and incidence of IOP above specified thresholds through Month 12, Month 24, and Month 36.
- Shift from APL2-GA 305 study baseline in ocular examination assessments including slit-lamp examination and indirect ophthalmoscopy through Month 12, Month 24, and Month 36.
- Incidence of subjects who lost letters based on NL-BCVA categories (≥15, ≥15 - < 30, ≥30 ETDRS letters) from APL2-GA-305 study baseline through Month 12, Month 24, and M nth 36.
- Change from APL2-GA-305 study baseline in central retinal thickness and central subfield thickness through Month 12, Month 24, and Month 36.
- Shift from APL2-GA-305 study baseline in subretinal fluid and cystoid spaces through Month 12, Month 24, and Month 36.
- Incidence of ADA directed against pegcetacoplan peptide or PEG through Month 12, Month 24, and Month 36.
- Change/shift from APL2-GA-305 study baseline in clinical labs and incidence of abnormal lab values through Month 12, Month 24, and Month 36.
- Change/shift from APL2-GA-305 study baseline in vital signs and incidence of abnormal vital signs through Month 12, Month 24, and Month 36.

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3. STUDY DESIGN

3.1. General Description

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 subjects with GA secondary to AMD.

This extension study will enroll approximately 1200 subjects from antecedent studies of APL2-103, APL2-303 and APL2-304 across approximately 250 multinational sites. Screening and baseline assessments can happen on the same day as th last visit in the antecedent study or within 60 days of the last visit. Subjects who meet all inclusion a d none of the exclusion criteria will be included in this study.

Subjects will receive pegcetacoplan, 15 mg/100 µL, monthly for up to 36 months (PM), if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Subjects will receive pegcetacoplan, 15 mg/100 µL, every other month for up to 36 months (PEOM), if they were in every other month (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.

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

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.

According to APL2-GA-305 protoco amendment 3.1 CAN, subjects in Canada can continue to receive treatment after Month 36 and their safety data will be collected during this time period. Due to the limited duration of this post-Month 36 treatment period, this safety data will be included in the correspondin analyses of safety data through Month 36,

The schedules of assessments pre ented in Protocol Amendment 3 are also available in Section 17.1.

3.2. Randomization

No randomization wa performed in the study APL2-GA-305. Pegcetacoplan treatment assignments (monthly or EOM) are based on treatment assignment in the antecedent studies.

Subjects will recei e monthly pegcetacoplan treatment if they were in the monthly treatment group (PM) in APL2-103/APL2-303/APL2-304. Subjects will receive EOM pegcetacoplan treatment if they were in the EOM treatment group (PEOM) in APL2-103/APL2-303/APL2-304. Subjects rand mized to sham monthly or sham every other month arms in APL2-303/APL2-304 studies will transition to PM and PEOM arms, respectively, in APL2-GA-305.

3.3. Masking

This is an open-label study. No masking of treatment is required.

3.4. Sample Size and Power Considerations

No formal power or sample size calculations will be made.

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

3.5. Definition of 12-Month Data, 24-Month Data, and 36-Month Data

3.5.1. Definition of 12-Month Data in the Month 12 Dataset

All screening and post-baseline data with a clinical date (ie, administration/assessment/ onset/start date) on or before the defined Month 12 data cutoff date will be included in the Month 12 Dataset. The 12-month data cutoff will include all data regardless of the type of study visit at which it was collected. This may include data collected at unscheduled visits or early termination visits if the visit date was on or before the 12-month data cutoff date. The Month 12 data cutoff is defined as:

- If the subject completed Month 12 visit, then the data cutoff will be the day that the Month 12 assessments are completed, or Study Day (based on APL2-GA-305 baseline) 376 if the subject did not complete the Month 12 visit due to missing visit.
- If the subject did not complete the Month 12 visit due to early termination, then the date of termination will be used as the Month 12 cutoff.
- The FAF data after subject's Month 12 visit or Study Day 376 will also be included only if the FAF data is within 1170 days of the antecedent study baseline.

3.5.2. Definition of 24-Month Data in the Month 24 Dataset

All screening and post-baseline data with a clinical date (ie, administration/assessment/ onset/start date) on or before the defined Month 24 data cutoff date will be included in the Month 24 Dataset. The 24-month data cutoff will include all data regardless of the type of study visit at which it was collected. This may include data collected at unscheduled visits or early termination visits if the visit date was on or before the 24 month data cutoff date. The Month 24 data cutoff is defined as:

- If the subject competed Month 24 visit, then the data cutoff will be the day that the Month 24 assessments are completed, or Study Day (based on APL2-GA-305 baseline) 736 if the subject did not complete the Month 24 visit due to missing visit.
- If the subject did not complete the Month 24 visit due to early termination, then the date of termination will be used as the Month 24 cutoff.
- The FAF data after subject's Month 24 visit or Study Day 736 will also be included only if the FAF data is within 1530 days of the antecedent study baseline.

3.5.3. Definition of 36-Month Data in the Month 36 (Final) Dataset

The Month 36 dataset will be based on data after all subjects have either completed the Month 36 visit in the study or discontinued the study early, and all data from the study are entered in the database and the database is reviewed, cleaned, and locked as the final dataset.

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3.6. Baseline Definitions

The following baseline definitions will be used in this study:

APL2-GA-305 Baseline: The baseline is defined as the last available non-missing assessment prior to first study drug administration in study APL2-GA-305.

Antecedent Study Baseline: The baseline is defined as the baseline value used in the antecedent study subject had enrolled in.

APL2-GA-305 Bilateral Treatment Baseline: The baseline is defined as the last available non-missing assessment prior to first study drug administration in the fellow eye.

3.7. Treatment Groups

Outputs will include:

- Using data from only APL2-GA-305 study
- Using integrated data from antecedent studies

For tables, figures, and listings in safety and efficacy analyses in APL2-GA-305, the subject will be assigned a treatment group according to both the an ecedent study treatment and the APL2-GA-305 treatments per the following categorization:

		Treatment group used in APL2-GA-305 analysis
Antecedent study	**APL2-GA-30**	
Pegcetacoplan monthly	Pegcet coplan monthly	PM to PM
Pegcetacoplan EOM	Peg etacoplan EOM	PEOM to PEOM
Sham monthly	P gcetacoplan monthly	SM to PM
Sham EOM	Pegcetacoplan EOM	SEOM to PEOM
Sham (monthly or EOM)	Pegcetacoplan (monthly or EOM)	Sham Pooled to Pegcetacoplan
Pegcetacoplan monthly or Sham monthly	Pegcetacoplan monthly	PM Total
Pegcetacoplan EOM or Sham EOM	Pegcetacoplan EOM	PEOM Total
Pegcetacoplan or Sham (monthly or EOM)	Pegcetacoplan (monthly or EOM)	Overall

For efficacy a alysis, subject will be assigned the treatment group based on antecedent study according to the treatment assigned when enrolled in antecedent study. For safety analysis, subject will be assigned the treatment group based on antecedent study according to the actual treatment received in antecedent study.

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For select efficacy summary tables based on APL2-GA-305 baseline, the following treatment groups will be presented:

- PM to PM
- PEOM to PEOM
- SM to PM
- SEOM to PEOM

For select efficacy summary tables based on antecedent study baseline, the following treatment groups will be presented:

- PM to PM
- PEOM to PEOM
- Sham pooled to pegcetacoplan

For study subjects and safety summary tables based on APL2 GA-305 baseline, the following treatment groups will be presented:

- PM to PM
- PEOM to PEOM
- SM to PM
- SEOM to PEOM
- PM Total
- PEOM Total
- Overall

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4. STATISTICAL ANALYSIS SETS

4.1. Screened Set

The screened set consists of all subjects who provided written informed consent and are screened for participation in this study. This population will only be used for the purposes of describing the subject disposition and for listing the data.

4.2. Enrolled Set

The enrolled set consists of all subjects who provided written informed consent and are enrolled in APL2-GA-305. Subjects will be analysed according to the treatment assigned when enrolled in antecedent study and APL2-GA-305.

4.3. Safety Set

The safety set consists of all enrolled subjects who receive at least one injection of Pegcetacoplan in APL2-GA-305. Subjects will be analysed according to the actual treatment received in antecedent study and APL2-GA-305.

4.4. Full Analysis Set

The full analysis set consists of all enrolled subjects who receive at least one injection of Pegcetacoplan in APL2-GA-305. Subjects will be analysed according to the treatment assigned when enrolled in antecedent study and APL2 GA-305.

4.5. Modified Full Analysis Set

The modified full analysis set consists of all subjects who are in APL2-303, APL2-304 antecedent study's ITT set, haven't been nrolled in APL2-103, and receive at least one injection of Pegcetacoplan in APL2-GA-305. Subjects will be analysed according to the treatment assigned when enrolled in antecedent study and APL2-GA-305.

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5. STUDY SUBJECTS

5.1. Disposition of Subjects

The number of subjects screened, passed screening, screened failed, and the reasons for screen failure will be presented overall.

The number of subjects enrolled, in each defined analysis set, and the antecedent study subject had enrolled in will be summarized by treatment group and overall.

The subject's disposition will be provided by treatment group and overall for the safety set. Subjects' disposition by region will also be provided for the safety set.

Overall summary of subjects' disposition includes:

- Number of subjects completed study (through Month 12 in the Month 12 dataset, or through Month 12 and Month 24 in the Month 24 d taset, or through Month 12, Month 24, and Month 36 in the Month 36 data et)

  Number of subjects discontinued from study and reason for discontinuation (prior to Month 12 in the Month 12 dataset, or prior to Month 12 and Month 24 in the Month 24 dataset, or prior to Month 12, Month 24, and Month 36 in the Month 36 dataset)

5.2. Demographic and Other Baseline Characteristics

Demographic and baseline characteristics will be t bulated using descriptive statistics by treatment group and overall using APL2-GA-305 baseline for safety set and full analysis set. Summaries will also be presented using antecedent study baseline for safety set and modified full analysis set.

The following variables will be included in the tables:

The demographic data are:

- Age (years) and Age g oup (<65 years, ≥65 - <75 years, ≥75 - <85 years, ≥85 years),
- Sex
- Race
- Ethnicity
- Geographic Region (United States vs. Rest of World)
- Country
- Weight (kg)
- Height (cm)
- Body Mass Index (kg/m^2)

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Baseline characteristics will be summarized for both study eye and fellow eye whenever applicable. Baseline characteristics include:

- Study eye laterality (OD, OS)
- Study eye status (better-seeing eye vs. worse-seeing eye, based on NL-BCVA – in the case of ties, study eye status will be classified as the better-seeing eye)
- GA lesion size (mm^2) (assessed by FAF)
- GA lesion size in categories, determined by reading center
  - $< 7.5\ mm^2$
  - $\geq 7.5\ mm^2$
- GA lesion size categories (tertiles based on antecedent study) – study eye only
- GA lesion location (subfoveal involvement v non-subfoveal involvement) (assessed by FAF)
- GA lesion location (distance to center point of the fovea $\geq$0.25mm and <0.25mm)
- GA focality (unifocal vs. multifocal) (assessed by FAF)
- Number of areas of atrophy (none, 1, 2-5, 6-10, 11-20, >20, cannot be determined) (assessed from FAF)
- Presence of double-layer sign (DLS) (assessed by SD-OCT) (only for antecedent study baseline)
- Central subfield thickn ss (CST) (assessed by SD-OCT)
- Presence of macular neovascularization (MNV) (ie, subclinical exudative AMD) (assessed by Optical Coherence Tomography Angiography (OCT-A))
- Presence of pseudodrusen (assessed by near-infrared reflectance imaging)
- Number of intermediate/large drusen (0-5, 6-10, 11-20, and >20) (assessed by color fundus photography)
- NL-BCVA in ETDRS letters
- NL-BCVA categories ($\geq$70, $\geq$60 - <70, $\geq$35 - <60, <35 ETDRS letters)
- NL-BCVA categories (<60 vs. $\geq$60 ETDRS letters)
- LL-BCVA in ETDRS letters
- LL-BCVA categories (tertiles based on antecedent study) – study eye only
- IOP
- LLD in ETDRS letters
- LLD categories (<20 vs. $\geq$ 20 ETDRS letters)
- LLD categories (tertiles based on antecedent study) – study eye only

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- NL-BCVA (<60 vs. ≥60 ETDRS letters) and LLD (<20 vs. ≥ 20 ETDRS letters) combinations
- Advanced AMD (fellow eye with: GA only, GA with exudative AMD, exudative AMD only, neither GA nor exudative AMD)
- GA laterality (bilateral GA vs. study eye GA Only)
- Presence of exudative AMD in fellow eye (based on medical history for antecedent study baseline; based on both medical history and Adverse Events for APL2-GA-305 baseline)
- Presence of exudative AMD in study eye (only for APL2-GA 305 baseline)
- Lens status:
    - Phakic
    - Pseudophakic
- Reading speed assessment method
- Monocular and binocular maximum corrected reading speed (with adjustment for reading inaccuracy)
- Monocular maximum reading speed categories (<60, 60-<160, ≥160 words per minute (wpm))
- Monocular maximum reading speed categories (tertiles based on antecedent study) – study eye only
- Mean FRI Index score
- FRI Level (1,2,3,4)
- NEI VFQ-25 distance activity subscale score
- NEI VFQ-25 near activity subscale score
- NEI VFQ-25 driving subscale score
- Number of subjects currently driving at baseline
- NEI VFQ-25 composite score

The following baseline characteristics will be summarized for those subjects who had the mesopic microperimetry performed in antecedent study APL2-304: (The measured distances to the atrophy border used to classify each anatomical region are based on antecedent study baseline.)

- Mean threshold sensitivity in (assessed by mesopic microperimetry)
    - Overall
    - Junctional zone (-250 to 250 µm)
    - Junctional zone (-375 to 375 µm)
    - Junctional zone (-500 to 500 µm)

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- Number of scotomatous points in (assessed by mesopic microperimetry)
    - Overall
    - Junctional zone (-250 to 250 µm)
    - Junctional zone (-375 to 375 µm)
    - Junctional zone (-500 to 500 µm)
- Fixation stability (95% BCEA) (assessed by microperimetry)
- Fixation stability (95% BCEA) categories (tertiles based on a tecedent study)

Duration between last visit of antecedent study and first dose of APL2-GA-305 (only for APL2-GA-305 baseline) will be summarized by treatment group both as a continuous summary and as a frequency and percent summary for:

- <7 days
- 7-30 days
- 30-60 days
- >=60 days

5.3. Medical Ocular and Non-ocular History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary version 23.1. Summaries will be pr sented by System Organ Class (SOC) and Preferred Term (PT) with counts and percentages by treatment group and overall for safety set. Each subject will be counted only o ce in each SOC or SOC/PT summary.

All ocular history will be summarized by SOC and PT with counts and percentages by treatment group and overall. The summari s will be produced separately for the study eye and the fellow eye. Any ocular condition associated with both eyes will be included in both summaries.

5.4. Prior and Concomitant Medications

Prior and concomitant m dications will be coded using World Health Organization (WHO) Drug Dictionary version WHO Drug Global B3-format March 2021. Non-ocular medications will be presented fo the safety set by anatomical therapeutic class (ATC) level 2 (therapeutic main group) and preferred term with counts and percentages by treatment group and overall. A subject who took more than one medication will be counted only once if these medications belong to the same extended ATC classification. In addition, concomitant ocular medications used in study eye will be summarized.

Similar summaries will be provided for the ocular medications used in the fellow eye. Any ophthalmological medications (ATC2 = 'Ophthalmologicals') that are not assigned to an eye will be presented under both eyes in the ocular medications tables and will not be presented in the non-ocular medications tables.

Prior medications will be defined as those medications taken prior to the date of first study drug administration in APL2-GA-305. Concomitant medications will be defined as those medications taken on or after the date of first study drug administration in APL2-GA-305.

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Medications started before the date of first study dosing in APL2-GA-305 and continuing into the treatment period are considered as both prior and concomitant medications.

Summaries will be provided for concomitant medications by treatment group and overall for the safety set.

5.5. Concomitant Procedures

Concomitant procedures will be coded using MedDRA version 23.1. Non-ocular procedures will be presented for the safety set by preferred term with counts and percentages by treatment group and overall. A subject who had more than one procedure will be counted only once in the summary. In addition, concomitant ocular procedures in study eye will be summarized. Similar summaries will be provided for the ocular procedures used in the fellow eye.

Concomitant procedures will be defined as those procedures taken on or after the date of first study drug administration in APL2-GA-305. Procedures started before the date of first study dosing in APL2-GA-305 and continuing into the treatment period are also considered as concomitant procedures.

5.6. Exposure to Investigational Product

5.6.1. Exposure to Investigational Product From APL2-GA-305 Baseline to Month 12, Month 24 and Month 36

For summary in the Month 12 dataset, exposure to the investigational product from APL2-GA-305 baseline to Month 11 will be summarized for safety set, injection in Month 12 will not be included. For summary in the Month 24 dataset, exposure to the investigational product from APL2-GA-305 baseline to Month 23 will be summarized for safety set, injection in Month 24 will not be included. For summary in the Month 36 dataset, exposure to the investigational product from APL2-GA-305 baseline to end of study (EOS) will be summarized for safety set.

The total number of injections received and total number of missed injections in each treatment group will be summarized by treatment group to support per-injection based TEAE rates.

The number of missed injections is defined as the scheduled injections missed up to completion or discontinuation of study treatment. The following categories for reason for missed injections will be summarized by treatment group using frequency counts and percentages based on the total number of missed injections: due to Covid-19 vs. non-Covid-19 reasons. The total number of injections received per subject will be summarized by treatment group both as a continuous summary and as a frequency and percent summary. In addition, the following categories of the total number of injections received per subject will be summarized by treatment group using frequency counts and percentages:

- 12 months summaries
  - Monthly: 1-3, 4-6, 7-9, 10-12
  - EOM: 1-2, 3-4, 5-6

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- 24 months summaries
  - Monthly: 1-3, 4-6, 7-9, 10-12 13-15 16-18 19-21 22-24
  - EOM: 1-2, 3-4, 5-6 7-8 9-10 11-12
- 36 months summaries
  - Monthly: 1-3, 4-6, 7-9, 10-12, 13-15, 16-18, 19-21, 22-24, 25-27, 28-30, 31-33, >=34
  - EOM: 1-2, 3-4, 5-6, 7-8, 9-10, 11-12, 13-14, 15-16, >=17

The number of subjects who received at least 75%, and less than 75% of the planned injections will be presented. For the first 12 months, subjects will be considered to have rec ived 75% of the planned injections if they received at least 9 (out of 12) injections for the Monthly group or 5 (out of 6) injections for the EOM group. For the first 24 months, s bjects will be considered to have received 75% of the planned injections if they received at least 18 (ou of 24) injections for the Monthly group or 9 (out of 12) injections for the EOM g oup. For the full 36 months, subjects will be considered to have received 75% of the planned injections if they received at least 27 (out of 36) injections for the Monthly group or 14 (out of 18) injections for the EOM group.

The number of subjects missing at least one injection and the number of missed injections per subject will be summarized by treatment group.

Additionally, the duration of treatment and compliance will be summarized by treatment group.

Duration of treatment in days will be defined as follows:

- Monthly group: (date of last injection in APL2-GA-305 + 30) – date of first injection in APL2-GA-305 + 1
- EOM group: (date of last injection in APL2-GA-305 + 60) – date of first injection in APL2-GA-305 + 1

The duration of treatment will be truncated to a subject's early termination date, Month 12 or Month 24 cutoff date or study completion date as appropriate.

Compliance (%) is defined a follows:

- Number of injections received × 100/ Number of scheduled injections up to discontinuation of study treatment, Month 12 or Month 24 cutoff date or study completion date.

Compliance ill be summarized in the following groups: <75%, ≥75% to <100%, 100%, and >100%.

For subjects treated bilaterally with pegcetacoplan, exposure to the investigational product in the fellow eye will be presented for safety set. Summary of total number of injections, number of missed injections, number of injections per subject, duration of treatment will be included.

To justify the midpoint between Monthly treatment and EOM treatment, duration of treatment in days will be defined as: (date of last injection of fellow eye in APL2-GA-305 + 45) – date of first injection of fellow eye in APL2-GA-305 + 1.

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5.6.2. Exposure to Investigational Product From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

For summary in the Month 12 dataset, exposure to the investigational product from antecedent study baseline to Integrated Month 35 will be summarized for modified full analysis set, injection in Integrated Month 36 will not be included. For summary in the Month 24 dataset, exposure to the investigational product from antecedent study baseline to Integrated Month 47 will be summarized for modified full analysis set, injection in Integrated Month 48 will not be included. For summary in the Month 36 dataset, exposure to the investigational product from antecedent study baseline to EOS will be summarized for modified full analysis set

The total number of injections received and total number of missed injections in each treatment group will be summarized by treatment group.

The number of missed injections is defined as the scheduled injections missed up to completion or discontinuation of study treatment. The total number of injecti ns received per subject will be summarized by treatment group both as a continuous summary and as a frequency and percent summary. In addition, the following categories of the total number of injections received per subject will be summarized by treatment group using frequency counts and percentages:

- Integrated 36 months summaries
  - Monthly: 1-6, 7-12, 13-18, 19-24, 25-30, 31-36
  - EOM: 1-3, 4-6, 7-9, 10-12, 13-15, 16-18
- Integrated 48 months summaries
  - Monthly: 1-6, 7-12 13-18 19-24, 25-30, 31-36, 37-42, 43-48
  - EOM: 1-3, 4-6, 7-9, 10 12, 13-15, 16-18, 19-21, 22-24
- Integrated 60 months summaries
  - Monthly: 1-6, 7-12, 13-18, 19-24, 25-30, 31-36, 37-42, 43-48, 49-54, >=55
  - EOM: 1-3, 4-6, 7-9, 10-12, 13-15, 16-18, 19-21, 22-24, 25-27, >=28

The number of subjects who received at least 75%, and less than 75% of the planned injections will be presented For the first 36 months, subjects will be considered to have received 75% of the planned injecti ns if they received at least 27 (out of 36) injections for the Monthly group or 14 (out of 18) injections for the EOM group. For the first 48 months, subjects will be considered to have rec ived 75% of the planned injections if they received at least 36 (out of 48) injections for the Monthly group or 18 (out of 24) injections for the EOM group. For the full 60 months, subjects will be considered to have received 75% of the planned injections if they received at least 45 (out of 60) injections for the Monthly group or 23 (out of 30) injections for the EOM group.

Duration of treatment in days will be defined as follows:

- Monthly group: (date of last injection in APL2-GA-305 + 30) – date of first injection in APL2-303/APL2-304 + 1
- EOM group: (date of last injection in APL2-GA-305 + 60) – date of first injection in APL2-303/APL2-304 + 1

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The duration of treatment will be truncated to a subject's early termination date, Month 12 or Month 24 cutoff date or study completion date as appropriate.

Compliance (%) is defined as follows:

- Number of injections received × 100/ Number of scheduled injections up to discontinuation of study treatment, Month 12 or Month 24 cutoff date or study completion date.

Compliance will be summarized in the following groups: <75%, ≥75% to <100%, 100%, and >100%.

Exposure to the investigational product from antecedent study baseline to In egrated Month 35, Integrated Month 47, and EOS will be repeated for modified full analysi set only after subjects received their first dose of pegcetacoplan. Summary of total number of injections, number of missed injections, number of injections per subject, duration of treatment will be presented.

5.7. Protocol Deviations

Important and non-important protocol deviations (PDV) will be assessed by sponsor personnel following Protocol Deviation Management Plan

A PDV is classified as important if there is the potential to significantly impact the completeness, accuracy, and/or reliability of the trial data or subject's rights, safety, or well-being. All PDVs will be identified and finalized prior to the analysis of the full 36 months data and documented.

PDVs will be presented for the safety set by deviation category, subcategory, and study specific category with counts and percentages by treatment group and overall from APL2-GA-305 Baseline to Month 36. In addition, similar summaries will be provided for important PDVs.

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6. EFFICACY ANALYSES

6.1. Estimands

6.1.1. Estimands Related to GA Lesion Within Each Treatment Group From APL2-GA-305 Baseline

The secondary estimand related to GA lesion within each treatment group from APL2-GA-305 baseline in the study is defined through the following 5 attributes:

- **Population:** GA subjects defined through inclusion and exclu ion criteria in full analysis set.
- **Treatment conditions:** The treatment regimen of interest in this study is PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM
- **Variable (or endpoint):** Change in total area of GA lesions in the study eye from APL2-GA-305 baseline measured by FAF to Month 12, Month 24, and Month 36, and total area of GA lesions in the study eye through Month 12, Month 24, and Month 36.
- **Strategy for addressing intercurrent events:** See description of intercurrent events below.
- **Population-level summary:** Least Square (LS) mean change of GA lesion from APL2-GA-305 baseline to Month 12, Month 24, and Month 36 within each treatment group according to mixed effect model for repeated measure (MMRM) analysis, and mean rate of change of GA lesion from APL2-GA-305 baseline to Month 12, Month 24, and Month 36 within each treatment group according to rate of change analysis.

The intercurrent event that will be considered is:

- Treatment discontinuation in the APL2-GA-305 study

The intercurrent events will be handled with a treatment policy strategy whereby any measured value will be used as is. Missing data resulting from these intercurrent events will be handled implicitly within the MMRM analysis that assumes missing at random (MAR).

6.1.2. Estimands Related to GA Lesion Within Each Treatment Group From Antecedent Study Baseline

The secondary estimand related to GA lesion within each treatment group from antecedent study baseline in the study is defined through the following 5 attributes:

- **Population:** GA subjects defined through inclusion and exclusion criteria in modified full analysis set.
- **Treatment conditions:** The treatment regimen of interest in this study is PM to PM, PEOM to PEOM, Sham Pooled to Pegcetacoplan.

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- **Variable (or endpoint):** Change in total area of GA lesions in the study eye from antecedent study baseline measured by FAF to Integrated Month 36, Integrated Month 48, and Integrated Month 60, and total area of GA lesions in the study eye through Integrated Month 36, Integrated Month 48, and Integrated Month 60.
- **Strategy for addressing intercurrent events:** See description of intercurrent events below.
- **Population-level summary:** LS mean change of GA lesion from antecedent study baseline to Integrated Month 36, Integrated Month 48, an Integrated Month 60 within each treatment group according to MMRM analysis, a d mean rate of change of GA lesion from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60 within each treatment group according to rate of change analysis.

The intercurrent event that will be considered is:

- Treatment discontinuation in the APL2-GA-305 tudy

The intercurrent events will be handled with a treatment policy strategy whereby any measured value will be used as is. Missing data resulting fr th intercurrent events will be handled implicitly within the MMRM analysis that assumes missing at random (MAR).

6.1.3. Estimands Related to GA Lesion Compared With Hypothetical Sham From Antecedent Study Baseline

The secondary estimand related to GA lesion o assess the effect of pegcetacoplan compared with hypothetical sham in the study from antecedent study baseline is defined through the following 5 attributes:

- **Population:** GA subjects defined through inclusion and exclusion criteria in modified full analysis set.
- **Treatment conditions:** The treatment regimen of interest in this study is PM to PM, PEOM to PEOM, hypothetical sham.
- **Variable (or endpoint):** Change in total area of GA lesions in the study eye from antecedent study baseline measured by FAF to Integrated Month 36, Integra d Month 48, and Integrated Month 60, and total area of GA lesions in the study eye through Integrated Month 36, Integrated Month 48, and Integrated Month 60.
- **Strategy for addressing intercurrent events:** See description of intercurrent events below.
- **Population-level summary:** Difference in LS mean change of GA lesion from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60 between pegcetacoplan and hypothetical sham according to MMRM analysis, and difference in mean rate of change of GA lesion from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60 between pegcetacoplan and hypothetical sham group according to rate of change analysis.

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The intercurrent events that will be considered are:

- Treatment discontinuation in the APL2-GA-305 study
- Subjects in Sham group in APL2- 303/APL2-304 received pegcetacoplan in APL2-GA-305

The intercurrent event of treatment discontinuation will be handled with a treatment policy strategy whereby any measured value will be used as is. Missing data resulting from these intercurrent events will be handled implicitly within the MMRM analysis that assumes MAR. The intercurrent event of Subjects in Sham group in APL2-303/APL2-304 received pegcetacoplan i APL2-GA-305 will be handled with a hypothetical strategy whereby data of these subjects in APL2-GA 305 will be excluded and imputed based on their APL2-303/APL2-304 data.

6.2. Analyses of Primary Efficacy Endpoint

Not applicable. The primary endpoint of this study is related to safety.

6.3. Analyses of Secondary Efficacy Endpoint related to GA Lesion

6.3.1. Analyses of Secondary Efficacy Endpoint related to GA Lesion From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

Efficacy analyses from APL2-GA-305 baseline to Month 12 will be performed in the Month 12 dataset in full analysis set. Efficacy analyses from APL2-GA-305 baseline to Month 24 will be performed in the Month 24 dataset in full ana ysis set. Efficacy analyses from APL2-GA-305 baseline to Month 36 will be performed in the Month 36 dataset in full analysis set.

The observed values for the total area of GA lesion size (mm^2) will be summarized by treatment group and visits for both the study eye and the fellow eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute value, and change from APL2-GA-305 baseline.

The mean change from APL2-GA-305 baseline in the total area of GA lesion size (mm^2) in the study eye ± the standard e ill be plotted over time by treatment group.

6.3.1.1. Main MMRM Analysis

The change from APL2-GA-305 to Month 12 in the total area of GA lesion size (mm^2) in the study eye will be summari ed and assessed with a MMRM approach in the full analysis set. The analysis model will include change from APL2-GA-305 baseline to Month 12 in the total area of GA lesion size (mm^2) in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, categorical) as a factor, the time × antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) and time × treatment as interaction terms. Note that the categorical covariates (ie, presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2)) will not be specified using the class statement in SAS, LS mean will be computed based on the observed frequency in the dataset. The LS mean change from APL2-GA-305 baseline to Month 12, and the corresponding 95% CI will be estimated from the model for each arm. Additional detail is provided in the sample code in Section 17.3.

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A common unstructured covariance matrix will be used to model the within-subject errors, the sandwich estimator (Diggle et al. 1994) will be used to estimate the standard errors (SE) of the fixed effects parameters, and the degrees of freedom will be partitioned into between-subject and within-subject portions. If there are convergence problems with the model, then a heterogeneous autoregressive (1) covariance matrix will be used. If convergence problems still exist, an autoregressive (1) covariance matrix will be used.

The LS mean of the change from APL2-GA-305 baseline in the total area of GA lesion(s) ± the standard error will be plotted over time by treatment group.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of cho oidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effe t APL2-GA-305 baseline GA lesion size as covariates, time (study month, categorical) as a factor, the time × APL2-GA-305 baseline GA lesion size and time × treatment as intera tion erms.

6.3.1.2. Main Rate of Change Analysis

The mean rate of change in GA area (ie, slope) from APL2-GA-305 baseline to Month 12 will be analysed by use of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") in full analysis set. A knot at Month 6 visit will be added which allows for the slope of lesion growth to differ between the two 6-month periods for each of the treatment groups.

The analysis model will include treatmen group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 6, interaction between time and antecedent study baseline GA l sion area (< 7.5 mm^2 or ≥ 7.5 mm^2), interaction between knot and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the GA lesion area (mm^2)

The mean rate of change slope), standard error, and confidence intervals will be estimated for the APL2-GA 305 baseline through Month 12 for each treatment group for each 6-month period as well as cumulatively. In addition, linear trend for mean rate of change of each 6-month periods wi hin each group will be tested. Further comparisons between 6-month periods may be performed to nderstand the lesion growth and treatment effect over time. Additional detail is provided in the sample code in Section 17.3.

A common unstructured covariance matrix will be used to model the within-subject errors, the sandwich estimator will be used to estimate the standard errors of the fixed effects parameters, and the degrees of freedom will be partitioned into between-subject and within-subject portions. If there are convergence problems with the model, then a heterogeneous autoregressive (1) covariance matrix will be used.

The mean rate of change from APL2-GA-305 baseline in the total area of GA lesion(s) ± the standard error will be plotted over time by treatment group.

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The rate of change analysis will be performed from APL2-GA-305 baseline to Month 24 with a knot at Month 12 visit, the analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot.

The rate of change analysis will also be performed from APL2-GA-305 baseline to Month 36 with a knot at Month 12 visit, and Month 24 visit, the analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of horoidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, knot at Month 24, interac ion between treatment and time, and interaction between treatment and knots.

6.3.1.3. Sensitivity Analysis

The observed values for the total area of GA lesion size (mm^2) excluding GA lesion assessments with an indeterminate boundary will be summarized by treatment group and visits for the study eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute value, and change from APL2-GA-305 baseline.

6.3.1.3.1. Sensitivity MMRM Analysis Excluding GA Lesion Assessments With an Indeterminate Boundary

The main MMRM analysis described in Section 6.3.1.1 will be repeated by excluding total area of GA lesion assessments with an ind terminate boundary of the study eye.

The main MMRM analysis described in Section 6.3.1.1 will also be repeated by excluding total area of GA lesion assessments with an indeterminate boundary due to poor image quality of the study eye.

6.3.1.3.2. Sensitivity Rate of Change Analysis Excluding GA Lesion Assessments With an Indeterminate Boundary

The main rate of change analysis described in Section 6.3.1.2 will be repeated by excluding total area of GA lesion assessments with an indeterminate boundary of the study eye.

The main rate of change analysis described in Section 6.3.1.2 will be repeated by excluding total area of GA lesion assessments with an indeterminate boundary due to poor image quality of the study eye.

6.3.1.4. Analysis Compared With the Fellow Eye

6.3.1.4.1. MMRM Analysis Compared With the Fellow Eye

The change from APL2-GA-305 baseline to Month 12 in the total area of GA lesion size (mm^2) in the study eye will be compared with the fellow eye for subjects with bilateral GA with fellow eyes satisfying the following characteristics at APL2-GA-305 baseline:

- baseline GA lesion size > 2.5 mm^2
- presence of any pattern of hyperautofluorescence in the junctional zone of GA

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The dependent variable, change from APL2-GA-305 baseline in GA lesion size at Month 6, and Month 12 for the respective eye (study or fellow) will be analyzed using a MMRM model in full analysis set. The model will include terms for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), eye (study or fellow), antecedent study baseline GA lesion area (<7.5 mm^2 or ≥7.5 mm^2), and difference between study eye and fellow eye GA lesion area at antecedent study baseline as fixed effects; time (study month, categorical) as a factor; time × treatment interaction term, antecedent study baseline GA lesion area (<7.5 mm^2 or ≥7.5 mm^2) × time interaction, difference between study eye and fellow eye GA lesion area at baseline × time interaction term, treatment × eye interaction term, eye × time interaction term, and time × treatment × eye interaction term. The covariance structure is a direct product unstructured. The sandwich estimator as described in Section 6.3.1.1 will be used to estimate the SEs of the fixed effects parameters.

The LS mean change from APL2-GA-305 baseline for each eye and difference between study eye and fellow eye at each assessment will be estimated from the model for each treatment group. The percentage difference in change from APL2-GA-305 ba eline in the study eye and fellow eye will be calculated within each group compared with the fellow eye change.

The MMRM analysis will also be performed from APL2 GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), eye (study or fellow), antecedent study baseline GA lesion area (<7.5 mm^2 or ≥7.5 mm^2), and difference between study eye and fellow eye GA lesion area at APL2-GA-305 baseline as fixed effects; time (study month, categorical) as a factor; time × treatment inte action term, difference between study eye and fellow eye GA lesion area at APL2-GA-305 baseline × time interaction term, treatment × eye interaction term, eye × time interaction term, and time × treatment × eye interaction term.

GA lesion measurements taken after initiation of pegcetacoplan treatment in the fellow eye will be censored in the above analysis

6.3.1.4.2. Rate of Change Analysis Compared With the Fellow Eye

The mean rate of change in GA area (ie, slope) from APL2-GA-305 baseline to Month 12 in the study eye will be compared with the fellow eye for subjects with bilateral GA with fellow eyes satisfying the characteris ics in Section 6.3.1.4.1. It will be analysed by use of a piecewise linear mixed effect model assuming time as continuous and piecewise linear (“piecewise slope model”) in full analysis set. A knot at Month 6 will be added which allows for the slope of lesion growth to differ between the two 6-month periods for each of the treatment groups.

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6.3.1.4.3. Analysis for Treated Fellow Eye

For subjects treated bilaterally with pegcetacoplan, the observed values for the total area of GA lesion size (mm^2) for treated fellow eye will be summarized by treatment group and visits in full analysis set.

Analysis visits for treat d fellow eye will be derived based on the analysis visit window mapping rules in Section 13.3. Summaries will present the descriptive statistics for APL2-GA-305 bilateral treatment baseline, absolute value, and change from APL2-GA-305 bilateral treatment baseline.

6.3.2. Analyses of Secondary Efficacy Endpoint Related to GA Lesion From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

Efficacy analyses from antecedent study baseline to Integrated Month 36 will be performed in the Month 12 dataset in modified full analysis set. Efficacy analyses from antecedent study baseline to Integrated Month 48 will be performed in the Month 24 dataset in modified full analysis set. Efficacy analyses from antecedent study baseline to Integrated Month 60 will be performed in the Month 36 dataset in modified full analysis set.

The observed values for the total area of GA lesion size (mm^2) will be summarized by treatment group and visits for both the study eye and the fellow eye. Summaries will present the descriptive statistics for antecedent study baseline, absolute value, and change from antecedent study baseline.

The mean change from antecedent study baseline in the total area of GA lesion size (mm^2) in the study eye ± the standard error will be plotted over time by treatment group.

6.3.2.1. Main Analysis – Observed Data

6.3.2.1.1. Main MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in the total area of GA lesion size (mm^2) in the study eye will be summarized and assessed with a MMRM approach in the modified full analysis set. The analysis model will include change from antecedent study baseline to Integrated Month 36 in the total area of GA lesion size (mm^2) in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, categorical) as a factor, the time × antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) and time × treatment as interaction terms. Note that the categorical covariates (i.e., presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) will not be specified using the class statement in SAS, LS mean will be computed based on the observed frequency in the dataset. Additional detail is provided in the sample code in Section 17.3.

A common unstructured covariance matrix will be used to model the within-subject errors, the sandwich estimator will be used to estimate the standard errors of the fixed effects parameters, and the degrees of freedom will be partitioned into between-subject and within-subject portions. If there are convergence problems with the model, then a heterogeneous autoregressive (1) covariance matrix will be used. The LS mean change from antecedent study baseline to Integrated Month 36, and the corresponding 95% CI will be estimated from the model for each arm. In addition, the difference in LS mean change from antecedent study baseline to Integrated Month 36, the corresponding 95% CI, and the 2-sided P-value will be estimated.

The percentage difference (100 x difference in LS mean change from antecedent study baseline to Integrated Month 36 between the arms / the reference group LS mean change from antecedent study baseline to Integrated Month 36) will also be presented. Note that this difference is to compare early vs late initiation of pegcetacoplan instead of treatment effect versus sham.

The LS mean of the change from antecedent study baseline in the total area of GA lesion(s) ± the standard error will be plotted over time by treatment group.

In addition, the main MMRM analysis will be repeated by antecedent study (APL2-303 and APL2-304).

The MMRM analysis will also be repeated from antecedent study baseline to Integrated Month 48, and from antecedent study baseline to Integrated Month 60.

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6.3.2.1.2. Supplemental Analysis of the Main MMRM Analysis

The change from antecedent study baseline to Integrated Month 36, Integrated Month 48 and Integrated Month 60 in the total area of GA lesion size (mm^2) in the study eye using MMRM approach described in Section 6.3.2.1.1 will also be repeated without pooling SM to PM and SEOM to PEOM groups together. Comparisons within each dose schedule (ie, PM to PM vs. SM to PM and PEOM to PEOM vs. SEOM to PEOM, respectively) will be conducted.

6.3.2.1.3. Main Rate of Change Analysis

The mean rate of change in GA area (ie, slope) from antecedent study baseline to Integrated Month 36 will be analysed by use of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope m del") in modified full analysis set. A knot at the Integrated Month 6, Integrated Month 12, Integrated Month 18, Integrated Month 24, and Integrated Month 30 visit will be added which allows for the slope of lesion growth to differ between each 6-month periods for each of the treatment groups.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Integrated Month 6, knot at Integrated Month 12, knot at Integrated Month 18, knot at Integrated Month 24, knot at Integrated Month 30, interaction between time and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), interaction between ach knot and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), interac ion between treatment and time, and interaction between treatment and each knot. The dependent variable will be the GA lesion area (mm^2).

A common unstructured covariance matrix will be used to model the within-subject errors, the sandwich estimator will be used to es imate the standard errors of the fixed effects parameters, and the degrees of freedom will be partitioned into between-subject and within-subject portions. If there are convergence problems with the model, then a heterogeneous autoregressive (1) covariance matrix will be used. The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for ea h 6-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

In addition, th LS mean difference between change from Integrated Month 24 to Integrated Month 30 and change from Integrated Month 18 to Integrated Month 24, the LS mean difference between change from Integrated Month 30 to Integrated Month 36 and change from Integrated Mo th 18 to Integrated Month 24, and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group. The LS mean difference between change from Integrated Month 24 to Integrated Month 30 and average of change from antecedent study baseline to Integrated Month 24, between change from Integrated Month 30 to Integrated Month 36 and average of change from antecedent study baseline to Integrated Month 24 and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group. Additional detail is provided in the sample code in Section 17.3.

The mean rate of change from antecedent study baseline in the total area of GA lesion(s) ± the standard error will be plotted over time by treatment group.

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The main rate of change analysis will be repeated by antecedent study (APL2-303 and APL2-304).

The rate of change analysis will be repeated from antecedent study baseline to Integrated Month 48 with a knot at the Integrated Month 12, Integrated Month 24, and Integrated Month 36. The LS mean difference between change from Integrated Month 24 to Integrated Month 36 and change from Integrated Month 12 to Integrated Month 24, the LS mean difference between change from Integrated Month 36 to Integrated Month 48 and change from Integrated Month 12 to Integrated Month 24, and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group. The LS mean difference between change from Integrated Month 24 to Integrated Month 36 and average of change from antecedent study baseline to Integrated Month 24, between change from Integrated Month 36 to Integrated Month 48 nd average of change from antecedent study baseline to Integrated Month 24 and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group.

The analysis will also be repeated from antecedent study baseline o Integrated Month 60 with a knot at the Integrated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48. The LS mean difference between change from Integrated Month 24 to Integrated Month 36 and change from Integrated Month 12 to Integrated Month 24, the LS mean difference between change from Integrated Month 36 to Integrated Month 48 and change from Integrated Month 12 to Integrated Month 24, the LS mean difference between change from Integrated Month 48 to Integrated Month 60 and change from Integrated Month 12 to Integrated Month 24, and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group. The LS m an difference between change from Integrated Month 24 to Integrated Month 36 and average of change from antecedent study baseline to Integrated Month 24, between change from Integrated Month 36 to Integrated Month 48 and average of change from antecedent study baseline to Integrated Month 24, between change from Integrated Month 48 to Integrated Month 60 and average of ch nge from antecedent study baseline to Integrated Month 24 and the corresponding 95% CI will be estimated from the main rate of change analysis for Sham Pooled to Pegcetacoplan group.

6.3.2.1.4. Supplemental Analysis of the Main Rate of Change Analysis

The change from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 6 in the total area of GA lesion size (mm^2) in the study eye using piecewise slope rate of change approach described in Section 6.3.2.1.3 will also be repeated without pooling SM to PM and SEOM to PEOM groups together. The comparison for pegcetacoplan and sham injection within each dose schedule (ie, PM to PM vs. SM to PM and PEOM to PEOM vs. SEOM to PEOM, respectively) will be conducted.

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6.3.2.4. Subgroup Analysis

Subgroup analyses will be performed to evaluate the consistency of the main MMRM analysis and main rate of change analysis results across subgroups defined by antecedent study baseline characteristics. Analyses will be performed for the main MMRM analysis and main rate of change analysis for each of the following subgroups (as appropriate per actual subgroup sample size, levels with low sample size may be pooled to allow for an analysis to be conducted).

In addition, MMRM compared with hypothetical sham and rate of change compared with hypothetical sham analyses will also be performed for each of the following subgroups in order to evaluate the consistency of the MMRM and rate of change compared with hypothetical sham analyses results across subgroups.

- Subgroups indicative of disease severity at antecedent study baseline
  - Study eye antecedent study baseline GA lesion size categories (tertiles based on antecedent study)
- Subgroups associated with GA progression or location of lesion development
  - Study eye antecedent study baseline GA focality (multifocal, unifocal)
  - Study eye antecedent study baseline GA lesion location (subfoveal involvement, without subfoveal involvement)
  - Study eye antecedent study baseline GA lesion loca ion (antecedent study baseline distance to center point of fovea ≥0.25mm and <0.25mm)

The approach described in Section 6.3.2.1.1, Section 6.3.2.1.3, Section 6.3.2.2.1, and Section 6.3.2.2.2 will be used for each subgroup analy i b ed on the data subset for the subject subgroup of interest. Antecedent study baseline covariates included in the main analysis but no longer relevant given the subgroup of interest will be excluded from the model.

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6.4. Analyses of Other Se ondary Efficacy Endpoints

Efficacy analyses from APL2-GA-305 baseline to Month 12 will be performed in the Month 12 dataset in full analysis set. Efficacy analyses from APL2-GA-305 baseline to Month 24 will be performed in the Month 24 dataset in full analysis set. Efficacy analyses from APL2-GA-305 baseline to Month 36 will be perf rmed in the Month 36 dataset in full analysis set.

Efficacy analyses from anteced nt study baseline to Integrated Month 36 will be performed in the Month 12 dataset in modified full analysis set. Efficacy analyses from antecedent study baseline to Integrated Month 48 will be performed in the Month 24 dataset in modified full analysis set. Efficacy analyses from antecedent study baseline to Integrated Month 60 will be performed in the Month 36 dataset in modified full analysis set.

6.4.1. Monocular Maximum Corrected Reading Speed

Maximum reading speed will be calculated per MNRead or Radner user manuals, with adjustment for reading inaccuracy. An additional step to cap resulting reading speed values at a maximum of 300 words per minute will be implemented. Values above 300 words per minute exceed values reported in the literature for adults with no vision impairment for MNRead (Calabrese et al. 2016) or Radner (Radner et al. 2002; Radner and Diendorfer 2014) assessments. Maximum reading speed will be calculated as the mean of the three highest nonzero reading speeds (or two, or one value, as available) (Baskaran et al. 2019; Patel et al. 2011), except when all words per minute are calculated as 0: then the maximum reading speed will be calculated as 0.

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6.4.1.1. Monocular Maximum Corrected Reading Speed From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for the monocular maximum corrected reading speed will be summarized by treatment group and visit for both the study eye and the fellow eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

The mean change from APL2-GA-305 baseline in the monocular maximum corrected reading speed of the study eye ± the standard error in the monocular maximum corrected reading speed of the study eye ± the standard error will be plotted over time by treatment group.

In addition, the categorical changes (improvements of ≥ 20 to <40, ≥ 40 to <60, ≥ 60 and minimal/no change (-20 to 20), worsening of ≥ 20 to <40, ≥ 40 to <60, ≥ 60) of monocular maximum corrected reading speed for the study eye will be summarized by treatment group and visit.

The shift from APL2-GA-305 baseline in the monocular maximum c rrected reading speed for the study eye categories over time will be presented by treatment group for the following categories:

- < 40 wpm (non-functional reading)
- 40 to < 80 wpm (spot reading: for short text such as price labels)
- 80 to <160 wpm (reasonably fluent oral reading: for long texts, such as newspapers)
- ≥ 160 wpm (fully fluent oral reading: r asonably accurate reading, with suitable expression [pitch, tone, volume, emphasis and rhythm in oral reading so that it sounds as effortless as speech], that leads to accurate and deep comprehension and motivation to read [Whittaker and Lovie-Kitchin 1993]).

6.4.1.1.1. MMRM Analysis

The change from APL2-GA-305 baseline to Month 12 in monocular maximum corrected reading speed in the study eye will be summarized and analyzed in a similar fashion using MMRM described in Section 6 3 1 1 The model will include change from APL2-GA-305 baseline to Month 12 in monocular maximum corrected reading speed in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline monocular maximum corrected reading speed as well as the chart type (MNRead or Radner) as covariates, time (in m nths) as a factor; the time × treatment interaction term as well as the antecedent study baseline mon cular maximum corrected reading speed × time interaction term.
Missing antecedent study baseline monocular maximum corrected reading speed values for analysis in MMRM models will be single-imputed as described in Section 13.6.6.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline monocular maximum corrected reading speed as well as the chart type (MNRead or Radner)

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as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline monocular maximum corrected reading speed × time interaction term.

The LS mean of the change from APL2-GA-305 baseline in the monocular maximum corrected reading speed of the study eye ± the standard error will be plotted over time by treatment group.

6.4.1.1.2. Rate of Change Analysis

The mean rate of change in monocular maximum corrected reading speed in the study eye from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), chart type (MNRead or Radner) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the monocular maximum corrected reading speed in the study eye.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the APL2-GA-305 baseline through Month 24 for each treatment group for each 12-month period as well as cumulatively.

The analysis will also be repeated from APL2-GA-305 baseline to Month 36 with a knot at Month 12 and Month 24.

6.4.1.2. Monocular Maximum Corrected Reading Speed From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

The observed values for the monocular maximum corrected reading speed will be summarized by treatment group and visit for both the study eye and the fellow eye. Summaries will present the descriptive statistics for antecedent study baseline, absolute values and change from antecedent study baseline data.

The mean change from antecedent study baseline in the monocular maximum corrected reading speed of the study eye ± the standard error in the monocular maximum corrected reading speed of the study eye ± the standard error will be plotted over time by treatment group.

In addition, the categorical changes (improvements of ≥ 20 to <40, ≥ 40 to <60, ≥ 60 and minimal/no change (-20 to 20), worsening of ≥ 20 to <40, ≥ 40 to <60, ≥ 60) of monocular maximum corrected reading speed for the study eye will be summarized by treatment group and visit.

The shift from antecedent study baseline in the monocular maximum corrected reading speed for the study eye categories over time will be presented by treatment group for the following categories:

- < 40 wpm (non-functional reading)
- 40 to < 80 wpm (spot reading: for short text such as price labels)
- 80 to <160 wpm (reasonably fluent oral reading: for long texts, such as newspapers)

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- ≥ 160 wpm (fully fluent oral reading: reasonably accurate reading, with suitable expression [pitch, tone, volume, emphasis and rhythm in oral reading so that it sounds as effortless as speech], that leads to accurate and deep comprehension and motivation to read).

6.4.1.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in monocular maximum corrected reading speed in the study eye will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1. The model will include change from antecedent study baseline to Integrated Month 36 in monocular maximum corrected reading speed in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM and Sh m Pooled to Pegcetacoplan), presence of exudative AMD in the fellow eye (yes or no) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline monocular maximum corrected reading speed as well as the cha t type (MNRead or Radner) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline monocular maximum corrected re ding speed × time interaction term.

The analysis will also be repeated from APL2-GA-305 baselin to Integrated Month 48, and from APL2-GA-305 baseline to Integrated Month 60

The LS mean of the change from antecedent study baseline in the monocular maximum corrected reading speed of the study eye ± the standard error will be plotted over time by treatment group.

6.4.1.2.2. Rate of Change Analysis

The mean rate of change in monocular maxim m corrected reading speed in the study eye from antecedent study baseline to Integrated Month 48 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.2.1.3 in modified full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), chart type (MNRead or Radner) as fixed effect, time (study month, continuous assuming linearity), knot at Integrated Month 12, kn t at Integrated Month 24, knot at Integrated Month 36, interaction between treatment and time, and in eraction between treatment and each knot. The dependent variable will be the monocular maximum corrected reading speed in the study eye.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 12-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will also be repeated from antecedent study baseline to Integrated Month 60 with a knot at Integrated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48.

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6.4.2. Binocular Maximum Corrected Reading Speed

6.4.2.1. Binocular Maximum Corrected Reading Speed From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for the binocular maximum corrected reading speed will be summarized by treatment group and visit. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

Categorical changes over time and categorical shifts from APL2-GA-305 baseline described in Section 6.4.1.1 will also be presented.

6.4.2.1.1. MMRM Analysis

The change from APL2-GA-305 baseline to Month 12 in binocular maximum corrected reading speed will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.1.1. The model will include change from APL2-GA-305 baseline to Month 12 in binocular maximum corrected reading speed as the dependent variable, treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline binocular maximum corrected reading speed as well as the chart type (MNRead or Radner) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline binocular maximum corrected reading speed × time interaction term. Missing antecedent study baseline monocular binocular corrected reading speed values for analysis in MMRM models will be single-imputed as described in Section 13.6.6.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline binocular maximum corrected reading speed as well as the chart type (MNRead or Radner) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline binocular maximum corrected reading speed × time interaction term.

6.4.2.1.2. Rate of Change Analysis

The mean rate of change in binocular maximum corrected reading speed from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), chart type (MNRead or Radner) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the binocular maximum corrected reading speed.

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The analysis will also be repeated from APL2-GA-305 baseline to Month 36 with a knot at Month 12 and Month 24.

6.4.2.2. Binocular Maximum Corrected Reading Speed From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

The observed values for the binocular maximum corrected reading speed will be summarized by treatment group and visit. Summaries will present the descriptive statistics for antecedent study baseline, absolute values and change from antecedent study baseline data.

Categorical changes over time and categorical shifts from antecedent study baseline described in Section 6.4.1.2 will also be presented.

6.4.2.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in binocular maximum corrected reading speed will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1. The model will include change from antecedent study baseline to Integrated Month 36 in binocular maximum corrected reading speed as the dependent variable, treatment group (PM to PM, PEOM to PEOM and Sham Pooled to Pegcetacoplan), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline binocular maximum corrected reading speed as well as the chart type (MNRead or Radner) as covariates, time (in months) as a factor; the time × treatment int raction term as well as the antecedent study baseline binocular maximum corrected reading speed × time interaction term.

The analysis will also be performed from APL2-GA-305 baseline to Integrated Month 48, and from APL2-GA-305 baseline to Integra ed Month 60. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization i the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesi n area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline binocular maximum corrected reading speed as well as the chart type (MNRead or Radner) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline binocular maximum corrected reading speed × time interaction term.

6.4.2.2.2. Rate of Change Analysis

The mean rate of change in binocular maximum corrected reading speed from antecedent study baseline to Integrated Month 48 will be analysed in a similar fashion using of a piecewise linear mixed effec model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.2.1.3 in modified full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), chart type (MNRead or Radner) as fixed effect, time (study month, continuous assuming linearity), knot at Integrated Month 12, knot at Integrated Month 24, knot at Integrated Month 36, interaction between treatment and time, and interaction between treatment and each knot. The dependent variable will be the binocular maximum corrected reading speed.

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The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 12-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will also be repeated from antecedent study baseline to Integrated Month 60 with a knot at Integrated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48.

6.4.3. NL-BCVA

NL-BCVA score is based on ETDRS letters.

6.4.3.1. NL-BCVA From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for the NL-BCVA score will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

In addition, the categorical changes (improvements of ≥15, ≥10 to <15, ≥5 to <10, and minimal/no change (-4 to 4), worsening of ≥5 to <10, and ≥10 to <15 and ≥15) for the study eye will be summarized by treatment group and vi it

The shift from APL2-GA-305 baseline in the NL-BCVA of the study eye categories (≥70, ≥60 - <70, ≥35 - <60, ≥20 - <35, <20 ETDRS letters ov r time will be presented by treatment group and visit. The above-mentioned ETDRS letter thresholds a e based on WHO definitions for vision impairment and blindness. WHO criteria were implemented in an attempt to capture the progressive nature of Geographic Atrophy and the ultimate t eatment goal of avoiding successive vision impairment and blindness through application of act ve treatment.

The mean change from APL2-GA-305 baseline in the NL-BCVA score for the study eye +/- the standard error will be plotted over time by treatment group.

6.4.3.1.1. MMRM Analysis

The mean change from APL2-GA-305 baseline to Month 12 in NL-BCVA score in the study eye will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.1.1 in full analysis set. The m del will include change from APL2-GA-305 baseline to Month 12 in NL-BCVA score n the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as the fixed effect; antecedent s udy baseline NL-BCVA score as a covariate, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline NL-BCVA score × time interaction term. Missing antecedent study baseline NL-BCVA scores for analysis in MMRM models will be single-imputed as described in Section 13.6.6. In addition, the LS mean change from APL2-GA-305 baseline for Month 10 through Month 12, and the corresponding 95% CI will be estimated from the MMRM model for each arm.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area

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(< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline NL-BCVA score as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline NL-BCVA score × time interaction term.

The LS mean of the change from APL2-GA-305 baseline in the NL-BCVA score for the study eye ± the standard error will be plotted over time by treatment group.

6.4.3.1.2. Rate of Change Analysis

The mean rate of change in NL-BCVA score (i.e., slope) will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 6, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the NL-BCVA score.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the APL2-GA-305 baseline through Month 12 for each treatment group for each 6-month period as well as cumulatively.

The analysis will be performed from APL2-GA 305 baseline to Month 24 with a knot at Month 12. T he analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of ch roidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and ante edent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the NL-BCVA score.

The analysis will also be repeated from APL2-GA-305 baseline to Month 36 with a knot at Month 12 and Month 24.

6.4.3.2. NL-BCVA From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

Efficacy analyses from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60 will be performed in modified full analysis set.

The observed lues for the NL-BCVA score will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descriptive statistics for antecedent study baseline, absolute values and change from antecedent study baseline data.

In addition, the categorical changes (improvements of ≥15, ≥10 to <15, ≥5 to <10, and minimal/no change (-4 to 4), worsening of ≥5 to <10, and ≥10 to <15 and ≥15) for the study eye will be summarized by treatment group and visit.

The shift from antecedent study baseline in the NL-BCVA of the study eye categories (≥70, ≥60 - <70, ≥35 - <60, ≥20 - <35, <20 ETDRS letters over time will be presented by treatment group and visit.

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The mean change from antecedent study baseline in the NL-BCVA score for the study eye +/- the standard error will be plotted over time by treatment group.

6.4.3.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in NL-BCVA score in the study eye will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1 in modified full analysis set.

Since time has been included in the MMRM model as a categorical variable, inclusion of all timepoints from the antecedent study will result in a large number of fix d effects and a large covariance matrix at Integrated Month 36, which may cause convergence issues. Moreover, from antecedent study NL-BCVA analysis, the results from analysis including all timepoints in the model and the results from the analysis only including a subset of timepoints in the model (Integrated Month 6, Integrated Month 12, Integrated Month 18 and Integrated Month 24) are highly consistent. To reduce the number of fixed effects param ter and size of the covariance matrix in the model, the change from integrated baseline fo only a subset of timepoints (Integrated Month 6, Integrated Month 12, Integrated Month 18, and Integrated Month 24) from antecedent study will be included in the analysis. All planned timepoints assessed across all treatment groups from the APL2-GA-305 study will be included in the analysis.

The model will include change from antecedent study baseline to Integrated Month 36 in NL-BCVA score in the study eye as the dep ndent variable, treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetac plan), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as the fixed effect; antecedent study baseline NL-BCVA score as a covariate, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline NL-BCVA score × time interaction term. In addition, the LS mean change from antecedent study baseline for Integrated Month 34 through Integrated Month 36, and the corresponding 95% CI will be estimated from the MMRM model for each arm. The difference in LS Mean, the corresponding 95% CI, and the 2-sided P-value will also be estimated.

The analysis will also be repeated from antecedent study baseline to Integrated Month 48, and from antecedent study baseline to Integrated Month 60.

The LS mean of the change from antecedent study baseline in the NL-BCVA score for the study eye ± the standard error will be plotted over time by treatment group.

6.4.3.2.2. Rate of Change Analysis

The mean rate of change in NL-BCVA score (ie, slope) will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.2.1.3 in modified full analysis set. Similar as Section 6.4.3.2.1, only a subset of visit (Integrated Month 6, Integrated Month 12, Integrated Month 18, and Integrated Month 24) from antecedent study will be included in the analysis.

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The analysis model will include treatment group (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Integrated Month 6, knot at Integrated Month 12, knot at Integrated Month 18, knot at Integrated Month 24, knot at Integrated Month 30, interaction between treatment and time, and interaction between treatment and each knot. The dependent variable will be the NL-BCVA score.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 6-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will also be repeated from antecedent study baseline to Integrated Month 48 with a knot at Integrated Month 12, Integrated Month 24, and Integrat d Month 36; and from antecedent study baseline to Integrated Month 60 with a knot at Int grated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48. The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 48 and integrated Month 60 for each treatment group for each 12-month period as well as cumulatively.

6.4.3.2.3. Time to Blindness and Severe Visual Impairment Analyses

Time to blindness and severe visual impairment analyses from antecedent study baseline to Integrated Month 36 will be performed in modified full analysis set.

- Time to blindness according to WHO criteria (NL-BCVA below 20 ETDRS letters)

An event of time to sustained decline in NL-BCVA below 20 letters is defined as the time (months) from first dose date of study drug in antecedent study to the first post antecedent study baseline assessment below 20 le ters that is confirmed at the following 4 months of visits without later recovery to 25 letters or more for subjects who have NL-BCVA>=20 at antecedent study baseline. Subjects with t th event are censored at their last post-baseline visit. Subjects with an event or censored will be summarized and described with Kaplan Meier methods.

A Cox proportional hazard model (Cox 1972) stratified by the stratification factors (presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) and adjusted for antecedent study baseline NL-BCVA score will be used. Efron (1977) method will be used for tied event times. The number of events in each treatment group, the hazard ratio, 95% CI, and p-value will be presented.

- Time to severe visual impairment (NL-BCVA below 35 ETDRS letters)

An event of time to sustained decline in NL-BCVA below 35 letters is defined as the time (months) from first dose date of study drug in antecedent study to the first post antecedent study baseline assessment below 35 letters that is confirmed at the following 4 months of visits without later recovery to 40 letters or more for subjects who have NL-BCVA>=35 at antecedent study baseline. Censoring rule and time to event calculation described above will be use. Subjects with an event or censored will be summarized and described with Kaplan Meier methods.

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A Cox proportional hazard model described above will be used. The number of events in each treatment group, the hazard ratio, 95% CI, and p-value will be presented.

The analysis will also be repeated from antecedent study baseline to Integrated Month 48, and from antecedent study baseline to Integrated Month 60.

6.4.4. LL-BCVA

LL-BCVA score is based on ETDRS letters.

6.4.4.1. LL-BCVA From APL2-GA-305 Baseline to Month 12, M nth 24, and Month 36

The observed values for the LL-BCVA score will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descript ve statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

In addition, the categorical changes (improvements of ≥15, ≥10 to <15, ≥5 to <10, and minimal/no change (-4 to 4), worsening of ≥5 to <10, nd ≥10 to <15 and ≥15) for the study eye will be summarized by treatment group and visit

The mean change from APL2-GA-305 study baseline in the LL-BCVA score for the study eye +/- the standard error will be plotted over time by treatment group.

6.4.4.1.1. MMRM Analysis

The mean change from APL2-GA-305 baseline to Month 12 in LL-BCVA score in the study eye will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.1.1 in full analysis set. The model will include change from APL2-GA-305 baseline to Month 12 in LL-BCVA score in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as the fixed effect; antecedent study baseline LL-BCVA score as a covariate, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline LL-BCVA score × time interaction term. Missing antecedent study baseline LL-BCVA scores for analysis in MMRM models will be single-imputed as described in Section 13.6.6.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow ye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 r ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline LL-BCVA score as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline LL-BCVA score × time interaction term.

The LS mean of the change from APL2-GA-305 baseline in the LL-BCVA score for the study eye ± the standard error will be plotted over time by treatment group.

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6.4.4.1.2. Rate of Change Analysis

The mean rate of change in LL-BCVA score (i.e., slope) from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be the LL-BCVA score.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the APL2-GA-305 baseline through Month 12 for each treatment group for each 12-month period as well as cumulatively.

The analysis will also be repeated from APL2-GA-305 baselin to Month 36 with a knot at Month 12 and Month 24.

6.4.4.2. LL-BCVA From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

The observed values for the LL-BCVA score will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descriptive statistics for antecedent study baseline, absolute values and change from antecedent study baseline data.

In addition, the categorical changes (impro ements of ≥15, ≥10 to <15, ≥5 to <10, and minimal/no change (-4 to 4), worsening of ≥5 to <10, and ≥10 to <15 and ≥15) for the study eye will be summarized by tr atment group and visit.

The mean change from antecedent tudy baseline in the LL-BCVA score for the study eye +/- the standard error will be plotted over time by treatment group.

6.4.4.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in LL-BCVA score in the study eye will be s mmarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1 in modified full analysis set.

As describe in Section 6.4.3.2.1, and since LL-BCVA will only be collected every 6 months in APL2-GA-305, from antecedent study LL-BCVA analysis, the results from analysis including all timepoints in the model and the results from the analysis only including a subset of timepoints in the model (Integrated Month 6, Integrated Month 12, Integrated Month 18, and Integrated Month 24) are highly consistent. To reduce the number of fixed effects parameter and size of the covariance matrix in the model, the change from integrated baseline for only a subset of timepoints (Integrated Month 6, Integrated Month 12, Integrated Month 18, and Integrated Month 24) from antecedent study will be included in the analysis. All planned timepoints assessed across all treatment groups from the APL2-GA-305 study will be included in the analysis.

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The model will include change from antecedent study baseline to Integrated Month 36 in LL-BCVA score in the study eye as the dependent variable, treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetacoplan), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as the fixed effect; antecedent study baseline LL-BCVA score as a covariate, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline LL-BCVA score × time interaction term. The difference in LS Mean, the corresponding 95% CI, and the 2-sided P-value will also be estimated.

The analysis will also be repeated from antecedent study baseline to Int grated Month 48, and from antecedent study baseline to Integrated Month 60.

The LS mean of the change from antecedent study baseline in the LL-BCVA score for the study eye ± the standard error will be plotted over time by treatment group

6.4.4.2.2. Rate of Change Analysis

The mean rate of change in LL-BCVA score (i.e., slope) from antecedent study baseline to Integrated Month 48 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.2.1.3 in modified full analysis set. Similar as Section 6.4.3.2.1, only a subset of visit (Integrated Month 6, Integrated Month 12, Integrated Month 18, and Integrated Month 24) from antecedent study will be included in the analysis.

The analysis model will include treatment gr up (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), ant cedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study mo th, continuous assuming linearity, knot at Integrated Month 12, knot at Integrated Month 24, knot at Integrated Month 36, interaction between treatment and time, and interaction between eatment and each knot. The dependent variable will be the LL-BCVA score.

The mean rate of chang (1 p), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 12-month period as well as cumula ively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will als be repeated from antecedent study baseline to Integrated Month 60 with a knot at Int grated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48.

6.4.5. Mean FRI Index Score

The mean FRI Index score will be calculated per the scoring algorithm in the FRI Index user's manual.

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6.4.5.1. Mean FRI Index Score From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for the mean FRI Index score will be summarized by treatment group and visit. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

The mean change from APL2-GA-305 baseline in the mean FRI Index score ± the standard error will be plotted over time by treatment group.

In addition, the mean FRI Index score will be converted to the FRI Level variable, as per the user manual, ranging from 1 (Unable to do) to 4 (Totally independent). The categorical changes from APL2-GA-305 baseline (improvements (an increase in FRI level), minimal/no change (no change in FRI level), and worsening (decrease in FRI level)) will be summarized by treatment group and visit. The shift from APL2-GA-305 baseline in the FRI level over time will be presented by treatment group.

6.4.5.1.1. MMRM Analysis

The change from APL2-GA-305 baseline to Month 12 in mean FRI Index score will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.1.1. The model will include change from APL2-GA-305 baseline to Month 12 in mean FRI Index score as the dependent variable, treatment group (PM to PM, PEOM to PEOM SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline mean FRI Index score as well as the antecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline mean FRI Index score × time interaction term. Missing antecedent study baseline FRI Index scores for analysis in MMRM models will be single-imputed as described in Section 13.6.6.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline FRI Index score as well as the antecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline FRI Index score × time interaction term.

The LS mean of the change from APL2-GA-305 baseline in the mean FRI Index score ± the standard error will be plotted over time by treatment group.

6.4.5.1.2. Rate of Change Analysis

The mean rate of change in mean FRI Index score from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

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The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), antecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be FRI Index score.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the APL2-GA-305 baseline through Month 12 for each treatment group for each 12 month period as well as cumulatively.

The analysis will also be repeated from APL2-GA-305 baseline to Month 36 with a knot at Month 12 and Month 24.

6.4.5.2. Mean FRI Index Score From Antecedent Study Bas line to Integrated Month 36, Integrated Month 48, and Integrated Month 60

The observed values for the mean FRI Index score will be summarized by treatment group and visit. Summaries will present the descriptive statistics for antecedent study baseline, absolute values and change from antecedent study baseline data.

The mean change from antecedent study baseline in the mean FRI Index score e ± the standard error will be plotted over time by treatment gr up.

In addition, the mean FRI Index score will be converted to the FRI Level variable, as per the user manual, ranging from 1 (Unable to do) to 4 (Totally independent). The categorical changes from antecedent study baseline (improvements (an increase in FRI level), minimal/no change (no change in FRI level), and worsening (decrease in FRI level)) will be summarized by treatment group and visit. The shift from antecedent study baseline in the FRI level over time will be presented by treatment g oup.

6.4.5.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 36 in mean FRI Index score will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1. The model will include change from antecedent study baseline to Integrated Month 36 in mean FRI Index score as he dependent variable, treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetacoplan), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; antecedent study baseline mean FRI Index score as well as the antecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline mean FRI Index score × time interaction term.

The analysis will also be repeated from antecedent study baseline to Integrated Month 48, and from antecedent study baseline to Integrated Month 60.

The LS mean of the change from antecedent study baseline in the mean FRI Index score ± the standard error will be plotted over time by treatment group.

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6.4.5.2.2. Rate of Change Analysis

The mean rate of change in FRI Index score from antecedent study baseline to Integrated Month 48 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.2.1.3 in modified full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2), antecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) s fixed effect, time (study month, continuous assuming linearity, knot at Integrated Month 12, knot at Integrated Month 24, knot at Integrated Month 36, interaction between treatment and time, and interaction between treatment and each knot. The dependent variable will be FRI Index score.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 12-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will also be repeated from antecedent study baseline to Integrated Month 60 with a knot at Integrated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48.

6.4.6. NEI VFQ-25 and NEI VFQ-39 Analyses

6.4.6.1. NEI VFQ-25 and NEI VFQ-39 Analyses From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

Efficacy analyses from APL2-GA-305 baseline to Month 12, Month 24, and Month 36 will be performed in full analysis set

Descriptive summary statistics f r APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data will be provided by treatment group and visit for the following NEI VFQ-25 and NEI VFQ 39 scores:

- NEI VFQ 25 distance activity subscale score
- NEI VFQ-39 distance activity subscale score
- NEI VFQ-25 composite score
- NEI VFQ-39 composite score
- NEI VFQ-25 near activity subscale score
- NEI VFQ-39 near activity subscale score
- NEI VFQ-25 driving subscale score (for subjects who are currently driving at APL2-GA-305 baseline)

The shift from APL2-GA-305 baseline in NEI VFQ score categories (>80, >65 - ≤80, >50 - ≤65, ≥35 - ≤50, <35) will be summarized by treatment group and visit for the scores described above.

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In addition, the categorical changes (improvements of >5 units and minimal/no change (-5 to 5), worsening of a decrease of >5 units) will be summarized by treatment group and visit for the following NEI VFQ-25 Scores: composite and near activity..

For the NEI VFQ-25 Driving subscale score, the number and percentage of subjects with a worsening driving outcome compared to APL2-GA-305 baseline will be summarized by treatment group and visit. Each visit will display the number of patients who were driving at APL2-GA-305 baseline with at least one of the worsening driving outcomes.

The categories to determine worsening driving outcomes are: conversion to no longer currently driving, increase in difficulty driving in familiar places in daytime, increase in difficult driving at night or stopped doing this due to vision, increase in difficulty driving in difficult conditions or stopped doing this due to vision.

6.4.6.1.1. MMRM Analysis

The change from APL2-GA-305 baseline to Month 36 in NEI VFQ-25 distance activity subscale score will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.1.1. The model will include change from APL2-GA-305 baseline to Month 36 in NEI VFQ-25 distance activity subscale score as the dependent variable, treatment group (PM to PM, PEOM to PEOM SM to PM, and SEOM to PEOM), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effects; APL2-GA-305 baseline NEI VFQ-25 distance activity subscale score as well as the APL2-GA-305 baseline study eye status (Better seeing eye vs. Worse-seeing eye) as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 NEI VFQ-25 distance activity subscal score × time interaction term.

The analysis will also be repeated for NEI FQ-25 composite score, NEI VFQ-25 near activity subscale score, and NEI VFQ-25 driving ubscale score.

6.4.6.2. NEI VFQ-25 and NEI VFQ-39 Analyses From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

Efficacy analyses from antecedent study baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60 will be performed in modified full analysis set.

Descriptive summary stat stics for antecedent study baseline, absolute values and change from antecedent study ba eline data will be provided by treatment group and visit for the following NEI VFQ-25 and NEI VFQ-39 scores:

- NEI VFQ-25 distance activity subscale score
- NEI VFQ-39 distance activity subscale score
- NEI VFQ-25 composite score
- NEI VFQ-39 composite score
- NEI VFQ-25 near activity subscale score
- NEI VFQ-39 near activity subscale score

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- NEI VFQ-25 driving subscale score (for subjects who are currently driving at APL2-GA-305 baseline)

The shift from antecedent study baseline in NEI VFQ score categories (>80, >65 - ≤80, >50 - ≤65, ≥35 - ≤50, <35) will be summarized by treatment group and visit for the scores described above.

In addition, the categorical changes (improvements of >5 units and minimal/no change (-5 to 5), worsening of a decrease of >5 units) will be summarized by treatment group and visit for the following NEI VFQ-25 scores: composite and near activity.

For the NEI VFQ-25 Driving subscale score, the number and percentage of subject with a worsening driving outcome compared to antecedent study baseline will be summarized by treatment group and visit. Each visit will display the number of patients who wer driving at antecedent study baseline with at least one of the worsening driving outcomes. The categories to determine worsening driving outcomes are: conversion to no longer currently driving, increase in difficulty driving in familiar places in daytime, increase in difficult driving at night or stopped doing this due to vision, increase in difficulty driving in difficult conditions or stopped doing this due to vision.

6.4.6.2.1. MMRM Analysis

The change from antecedent study baseline to Integrated Month 60 in NEI VFQ-25 distance activity subscale score will be summarized and analyzed in a similar fashion using MMRM described in Section 6.3.2.1.1. The model will include change from antecedent study baseline to Integrated Month 60 in NEI VFQ-25 distance activity subscale score as the dependent variable, treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetacoplan), presence of exudative AMD in the fellow eye (yes or no), and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effec s; antecedent study baseline NEI VFQ-25 distance activity subscale score as well as the ntecedent study baseline study eye status (Better-seeing eye vs. Worse-seeing eye) as covariates, tim (in months) as a factor; the time × treatment interaction term as well as the antecedent study baseline NEI VFQ-25 distance activity subscale score × time interaction term.

The analysis will also b p ated for NEI VFQ-25 composite score, NEI VFQ-25 near activity subscale score, and NEI VFQ-25 driving subscale score.

6.4.7. Mean Threshold Sensitivity Based on Mesopic Microperimetry

Mean threshold sensitivity of all points will be determined from mesopic microperimetry as an assessment of the macular functional response. The measured distances to the atrophy border will be used to clas ify each of the 68 test points into distinct anatomical regions, namely, junctional zone points at distances ≥−250 to ≤250 µm, distances ≥−375 to ≤375 µm, and distances ≥−500 to ≤500 µm from the GA lesion border.

Mean sensitivity in a given region is defined as the arithmetic mean of the measured pointwise sensitivity of each point in that region, with the sensitivity of points of dense scotoma considered as 0 dB.

The mean change from APL2-GA-305 baseline in the mean threshold sensitivity of all points of the study eye ± the standard error will be plotted over time by treatment group.

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Data that is not acceptable quality for the microperimetry analysis, as identified by the reading center per the Imaging Charter, will be excluded in the analysis. An exam with no apparent operational and patient performance issues (e.g., high fixation loss), and no relevant adverse event, with all 68 points scotomatous (non-responsive) that is not sustained in prior or subsequent assessments, or where the magnitude of increase in number of scotomatous points in such that it does not clinically align with the spatial distribution of the GA lesion(s) will also be excluded in the analysis.

6.4.7.1. Mean Threshold Sensitivity From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for mean threshold sensitivity of all points in th study eye and the fellow eye will be summarized by treatment group and visit. Mean sensitivity for each anatomical region (junctional zone [-250 µm to 250 µm], junctional zone [-375 µm to 375 µm], and junctional zone [-500 µm to 500 µm] in the study eye will be summarized by treatment group and visit.
Mean sensitivity for junctional zone (-250 µm to 250 µm) will also be summarized in the fellow eye by treatment group and visit. Summaries will present the d scriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

6.4.7.1.1. MMRM Analysis

Change from APL2-GA-305 baseline in mean threshold sensitivity of all points in the study eye will be summarized and analyzed in a similar fashion as the MMRM analysis described in Section 6.3.1.1. The MMRM model will in lude ovariates for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), time (in months), presence of exudative AMD in the fellow eye (yes or no), ante edent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), antecedent study baseline mean sensitivity of all points, and time × treatment, time × antecedent study baseline mean sensitivity of all points in interaction term.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM t PM, d SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline mean sensitivity of all points as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 bas line mean sensitivity of all points × time interaction term.

The LS mean change from APL2-GA-305 baseline in the mean threshold sensitivity of all points of the study eye ± the standard error will be plotted over time by treatment group.

Only those subjects who had mesopic microperimetry performed in study APL2-304 will be included in these analyses.

The MMRM analysis described above will be repeated for the following:

- Mean threshold sensitivity for junctional zone (-250 µm to 250 µm).
- Mean threshold sensitivity for junctional zone (-375 µm to 375 µm).
- Mean threshold sensitivity for junctional zone (-500 µm to 500 µm).

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The MMRM model will include covariates for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), time (in months), presence of exudative AMD in the fellow eye (yes or no), antecedent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), APL2-GA-305 baseline mean sensitivity of points in anatomical region, and time × treatment, time × APL2-GA-305 baseline mean sensitivity of points in anatomical region in interaction terms.

6.4.7.1.2. Rate of Change Analysis

The mean rate of change in mean sensitivity of all points from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise lin ar mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in th fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7 5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and kno The dependent variable will be mean sensitivity of all points.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the APL2-GA-305 baseline through Month 12 for each treatment group for each 12-month period as well as cumulatively.

The analysis will also be repeated from APL2-GA 305 baseline to Month 36 with a knot at Month 12 and Month 24.

Only those subjects who had mes pic microperimetry performed in study APL2-304 will be included in these analyses.

The rate of change analysis d scribed above will be repeated for the following:

- Mean threshold sensitivity for junctional zone (-250 µm to 250 µm).
- Mean threshold sensitivity for junctional zone (-375 µm to 375 µm).
- Mean threshold sensitivity for junctional zone (-500 µm to 500 µm).

Sensitivity analy es of mean threshold sensitivity will be performed whereby microperimetry exams with fixation loss >20% are excluded from the sensitivity analyses. Additional analyses of mean threshold sensitivity may be performed by limiting to number of points that are not scotomatou at APL2-GA-305 baseline.

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6.4.7.2. Mean Threshold Sensitivity From Antecedent Study Baseline to Integrated Month 36, Integrated Month 48, and Integrated Month 60

The observed values for mean threshold sensitivity of all points in the study eye and the fellow eye will be summarized by treatment group and visit. Mean sensitivity for each anatomical region (junctional zone [-250 µm to 250 µm], junctional zone [-375 µm to 375 µm], and junctional zone [-500 µm to 500 µm] in the study eye will be summarized by treatment group and visit. Mean sensitivity for junctional zone (-250 µm to 250 µm) will also be summarized in the fellow eye by treatment group and visit. Summaries will present the descriptive statistics for antecedent study baseline, absolute value, and change from antecedent study baselin

The mean change from antecedent study baseline in the mean threshold sens tivity of all points of the study eye ± the standard error will be plotted over time by treatment group.

6.4.7.2.1. MMRM Analysis

Change from antecedent study baseline in mean threshold sensitivity of all points in the study eye will be summarized and analyzed in a similar fashion as he MMRM analysis described in Section 6.3.2.1.1. The MMRM model will include covariates for treatment group (PM to PM, PEOM to PEOM, and Sham Pooled to Pegcetacoplan) time (in months), presence of exudative AMD in the fellow eye (yes or no), antecedent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), antecedent study baseline mean sensitivity of points in the anatomical region, and time × treatment, time × antecedent study baseline mean sensitivity of points in the anatomical region in interaction term.

The analysis will also be repeated from antecedent study baseline to Integrated Month 48, and from APL2-GA-305 baseline to Int grated Month 60.

The LS mean change from anteceden study baseline in the mean threshold sensitivity of all points of the study eye ± the standard error will be plotted over time by treatment group.

Only those subjects who had mesopic microperimetry performed in study APL2-304 will be included in these analyses.

The MMRM analysis described above will be repeated for the following:

- Mean threshold s nsitivity for junctional zone (-250 µm to 250 µm)
- Mean thre hold sensitivity for junctional zone (-375 µm to 375 µm)
- Mean threshold sensitivity for junctional zone (-500 µm to 500 µm)

6.4.7.2.2. Ra of Change Analysis

The mean rate of change in mean sensitivity of all points from antecedent study baseline to Integrated Month 48 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear (“piecewise slope model”) described in Section 6.3.2.1.3 in modified full analysis set.

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The analysis model will include treatment group (PM to PM, PEOM to PEOM and and Sham Pooled to Pegcetacoplan), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No), antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity, knot at Integrated Month 12, knot at Integrated Month 24, knot at Integrated Month 36, interaction between treatment and time, and interaction between treatment and each knot. The dependent variable will be mean sensitivity of all points.

The mean rate of change (slope), standard error, and confidence interval will be estimated for the antecedent study baseline through Integrated Month 36 for each treatment group for each 12-month period as well as cumulatively. In addition, the estimated difference in slopes along with the 95% CIs and p-value will be reported between treatment groups.

The analysis will also be repeated from antecedent study baseline to Integrated Month 60 with a knot at Integrated Month 12, Integrated Month 24, Integrated Month 36, and Integrated Month 48.

Only those subjects who had mesopic microperimetry performed in study APL2-304 will be included in these analyses.

The rate of change analysis described above will be repeated for the following:

- Mean threshold sensitivity for junctional zone (-250 µm to 250 µm)
- Mean threshold sensitivity for juncti nal zone (-375 µm to 375 µm)
- Mean threshold sensitivity for juncti nal zone (-500 µm to 500 µm)

Sensitivity analyses of mean threshold sensitivity will be performed whereby microperimetry exams with fixation loss >20% ar excluded from the sensitivity analyses. Additional analyses of mean threshold sensitivity may be performed by limiting to number of points that are not scotomatous at antecedent study baseline.

6.4.8. Scotomatous Points based on Mesopic Microperimetry

The number of absolute scotomatous points will be determined from mesopic microperimetry as an assessment of the macular functional response. The measured distances to the atrophy border were used to classify each of the 68 test points into distinct anatomical regions, namely, junctional zone points at distance ≥−250 to ≤250 µm, distances ≥−375 to ≤375 µm, and distances ≥−500 to ≤500 µm from the GA lesion border. The number of scotomatous points in a given region is defined as the number of dense scotomas in a given region.

Data that is not acceptable quality for microperimetry analysis, as identified by the reading center per the Imaging Charter, will be excluded in the analysis. An exam with no apparent operational and patient performance issues (e.g., high fixation loss), and no relevant adverse event, with all 68 points scotomatous (non-responsive) that is not sustained in prior or subsequent assessments, or where the magnitude of increase in number of scotomatous points in such that it does not clinically align with the spatial distribution of the GA lesion(s) will also be excluded in the analysis.

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6.4.8.1. Scotomatous Points From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for number of scotomatous points in the study eye and the fellow eye will be summarized by treatment group and visit. The observed values for number of scotomatous points for each anatomical region (junctional zone [-250 µm to 250 µm], junctional zone [-375 µm to 375 µm], and junctional zone [-500 µm to 500 µm] in the study eye will be summarized by treatment group and visit. Number of scotomatous points for junctional zones (-250 µm to 250 µm) will also be summarized in the fellow eye by treatment group and visit. Summaries will present the descriptive statistics for APL2-GA-305 bas line, absolute values and change from APL2-GA-305 baseline data.

The mean change from APL2-GA-305 baseline number of scotomatous p ints of the study eye ± the standard error will be plotted over time by treatment group.

6.4.8.1.1. MMRM Analysis

Change from APL2-GA-305 baseline in absolute scotomatous points in the study eye will be summarized and analyzed in a similar fashion as the MMRM analysis described in Section 6.3.1.1. The MMRM model will include covariates for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), time (in months), presence of exudative AMD in the fellow eye (yes or no), antecedent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), antecedent study baseline number of scotomatous points, and time × treatment, time × antecedent study baseline number of scotomatous points in interaction term.

The analysis will also be performed from APL2-GA-305 baseline to Month 24, and from APL2GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline number of scotomatous points as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline number of scotomatous points × time interaction term.

The LS mean change from APL2-GA-305 baseline in number of scotomatous points of the study eye ± the standard error will be plotted over time by treatment group.

Only those subje ts who had mesopic microperimetry performed in study APL2-304 will be included in these analyses.

The MMRM analysis described above will be repeated for the following:

- Number of scotomatous points for junctional zone (-250 µm to 250 µm)
- Number of scotomatous points for junctional zone (-375 µm to 375 µm)
- Number of scotomatous points for junctional zone (-500 µm to 500 µm)

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The MMRM model will include covariates for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), time (in months), presence of exudative AMD in the fellow eye (yes or no), antecedent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), APL2-GA-305 baseline number of scotomatous points of anatomical region, total number of points in anatomical region based on APL2-GA-305 baseline and time × treatment, time × APL2-GA-305 baseline number of scotomatous points of anatomical region, time × total APL2-GA-305 baseline number of points of anatomical region in interaction terms.

6.4.8.1.2. Rate of Change Analysis

The mean rate of change in number of scotomatous points from APL2-GA-305 baseline to Month 24 will be analysed in a similar fashion using of a piecewise linear mixed effect model assuming time as continuous and piecewise linear ("piecewise slope model") described in Section 6.3.1.2 in full analysis set.

The analysis model will include treatment group (PM to PM, PEOM o PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, time (study month, continuous assuming linearity), knot at Month 12, interaction between treatment and time, and interaction between treatment and knot. The dependent variable will be number of scotomatous points.

The mean rate of change (slope), standard error, and onfidence interval will be estimated for the APL2-GA-305 baseline through Month 12 for e ch treatment group for each 12-month period as well as cumulatively.

The analysis will also be repeated from APL2-GA-305 baseline to Month 36 with a knot at Month 12 and Month 24.

Only those subjects who had mesopic microperimetry performed in study APL2-304 will be included in these analyses

The rate of change analysis described above will be repeated for the following:

- Number of scotomatous points for junctional zone (-250 µm to 250 µm)
- Number of scotomatous points for junctional zone (-375 µm to 375 µm)
- Number of scotomatous points for junctional zone (-500 µm to 500 µm)

Sensitivity analyses of number of scotomatous points will be performed where microperimetry exams with fixation loss >20% are excluded from the sensitivity analyses. Additional analyses of number of scotomatous points may be performed by limiting to number of points that are not scotomatous at APL2-GA-305 baseline.

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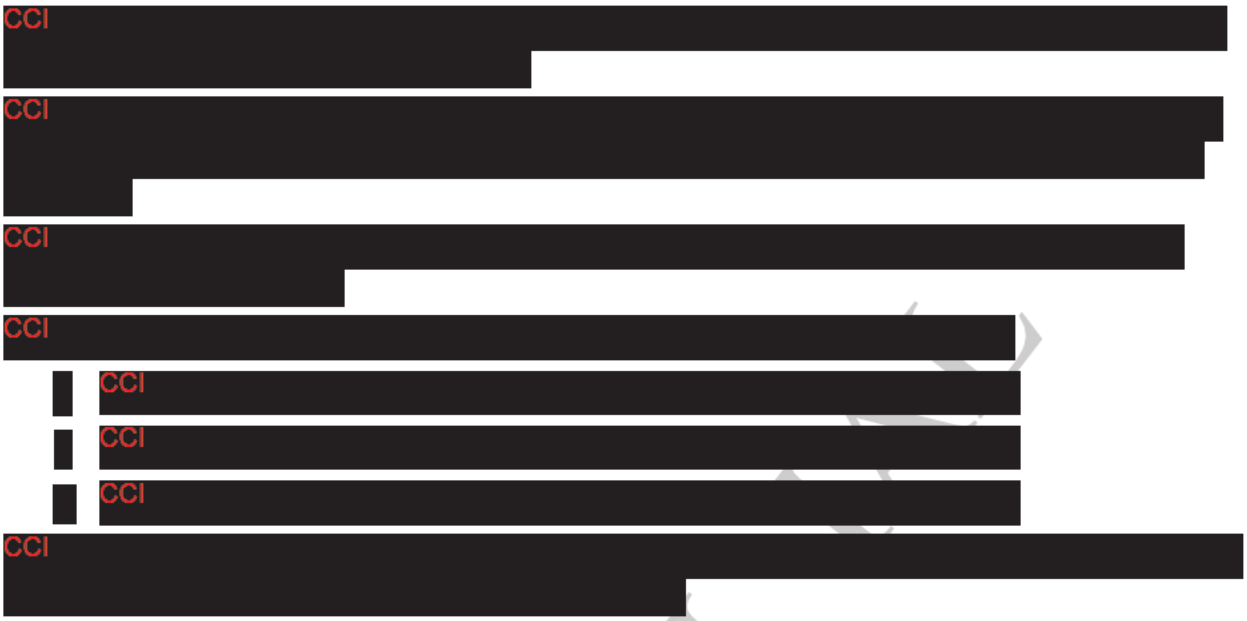
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6.4.9. Other Microperimetry Endpoints

The following analyses will be performed for additional microperimetry parameters, including 95% BCEA and number of points with a clinically significant decrease in mean sensitivity.

6.4.9.1. Other Microperimetry Endpoints From APL2-GA-305 Baseline to Month 12, Month 24, and Month 36

The observed values for 95% BCEA will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

Change from APL2-GA-305 baseline in 95% BCEA in the study eye will be summarized and analyzed in a similar fashion as the MMRM analysis described in Section 6.3.1.1. The MMRM model will include covariates for treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM) time (in months), presence of exudative AMD in the fellow eye (yes or no), antecedent study baseline GA lesion area (<7.5 mm^2, or ≥7.5 mm^2), antecedent study baseline 95% BCEA, and time × treatment, time × antecedent study baseline 95% BCEA in interaction term.

The observed values for number of points with a clinically significant decrease in mean sensitivity, defined as a decrease of more than 4 dB. will be summarized by treatment group and visit for both the study and the fellow eye. Summaries will present the descriptive statistics for APL2-GA-305 baseline, absolute values and change from APL2-GA-305 baseline data.

The above analyses will also be performed from APL2-GA-305 baseline to Month 24, and from APL2-GA-305 baseline to Month 36. The analysis model will include treatment group (PM to PM, PEOM to PEOM, SM to PM, and SEOM to PEOM), presence of choroidal neovascularization in the fellow eye at antecedent study baseline (Yes, No) and antecedent study baseline GA lesion area (< 7.5 mm^2 or ≥ 7.5 mm^2) as fixed effect, APL2-GA-305 baseline 95% BCEA as covariates, time (in months) as a factor; the time × treatment interaction term as well as the APL2-GA-305 baseline 95% BCEA × time interaction term.

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Only those subjects who had mesopic microperimetry performed in study APL2-304 and APL2-305 will be included in these analyses.

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6.5. Multiplicity Adjustment

No multiplicity adjustments will be made. There are no hypotheses being tested.

7. SAFETY ANALYSES

Safety analyses from APL2-GA-305 baseline to Month 12 will be performed in the Month 12 dataset in safety set. Safety analyses from APL2-GA-305 baseline to Month 24 will be performed in the Month 24 dataset in safety set. Safety analyses from APL2-GA-305 baseline to Month 36 will be performed in the Month 36 dataset in safety set.

Safety variables include AEs, deaths, clinical laboratory results, vital signs, incidence of ADA against pegcetacoplan, ocular assessments (eg, NL-BCVA, IOP and ophthalmic examinations), and ocular imaging.

The baseline value for safety variables is defined in Section 3.6. Last Observed Value (LOV) will be defined as the last valid assessment obtained after the APL2 GA-305 baseline.

7.1. Adverse Events

7.1.1. Adverse Events

AEs will be coded using MedDRA version 23.1 and summariz d separately for those occurred in the study eye, those in the fellow eye, ocular, and non-ocular events.

An AE will be considered a TEAE if it has a start date on or after the first dose of investigational product in APL2-GA-305 or if it has a start date before the date of the first dose of investigational product in APL2-GA-305 but increases in se erity on or after the date of the first dose of investigational product in APL2-GA-305

An overall summary of the number of subjects with TEAEs will be presented, including the number and percentage of subjects with

- Any TEAEs
- TEAEs related to study drug (evaluated by the investigator as definitely related, possibly related)
- TEAEs relat d t t dy drug injection procedure
- All TEAE by maximum severity
- Serious TEAEs
- Serious TEAEs related to study drug (evaluated by the investigator as definitely related, possibly related)
- Se ious TEAEs related to study drug injection procedure
- Serious TEAEs by maximum severity
- TEAEs leading to interruption of study treatment
- TEAEs leading to study discontinuation
- TEAEs leading to death

This overall summary will also include the total number of TEAEs reported.

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The number and percentage of subjects reporting TEAEs in each treatment group and overall will be tabulated by SOC and PT for all of the categories in the list above. If more than 1 AE occurs with the same preferred term for the same subject, then the subject will be counted only once for that preferred term using the most severe and most related occurrence for the summarization by severity and by relationship to investigational product. All SOC and PT summaries will be ordered alphabetically by SOC and within SOC, by descending order of the total number of subjects in the overall, PM total, and PEOM total groups.

Ocular TEAEs will also be presented by SOC and PT for study eye for subjects with concomitant anti-VEGF injection and subjects without concomitant anti-VEGF injection.

In addition, the number and percentage of subjects reporting adverse drug reactions in study eye in each treatment group and overall will be summarized by category and PT.

7.1.2. Adverse Events of Special Interest

AEs of special interest will include:

- Exudative AMD
- Increased intraocular pressure
- Intraocular inflammation
- Endophthalmitis
- Optic ischemic neuropathy

7.1.2.1. TEAEs of Endophthalmiti and Intraocular Inflammation

Endophthalmitis and intraocular inflammation ocular TEAEs will be presented by PT for study eye and fellow eye. Endophthalmitis and intraocular inflammation ocular TEAEs in the study eye will also be presented on a subject in idence basis and a per-injection basis (ie, number of events/total number of injections given). Intraoc lar inflammation ocular TEAEs in the study eye on a subject incidence as well as a per-injection basis will also be presented by maximum severity.

7.1.2.2. TEAEs of Increased Intraocular Pressure

Ocular TEAEs associated with increased intraocular pressure will be presented by PT for study eye. This will include PTs of glaucoma, ocular hypertension and IOP increased. Subjects with ocular TEAEs associated with intraocular pressure will also be summarized by duration of the TEAEs, resolved time from the treatment, and medical history of glaucoma and ocular hypertension.

7.1.2.3. TEAEs of Optic Ischemic Neuropathy

No separate analysis will be performed for TEAEs of optic ischemic neuropathy.

7.1.2.4. TEAEs of New Onset Exudative AMD

Unless otherwise specified, subjects with previous exudative AMD reported in the medical history or as an AE from antecedent study in the corresponding eye will be excluded from the analysis described below. For subjects who experience a TEAE of “Choroidal neovascularization” or “Neovascular AMD” (“Exudative AMD TEAE”), the following summaries will be performed:

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- Overall summary of Exudative AMD

The overall summary table described in Section 7.1.1 will be repeated replacing “TEAEs” with “Exudative AMD TEAEs”. This will be reported for the study eye in the safety set.

- Incidence of Exudative AMD TEAEs
    - Incidence of Exudative AMD TEAEs from APL2-GA-305 baseline through Month 12

The incidence and rate per 100 subject-years from APL2-GA-305 baseline through Month 12 of Exudative AMD TEAEs from APL2-GA-305 baseline in the study eye and fellow eye will be presented by treatment group and overall. Subjects at risk for each time period are defined as subjects without previous exudative AMD in the medical history and without exudative AMD reported as an AE before that time period. In addition, the analysis will be repeated by fellow eye exudative AMD status at APL2-GA-305 baseline.

Kaplan Meier plot for the time to development of Exudative AMD TEAEs from APL2-GA-305 baseline in the study eye will be presented by treatment group in the safety set.

    - Incidence of Exudative AMD TEAEs from APL2-GA-305 baseline through Month 24

The incidence and rate per 100 subject-years from APL2-GA-305 baseline through Month 12, from Month 12 through Month 24, and from APL2-GA-305 baseline through Month 24 of Exudative AMD TEAEs from APL2-GA-305 b seline in the study eye and fellow eye will be presented by treatment group and overall. In addition, the analysis will be repeated by fellow eye exudative AMD status at APL2-GA-305 baseline.

Kaplan Meier plot for the time to development of Exudative AMD TEAEs from APL2-GA-305 baseline in the study eye will be presen ed by treatment group in the safety set.

    - Incidence of Exudative AMD TEAEs from APL2-GA-305 baseline through Month 36

The incidence and rate per 100 subject-years from APL2-GA-305 baseline through Month 12, from Month 12 through Month 24, from Month 24 through Month 36, and from APL2-GA-305 baseline through Month 6 of Exudative AMD TEAEs from APL2-GA-305 baseline in the study eye and fellow eye will be presented by treatment group and overall. In addition, the analysis will be repeated by f llow eye exudative AMD status at APL2-GA-305 baseline.

Kaplan Meier plot for the time to development of Exudative AMD TEAEs from APL2-GA-305 baseline in th study eye will be presented by treatment group in the safety set.

- Characteristics of the Exudative AMD TEAEs from APL2-GA-305 baseline through Month 12 in the Month 12 dataset, from APL2-GA-305 baseline through Month 24 in the Month 24 dataset, and from APL2-GA-305 baseline through Month 36 in the Month 36 dataset.

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The characteristics of the Exudative AMD TEAEs in the study eye will be presented at APL2-GA-305 baseline, study visit preceding exudation, study visit at exudation, at Month 12 (or Month 24 or Month 36), and LOV for characteristics based on SD-OCT and baseline, study visit at exudation in the safety set for subjects with an Exudative AMD TEAE in the study eye. The following characteristics will be presented by treatment group:

  - Presence of cystoid spaces on SD-OCT
  - Central (center point) retinal thickness on SD-OCT
  - Central subfield thickness on SD-OCT
  - Presence of subretinal fluid on SD-OCT
  - Presence of Exudative AMD on FA
  - Exudative AMD type on FA
- Anti-VEGF therapy for Exudative AMD TE Es from APL2-GA-305 baseline through Month 12 in the Month 12 dataset, from APL2-GA-305 baseline through Month 24 in the Month 24 dataset, and from APL2-GA-305 baseline through Month 36 in the Month 36 dataset.

A summary of concomitant anti-VEGF therapy for subjects with new exudative AMD in the study eye will be provided by treatment group and overall in the safety set for subjects with an Exudative AMD TEAE in the study eye. This summary will include the total number of subjects that received any anti-VEGF for new exudative AMD as well as the average number of injections per month post exudative AMD. There will also be a breakdown by preferred term of anti-VEGF therapy and the average number of injections per month for each term. Subjects will be presented by the number of injections received for that medication.

- NL-BCVA score for Exudative AMD TEAEs from APL2-GA-305 baseline through Month 12 in the Mo th 12 dataset, from APL2-GA-305 baseline through Month 24 in the Month 24 dataset, and from APL2-GA-305 baseline through Month 36 in the Month 36 data t

NL- BCVA scores at the baseline visit, study visit preceding exudation, the study visit at the exudation, at Month 12 (r Month 24 or Month 36), and LOV will be presented for all subjects with an Exudative AMD TEAE in the study eye by treatment group. In addition, the change in NL-BCVA scores fr m APL2-GA-305 baseline, the visit prior to the exudation, and the exudation visit will be presented where appropriate.

7.1.3. Adverse Events Related to Retinal Detachment

Retinal detachment ocular TEAEs will be presented by PT for study eye and fellow eye. Retinal detachment ocular TEAEs in the study eye will also be presented on a subject incidence basis and a per-injection basis (ie, number of events/total number of injections given).

7.1.4. Adverse Events of Subjects Being Treated Bilaterally With Pegcetacoplan

For subjects being treated bilaterally with pegcetacoplan, an AE will be considered an TEAE for bilateral analyses if it has a start date on or after the first dose of investigational product in APL2-GA-305 for the fellow eye

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All summaries of TEAEs, AEs of special Interest, AEs related to retinal detachment will be presented for subjects being treated bilaterally with pegcetacoplan.

7.2. Clinical Laboratory Data

All laboratory parameters collected at each center's local laboratory will be normalized by converting values in original units to values in SI units and classified as normal, low, or high based on normal ranges supplied by the local laboratories and upon employing standardization.

Observed and change from APL2-GA-305 baseline clinical laboratory data (hematology, chemistry and urinalysis) will be summarized by treatment group and overall, from APL2-GA-305 baseline through Month 12 in the Month 12 dataset, from APL2-GA-305 baseline through Month 24 in the Month 24 dataset, and from APL2-GA-305 baseline through Month 36 in th Month 36 dataset for the following clinical laboratory variables.

Hematology Hemoglobin, hematocrit, red blood cells (RBC) platelet count, white blood cell count (WBC). – total and differential

Biochemistry Aspartate transaminase, alanine transaminase, alkaline phosphatase, sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), bilirubin (total, direct and indirect), creatinine, creatine kinase, glucose, and albumin.

Urinalysis Glucose, specific gravity, blood, ketones, protein, bilirubin, pH, urobilinogen, leukocyte esterase, and nit ite.

Clinical laboratory test values are potentially linically significant (PCS) if they meet either the low or high PCS criteria listed in Table 1. The number and percentage of subjects with baseline and/or post-baseline PCS values will be tabulated by treatment group and overall. The percentages will be calculated relative to the number of subjects with available values for each lab parameter in each treatment group at the analysis visit The numerator is the total number of subjects with at least 1 PCS value at the analysis visi A supportive listing of subjects with post-baseline PCS values will be provided including the subject n mber, site, baseline, and post-baseline values.

Table 1: Criteria for Potentially Clinically Significant Laboratory Tests

Parameter	SI unit	Lower limit	Higher limit
Biochemistry			
Albumin	g/L	<25 g/L	
Alanine Am notransferase (ALT)	U/L		≥3*ULN
Alkaline Phosphatase (ALP)	U/L		≥3*ULN
Aspartate Aminotransferase (AST)	U/L		≥3*ULN
Bilirubin, Direct	umol/L		>1.5*ULN
Bilirubin, Total	umol/L		>1.5*ULN
Bicarbonate	mmol/L	<LLN	
Blood Urea nitrogen	mmol/L		>2.5*ULN
Chloride	mmol/L	<90 mmol/L	>115mmol/L

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Descriptive statistics will be used for continuous data and frequency counts and percentages for categorical data. A shift table fr m baseline, by treatment group and protocol specified time points, of normal, abnormal low, and abnormal high records will also be summarized for hematology and chemi t y d ta with marginal totals using frequency counts and percentages.

7.3. Vital Sign

Descriptive statis ics for vi al signs (eg, systolic and diastolic blood pressure, respiratory rate, temperature, and pulse rate) and their changes from APL2-GA-305 baseline at each post-baseline visit through Month 12 in the Month 12 dataset, Month 24 in the Month 24 dataset, and Month 36 in the Month 36 dataset will be presented by treatment group and overall.

Vital sign values will be considered PCS if they meet both the observed value criteria and the change from APL2-GA-305 baseline criteria listed in Table 2. The number and percentage of subjects with PCS at APL2-GA-305 baseline and/or post-baseline values will be tabulated by treatment group and overall. The percentages will be calculated relative to the number of subjects with values for each vital sign parameter in each treatment group at the analysis visit. The numerator is the total number of subjects with at least 1 PCS vital sign value at the analysis visit.

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7.4. Physical Examination Findings

Any relevant findings from the baseline physical examination are to be reported on the medical history. Any relevant findings from the post-baseline physical examination are to be reported as AE's. No separate physical examination findings were collected to summarize.

7.5. Complete Ophthalmic Exam

Results of the ocular assessments will be summ rized by shift tables showing the shift from APL2-GA-305 baseline in the individual slit- amp examination and indirect ophthalmoscopy endpoint in safety set. These will be provided by treatment group for study eye and fellow eye at Month 12, Month 24, Month 36 and LOV

Any relevant findings from the post-bas line ophthalmic examination are to be reported as AEs.

The change from APL2-GA-305 baseline in (first measurement of the day) IOP will be summarized over time by treatment group. In addition, the incidence of IOP above specified thresholds (ie, >21 mmHg at pre-inje ti (first measurement of the day); >30 mmHg post injection) will be summarized by timepoint, treatment group and overall.

The mean change from APL2-GA-305 baseline in IOP ± the standard error will be plotted over time by treatmen group.

For subjects treated bilaterally with pegcetacoplan, baseline will be defined as the last available non-missing assessment prior to the first dose of investigational product in APL2-GA-305 for the fellow eye. Change from baseline in IOP will be summarized by treatment group.

7.6. NL-BCVA

The number and percentage of subjects who lost letters compared with APL2-GA-305 baseline at each visit based on NL-BCVA in the study and fellow eye will be presented. The three categories are >=15, ≥15- < 30 and ≥30 ETDRS letters. This analysis will be performed from APL2-GA-305 baseline at each post-baseline visit through Month 12 in the Month 12 dataset, Month 24 in the Month 24 dataset, and Month 36 in the Month 36 dataset will be presented by treatment group and overall in safety set.

7.7. Other Ophthalmology Imaging Assessments

Other ophthalmology imaging assessments include Digital Color Fundus Photographs (DCFP), FA, SD-OCT and OCT-A. Unless otherwise stated, ophthalmology imaging assessments data will be summarized by treatment group. Summaries will be presented separately by study eye and by fellow eye in safety set:

- DCFP
    - Shift from baseline in the presence/absence of hemorrhage at each visit
- FA
    - Unless otherwise specified, subjects with previous ex dative AMD reported in the medical history or as an AE from antecedent study in the corresponding eye will be excluded from the analysis described below
        - Incidence of new exudative AMD. This ill be summarized as the cumulative number of exudative AMD events by each visit and the cumulative incidence by that visit based on Kaplan Meier methods
        - Incidence of new exudative AMD by type (classic, occult, classic & occult, disciform scar) at first emergence will be summarized at each visit for the cumulative number of events
        - Total exudative AMD size (diameter) at first emergence will be summarized at ea h vis t for the cumulative number of events
- SD-OCT

The SD-OCT assessment of central etinal hickness will be assessed by up to three readers per assessment. If assessments by only two independent readers are available, then the median of the 2 readings will be used in the alculation of summary statistics. If assessments by three independent readers are available, then the median of the three readings will be used for the summary calculations. For presence/absence of subretinal fluid, the most frequently assessed decision per assessment will be used. If present or absent is assessed equal number of times per assessment, then pres nt will be used.

- Descriptive statistics on central subfield thickness, and change from APL2-GA-305 bas line at each visit
- Plot of the mean change from APL2-GA-305 baseline in central subfield thickness in the study eye ± the standard error over time by treatment group
- Descriptive statistics on central (center point) retinal thickness, and change from APL2-GA-305 baseline at each visit
- Shift from APL2-GA-305 baseline in the presence/absence of subretinal fluid at each visit
- Shift from APL2-GA-305 baseline in the presence/absence of cystoid spaces at each visit

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- OCT-A
  - Incidence of subclinical exudative AMD (referred to as MNV in the datasets) determined by OCT-A in eyes without previous exudative AMD reported in the medical history or as an AE in the corresponding eye at each visit. This analysis will be performed based on APL2-GA-305 baseline in safety set.

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8. PHARMACOKINETICS ANALYSIS

No pharmacokinetic analyses are planned for this study.

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9. PHARMACODYNAMIC ANALYSIS

No pharmacodynamic analyses are planned for this study.

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10. OTHER ANALYSIS

10.1. Immunogenicity

Immunogenicity analyses will only be performed from APL2-GA-305 baseline to Month 24 in the Month 24 dataset and from APL2-GA-305 baseline to Month 36 in the Month 36 dataset in safety set. Immunogenicity data will be listed and summarized separately for anti-pegcetacoplan peptide antibody and anti-PEG antibody results. A sample and subject level summary table will be presented as described below.

Sample Level Summary

The number of evaluable (ADA-positive, ADA-negative, and ADA-inc nclusive) and unevaluable samples will be summarized by treatment group and overall. The number and percentage of each ADA sample classification will be summarized by treatment gro p and overall in the evaluable samples. In addition, the number and percentage of baseline and pos dose ADA positive samples along with the titer range for each will also be summarized by treatment group and overall in samples that are ADA positive.

ADA samples will be classified as follows:

- ADA-Positive Sample – when the sample is positive in the confirmatory assay
- ADA-Negative Sample – when the sample is negative in the screening assay or the confirmatory assay, and drug is at a level that does not interfere with the ADA method
- ADA-Inconclusive Sample – when the sample is negative in the screening assay or the confirmatory assay, and drug is at a level that interferes with the ADA method, then the sample is considered inconclusive
- Unevaluable Sample – when a sample could not be tested for ADA status due to inadequate sampl volume, mishandling, or errors in sample collection, processing, storage, etc.

Subject Level Summary

The number and percentage of subjects with pre-existing ADAs will be summarized by treatment group and overall in the subjects with a baseline sample result. In addition, the number and percentage of su jects wi h an ADA positive response, ADA negative response, and ADA inconclusive respo se as well as the type and kinetics of the positive ADA response will be summarized by treatment group and overall in the evaluable subjects. The subject summary table will includ a summary by treatment group and overall for the ADA population parameters.

Pre-existing ADA will be defined as follows: any subject with an ADA positive baseline sample from the total subjects with a baseline sample result.

Evaluable subjects will be defined as follows: a subject with at least one sample taken with a reportable result after first dosing during the treatment or follow-up period.

Evaluable subjects will be classified as follows for ADA response:

- ADA-Positive Subject – An evaluable subject with at least one pre-dose sample and one treatment-emergent or treatment-boosted ADA-positive sample at any time after dosing

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- ADA-Negative Subject – An evaluable subject without a treatment-emergent or treatment-boosted ADA-positive sample during the treatment or follow-up period
- ADA-Inconclusive Subject – An evaluable subject who cannot be classified as either ADA-positive or ADA-negative (eg, assay drug tolerance issues, post-dose positive without a baseline sample, positive baseline and positive post-dose sample without a titer value, etc.)

ADA positive responses will be classified as follows:

- Treatment-Boosted ADA Response – An evaluable subject with a baseline ADA positive sample and a post-dose ADA positive sample that is ≥ 4x the baseline titer (eg, baseline titer of 10 vs. post-dose titer of 40)
- Treatment-Emergent ADA Response – An evaluable subject with a baseline ADA negative sample and an ADA positive sample after treatment, ADA developed de novo

The kinetics of ADA positive responses will be classified as follows:

- Transient ADA Response
  - Treatment-emergent positive subjects are classified as having a transient response if they have only a single ADA positive sample (that was not the last assessment), or more than 1 ADA positive sample where the first and last ADA positive samples are separated by a period of less than 112 days (16 weeks), irrespective of any negative and positive samples in between.
  - Treatment-boosted ADA positive subjects are classified as having a transient response if they have only a single ADA boosted sample (that was not the last assessment), or more tha 1 positive boosted sample where the first and last ADA positive samples are eparat d by a period of less than 112 days (16 weeks), irrespective of any negative and positive samples in between.
- Persistent ADA Response
  - Treatment-emergent positive subjects are classified as having a persistent response if they have more than 1 positive ADA sample ≥ 112 days (16 weeks) apart, or a positive ADA sample at the last timepoint with no further results available
  - Treatmen boosted ADA positive subjects were classified as having a persistent re ponse if they have more than 1 positive boosted sample ≥ 112 days (16 weeks) apart, r a positive boosted sample at the last timepoint with no further results available
- U classified Response
  - Any ADA positive subject that cannot be defined as having a transient or persistent ADA response

ADA population parameters are derived as follows:

- ADA Prevalence – The proportion of all ADA positive subjects, including pre-existing ADA, computed as a percentage of the total number of evaluable and unevaluable subjects

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- ADA Incidence – The sum of all ADA positive treatment-emergent and treatment-boosted subjects computed as a percentage of the total number of evaluable subjects. Note: This population parameter is the same as the percentage of subjects with an ADA positive response.

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11. INTERIM ANALYSIS

An Interim analysis to assess the efficacy and safety of subjects based on all data through the Month 6 visit in APL2-GA-305 study from a data cut taken on 01 February 2023 is planned for this study. Additional interim analysis may be performed at Month 18 or Month 30 for specific reasons (eg, providing data to a regulatory agency).

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12. 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. A charter for the DMC as well as a DMC SAP are prepared separately.

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13. DATA HANDLING CONVENTIONS

13.1. General Data Reporting Conventions

Continuous variables will be summarized using the number of non-missing observations (n), mean, SD, median, quartile 1, quartile 3, minimum, and maximum. Categorical variables will be summarized using frequencies and percentages. Unless stated otherwise, for all percentages, the number of subjects in the analysis population for the treatment group will be the denominator.

Unless otherwise specified, the estimated mean and median for a set of values should be printed out to 1 more decimal place than the original values, and standard deviati ns should be printed out to 2 more decimal places than the original values. Quartile 1 and quartile 3 should be printed out to 1 more decimal place than the original values. The minimum and maximum should report the same number of decimal places as the original values. Pe centages will be displayed with 1 decimal place; except percentages will not be presented when he count is zero and 100% will be presented as an integer. P-value will be displayed with 4 decimal places.

For the following derived endpoints, the original values will be considered as: 1 decimal place for GA lesion size data, 0 decimal place for reading speed, NL-BCVA, LL-BCVA, and NEI-VFQ data, 2 decimal places for FRI data, 1 decimal place for an threshold sensitivity data, and 0 decimal place for scotomatous points data.

13.2. Definition of Relative Study Days

The following relative study days definitions will be used in this study:

- Relative study days based on APL2-GA-305 baseline: defined as number of days relative to the first dose date of his study drug in APL2-GA-305 which is designated as Day 1, and the preceding day is Day -1, the day before that is Day -2, etc.
    - If evaluation da e is on or after first dose date in APL2-GA-305, then relative study days are calculated as:

      Evaluation date - first dose date of study drug in APL2-GA-305 + 1.
    - If evalu tion date is before first dose date in APL2-GA-305, then relative study days are c lculated as

      E aluation date - first dose date of study drug in APL2-GA-305.

Relative study days based on APL2-GA-305 baseline take negative values if evaluation date occurs prior to first dose date in APL2-GA-305 and take positive values if evaluation date occurs on or after first dose date of study drug in APL2-GA-305.

- Relative study days based on antecedent study baseline: defined as number of days relative to the first dose date of study drug in antecedent study which is designated as Day 1, and the preceding day is Day -1, the day before that is Day -2, etc.
    - If evaluation date is on or after first dose date in antecedent study, then relative study days are calculated as:

      Evaluation date - first dose date of study drug in antecedent study + 1.

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- If evaluation date is before first dose date in antecedent study, then relative study days are calculated as

  Evaluation date - first dose date of study drug in antecedent study.

Relative study days based on antecedent study baseline take negative values if evaluation date occurs prior to first dose date in antecedent study and take positive values if evaluation date occurs on or after first dose date of study drug in antecedent study.

13.3. Definition of Visit Windows

Two analysis visits will be used for this study. APL2-GA-305 analysis visit (APL2-GA-305 Baseline, Month 1, Month 2, etc.) is based on APL2-GA-305 baselin Integrated study visit (Antecedent study baseline, …, Integrated Month 24, Integrated Month 25, Integrated Month 26, etc.) is based on antecedent study baseline.

All assessments of study APL2-GA-305 occurring on or before the first date of dosing in APL2-GA-305 (Analysis Study Day (ADY) ≤ 1) will be assigned to the APL2-GA-305 Baseline analysis visit window.

Table 3, Table 4, Table 5, and Table 6 present the APL2 GA-305 analysis visit window mapping for all scheduled, unscheduled and early term visits based on APL2-GA-305 baseline. Table 7, Table 8, Table 9, and Table 10 present the integrated analysis visit window mapping for all visits based on Antecedent Study baseline. Analy is visit derived previously in APL2-303 and APL2-304 will be used from antecedent study aseline through Integrated Month 24.
For integrated analysis visit after Integrated Month 24, in the case that multiple scheduled, unscheduled, or early termination visits are in the same integrated analysis window, the one closest to the target date will be used. For micrope imetry assessments, if assessment with 'MP' and assessment with 'MP2' of the modality variable within the same analysis window, assessment with 'MP' of the modality variable will be used.

Table 3: Analysis Visit Window vs. APL2-GA-305 Baseline – Monthly Assessments

APL2-GA-305 analysis visit	**Target Study day based on APL2-GA-305 baseline**	CCI [redacted]
Baseline	1	
Month 1	30	
Month 2	60	
Month 3	90	
Month 4	120	
Month 5	150	
Month 6	180	
Month 7	210	
Month 8	240	
Month 9	270	

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Table 3: Analysis Visit Window vs. APL2-GA-305 Baseline – Monthly Assessments

APL2-GA-305 analysis visit	Target Study day based on APL2-GA-305 baseline	CCI [redacted]
Month 10	300	
Month 11	330	
Month 12	360	
Month 13	390	
Month 14	420	
Month 15	450	
Month 16	480	
Month 17	510	
Month 18	540	
Month 19	570	
Month 20	600	
Month 21	630	
Month 22	660	
Month 23	690	
Month 24	720	
Month 25	750	
Month 26	780	
Month 27	810	
Month 28	840	
Month 29	870	
Month 30	900	
Month 31	930	
Month 32	960	
Month 33	990	
Month 34	1020	
Month 35	1050	
Month 36	1080	

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Table 4: Analysis Visit Window vs. APL2-GA-305 Baseline – Every Other Month Assessments

APL2-GA-305 analysis visit	**Target Study day based on APL2-GA-305 baseline**	CCI [redacted]
Baseline	1	
Month 2	60	
Month 4	120	
Month 6	180	
Month 8	240	
Month 10	300	
Month 12	360	
Month 14	420	
Month 16	480	
Month 18	540	
Month 20	600	
Month 22	660	
Month 24	720	
Month 26	780	
Month 28	840	
Month 30	900	
Month 32	960	
Month 34	020	
Month 36	1080	

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Table 5: Analysis Visit Window vs. APL2-GA-305 Baseline – Every 6 Months Assessments

APL2-GA-305 analysis visit	Target Study day based on APL2-GA-305 baseline
Baseline	1
Month 6	180
Month 12	360
Month 18	540
Month 24	720
Month 30	900
Month 36	1080

CCI [redacted]

Table 6: Analysis Visit Window vs. APL2-GA-305 Baseline – Every 12 Months Assessments

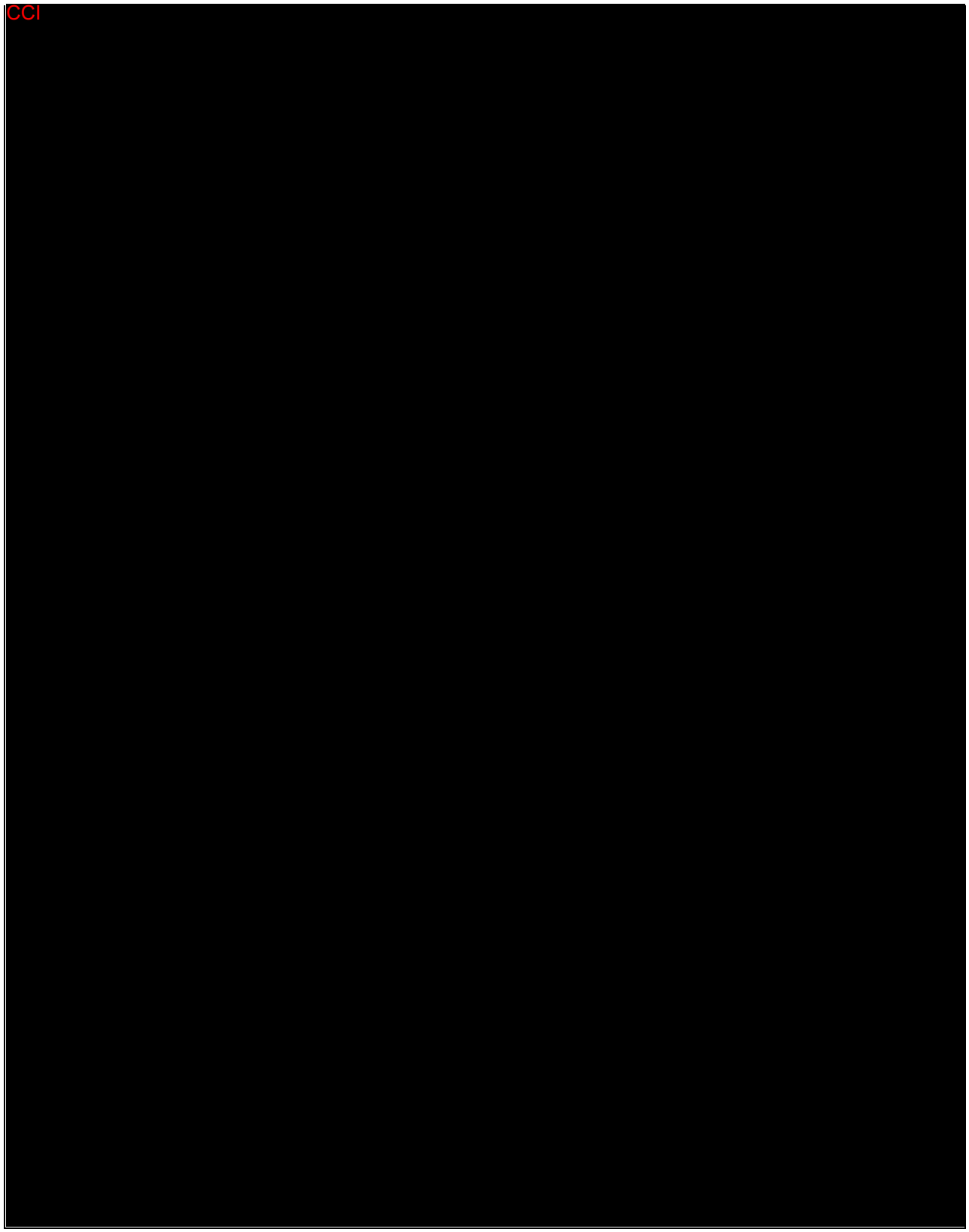
APL2-GA-305 analysis visit	Target Study day based on APL2-GA-305 bas line
Baseline	1
Month 12	360
Month 24	720
Month 36	1080

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13.4. Derived Efficacy Endpoints

13.4.1. GA Lesion Size

For all independent ophthalmic assessments (performed by DARC laboratory), which includes GA lesion size, if assessments by only two independent readers are available, then the median of the 2 readings will be used in the calculation of summary statistics. If assessments by three independent readers are available, then the median of the three readings will be used for the summary calculations.

In the case that the GA lesion size has an indeterminate boundary noted, hen the lesion size for this indeterminate boundary will be used in all analyses of GA lesion size unless otherwise noted in the case that primary lesions size assessment for an individual reader is missing.

13.4.2. MNRead Reading Chart

13.4.2.1. Reading Speed

13.4.2.1.1. Without Adjustment for Reading Inaccuracy

Any print size with “Not Done” will have the associated wpm marked as 0.

Reading speed (wpm) = 600 / (reading time in seconds)

If reading speed >300 wpm, reading speed = 300.

13.4.2.1.2. With Adjustment for Reading Inaccuracy

Any print size with “Not Done” w ll have the associated wpm marked as 0.

Reading speed (wpm) = 60 (10 – errors) / (reading time in seconds)

If reading speed >300 wpm, re ding speed = 300.

If 10 or more errors were made in a sentence (implying wpm<0), then the reading speed for that sentence can be assumed to be zero (wpm).

13.4.2.2. Maximum Reading Speed

Maximum reading speed will be calculated as the mean of the three highest nonzero reading speeds (or 2 or 1 if that is all that exists). For subjects having <u>all</u> wpm values = 0, the maximum reading sp ed will be set to 0. Reading speed will equal 0 wpm at each print size for which (time=0) or Not Done (indicating no words in the sentence could not be read or sentence was not attempted due to vision) is checked for that print size.

13.4.3. Radner Reading Chart

13.4.3.1. Reading Speed

13.4.3.1.1. Without Adjustment for Reading Inaccuracy

Reading Speed (wpm) = 14 / (time in seconds) x 60 = 840 / (time in seconds)

If reading speed >300 wpm, reading speed = 300.

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13.4.3.1.2. With Adjustment for Reading Inaccuracy

Reading Speed (wpm) = (14 – errors)/ (time in seconds) x 60

If 14 or more errors were made in a sentence (implying wpm<0), then the reading speed for that sentence can be assumed to be zero (wpm).

If reading speed >300 wpm, reading speed = 300.

13.4.3.2. Maximum Reading Speed

Maximum reading speed will be calculated as the mean of the three highest nonzero reading speeds (or 2 or 1 if that is all that exists). For subjects having all wpm value = 0, the maximum reading speed will be set to 0. Reading speed will equal 0 wpm at each print size for which (time=0) or Not Done (indicating no words in the sentence could not be read or sentence was not attempted due to vision) is checked for that print size.

13.4.4. NL-BCVA and LL-BCVA

13.4.4.1. BCVA Letter Score

- If the 4-meter score is >19 letters read correctly, the visual acuity score is the sum of total letters correctly read at 4 meters plus the addition of 30.
- If the 4-meter score is ≤19 letters read correctly and letters are read correctly at 1-meter distance, the visual acuity sc re is the sum of total letters read correctly at 4 meters and total letters read corr ctly at the 1-meter distance.
- If the 4-meter score is ≤19 le ters read correctly and 1-meter score is missing, the visual acuity score will be missing.
- If the 4-meter score is missing but 1-meter score is available, the visual acuity score is total letters read corr ctly at the 1-meter distance.
- If no letters are read correctly at either the 4-meter distance or the 1-meter distance, the visual acuity score is 0.

13.4.4.2. Conversion of BCVA Letter Score to Snellen Equivalent

Conversions betw en letter, logMAR, and Snellen visual acuity scores are available in Beck et al. 2003 and Holladay 2004. Letter scores are converted to logMAR equivalents using the formula logMAR = 1.7 – (.02) (letter score). With this conversion, a 5-letter difference in visual acuity is equi alent to a difference of 0.1 logMAR and to one Snellen line. Conversion from logMAR to Snellen can be done after rounding logMAR values to one decimal place following Table 1 in Holladay 2004.

13.4.5. Mean FRI Index Score and FRI Level

Follow Section 4.3.2 of FRI Index User Manual (Version 1.4).

SAS code for scoring FRI Index and FRI Level is available in Appendix C of FRI Index Under Manual (Version 1.4).

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13.4.6. NEI VFQ-25 Scores

Scoring VFQ-25 with or without optional item is a two-step process:

- First, original numeric values from the survey are re-coded following the scoring rules outlined in Table 2 of user's manual. All items are scored so that a high score represents better functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. In this format, scores represent the achieved percentage of the total possible score, eg, a score of 50 represents 50% of the highest possible score.
- In step 2, items within each sub-scale are averaged together to c eate the 12 sub-scale scores, Table 3 of user's manual indicates which items contribute to each specific sub-scale. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Sub-scales with at least one item answered can be used to generate a sub-scale score. Hence, scores represent the average for all items in the sub-scale that the respondent answered.

13.4.6.1. NEI VFQ-25 Distance Activity Subscale Score

Average of items 8, 9, and 14.

13.4.6.2. NEI VFQ-25 Near Activity Subscal Score

Average of items 5, 6, and 7.

13.4.6.3. NEI VFQ-25 Driving Subscale Score

For subjects who are currently dri ing at baseline only. Average of items 15c, 16, and 16a.

13.4.6.4. NEI VFQ-25 Composite Score

To calculate an overall composite score for the VFQ-25, simply average the vision-targeted sub-scale scores, excluding the general health rating question.

13.4.7. NEI VFQ 39 Scores

For subjects responded to additional questions A1-A13, VFQ-39 subscale scores can be calculated using Table 4 of user's manual.

13.4.7.1. NEI VFQ-39 Distance Activity Subscale Score

Average of items 8, 9, 14, A6, A7, and A8.

13.4.7.2. NEI VFQ-39 Near Activity Subscale Score

Average of items 5, 6, 7, A3, A4, and A5.

13.4.7.3. NEI VFQ-39 Composite Score

Calculated by simply averaging the vision related subscales, excluding the general health rating question.

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13.5. Repeated or Unscheduled Assessments of Safety Parameters

If a subject has repeated assessments before the start of investigational product, then the results from the final assessment made prior to the start of investigational product will be used as baseline. If end-of-study assessments are repeated or unscheduled, the last post-baseline assessment will be used as the end of study assessment for generating descriptive statistics.

13.6. Handling of Missing, Unused, and Spurious Data

For antecedent study, APL2-103, APL2-303, and APL2-304, imputed data for missing, unused and spurious data based on rules stated in these studies will be used. The following rules will only be applied to APL2-GA-305 data.

13.6.1. Missing Date of Investigational Product

When the date of the last dose of investigational product in APL2 GA-305 is missing for a subject in the Safety set, all efforts should be made to obt in the date from the investigator.

13.6.2. Missing Date Information for Prior or Concomitant Medications (Therapies/Procedures)

If either the start or stop date of medication is missing, the worst or most conservative case will be considered when assigning medications to categories. So, for a missing start date (where stop date is after date of first dose in APL2-GA-305 or missing) the date will be imputed as the date of first dose in APL2-GA-305; for a missing stop date the date will be imputed as the last study date.

13.6.2.1. Incomplete Start Date

The following rules will be applied t impute the missing numerical fields. If the stop date is complete and the imputed start date is after the stop date, then the start date will be imputed using the stop date.

13.6.2.1.1. Missing Day and Month

If the year of the incomplete start date is the same as the year of the date of the first dose of investigational product in APL2-GA-305, then the day and month of the date of the first dose of investigational p oduct in APL2-GA-305 will be assigned to the missing fields.

If the year of the incomplete start date is before the year of the date of the first dose of investigational product in APL2-GA-305, then December 31 will be assigned to the missing fields.

If the year of he incomplete start date is after the year of the date of the first dose of investigational product in APL2-GA-305, then 01 January will be assigned to the missing fields.

13.6.2.1.2. Missing Month Only

The day will be treated as missing and both month and day will be replaced according to the above procedure.

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13.6.2.1.3. Missing Day Only

If the month and year of the incomplete start date are the same as the month and year of the date of the first dose of investigational product in APL2-GA-305, then the day of the date of the first dose of investigational product in APL2-GA-305 will be assigned to the missing day.

If either the year is before the year of the date of the first dose of investigational product in APL2-GA-305 or if both years are the same but the month is before the month of the date of the first dose of investigational product in APL2-GA-305, then the last day of the month will be assigned to the missing day.

If either the year is after the year of the date of the first dose of investigational product in APL2-GA-305 or if both years are the same but the month is after the month of the date of the first dose of investigational product in APL2-GA-305, then the first day of the month will be assigned to the missing day.

13.6.2.2. Incomplete Stop Date

The following rules will be applied to impute the missing num rical fields. If the imputed stop date is before the start date (imputed or non-imputed start date), then the imputed stop date will be equal to the start date.

13.6.2.2.1. Missing Day and Month

If the year of the incomplete stop date is the same as the year as of the last study date, then the day and month of the date of the last study d te will be assigned to the missing fields.

If the year of the incomplete stop date is before the year of the last study date, then 31 December will be assigned to the missing fields.

If the year of the incomplete stop date is after the year of the last study date, then 01 January will be assigned to the missing fields

13.6.2.2.2. Missing Month Only

The day will be treated as missing and both month and day will be replaced according to the above procedure.

13.6.2.2.3. Missing Day Only

If the month and year of the incomplete stop date are the same as the month and year of the last study date, hen the day of the last study date will be assigned to the missing day

If either the year is before the year of the last study date or if both years are the same, but the month is before the month of the last study date, then the last day of the month will be assigned to the missing day

If either the year is after the year of the last study date or if both years are the same, but the month is after the month of the last study date, then the first day of the month will be assigned to the missing day.

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13.6.3. Missing Date Information for Adverse Events

Events with missing or partial dates will be handled such that in the absence of contradictory information an AE is treatment emergent. So, for a missing start date (where stop date is after first dosing date in APL2-GA-305 or missing) the date will be imputed as the first dose date in APL2-GA-305; for a missing stop date the date will be imputed as the last study date. If a partial date is recorded, the following convention will be used to assign the AE.

13.6.3.1. Incomplete Start Date

If a start date is missing the day information and month/year is the same as first dose date in APL2-GA-305 then use first dose date in APL2-GA-305, else '01' will be u ed for the day; if a start date is missing the month and the year is the same as first dose dat in APL2-GA-305 then use first dose date in APL2-GA-305, else January will be used for the start month.

If AE end date is earlier than treatment start date in APL2 GA-305 (ie, could be inferred by any combination of year/month/day), then any missing part of AE start date will be imputed based on the AE end date.

13.6.3.2. Incomplete Stop Date

If a stop date is missing the day information and month/year is same as last study date then use last study date, else last day of the given month will be used for the stop day; if a stop date is missing the month and year is the same as last study date then use last study date, else December will be used for the stop month.

13.6.4. Missing Severity Assessm nt for Adverse Events

If severity is missing for an AE starting prior to the date of the first dose of investigational product in APL2-GA-305, then a severity of "Mild will be assigned. If the severity is missing for an AE starting on or after the date of the first dose of investigational product in APL2-GA-305, then a severity of "Severe" will be assigned. The imputed values for severity assessment will be used for incidence summaries, while the actual values will be used in data listings.

13.6.5. Missing Relationship to Investigational Product for Adverse Events

If the relationship to investigational product is missing for an AE starting on or after the date of the first dose f investigational product in APL2-GA-305, a causality of "Related" to the investigational product will be assigned. The imputed values for relationship to the investigational product will be used for incidence summaries, while both the actual and the imputed valu will be presented in data listings.

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13.6.6. Missing Antecedent Study Baseline Values for Secondary Efficacy Endpoints

For secondary efficacy endpoints (monocular maximum corrected reading speed, binocular maximum reading speed, NL-BCVA, LL-BCVA, mean FRI index score, mean threshold sensitivity [subjects who had mesopic microperimetry performed in study APL2-304], and number of scotomatous points [subjects who had mesopic microperimetry performed in study APL2-304]) based on APL2-GA-305 Baseline to Month 12, if the antecedent study baseline value in the covariates of MMRM models based on APL2-GA-305 baseline is missing, the missing values will be single-imputed with the median of distribution in full analysis set at antecedent study baseline.

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14. ANALYSIS SOFTWARE

Statistical analyses will be performed using Version 9.4 (or newer) of SAS® on a suitably qualified environment.

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15. CHANGES TO ANALYSIS SPECIFIED IN PROTOCOL

No changes were made to the analyses specified in the protocol.

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17. APPENDIX

17.1. Schedule of Activities

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Table 11: 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	10	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
IOP measurement [a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Char (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

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Table 11: 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	10	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	
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
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										
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	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 Receivin 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; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

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[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 dil ting the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select subjects [those who had the assessment performed in the antecedent study]) wi be performed post dilation.

[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 uld be captured prior to dosing on dosing days. If a subject 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 is suspected, SD-OCT, FFA and OCT-A (select subjects [those who had the assessment performed in he 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 i 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 appr al 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 subjects will be contacted by study site staff with n 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 oc lar 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 fter 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 subject passes gross vision test, the subject may leave the site. If subject fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site If ssa y, antiglaucomatous medication can be given to lower the IOP. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the subject 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 treatm nt 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, pr scription a d over-the-counter medications) used by the subject throughout the subject's participation in the study.

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

[r] Subjects who developed exu ation related to exudative AMD 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 mus nly be re started if disease activity is detected by the investigator.

[s] At screening, serum pregnancy te hould be performed for women of childbearing potential. If positive, subject 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.

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Table 12: 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
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

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Table 12: 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**	
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]						x						x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x	x	
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
Schedule of Activities for Participants Receiving Fellow Eye Treatment ith Peg etacoplan													
Fellow eye IOP measurement	To be completed prior to llow eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR [h]	To be collected on the day of itiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration [o]	Regimen er PI's discretion												
Fellow eye postinjection assessment [k]	T be comple ed following fellow eye pegcetacoplan administration												

Abbreviations: Ab = antibody; BCVA = bes corrected visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fun us fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance est-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; 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.

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[f] Microperimetry assessments (select subjects [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 subject 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 is suspected, SD-OCT, FFA and OCT-A (select in the study eye is suspected, SD-OCT, FFA and OCT-A (select subjects [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 occ rs 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 pegc coplan adm nistration 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 inc ude a gross assessment of vision (finger-counting, handmotion, then light perception when applicable). If subject passes gross vision test, the subject may leave the site. If subjec fails gross ision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site. If necessary, antiAntiglaucomatous medication or glaucomato anterior chamber (medication can be given to lower the IOP.AC) If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from tap can be used to lower the p vious measurement until the subject passes gross vision test and IOP is ≤30 mm Hg. Note: if to the study eye is treated with an antiappropriate range to allow for VEGF injection during the same visit as pegcetacoplan, pegcetacoplan injection or after the the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment with anti-VEGF must is necessary to lowe he IOP, the increase in the IOP should be performed first. The pre- recorded as an AE and post-antimedication/AC tap should be recorded as a concomitant medication/concomitant procedure. VEGF If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the subject passes gross ision test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an antiIOP VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must be performed f st. The pre- and post-antiVEGF IOP values must be measured and recorded on the eCRF.
[l] Record concomitant medications (ie, prescription and over-the-counter medications) u d by he subject throughout the subject's participation in the study.
[m] For subjects who discontinue the study early, the early termination assessme ts should b perfo med after a minimum of 30 days have passed from the last dosing visit. If a subject reports for a scheduled visit and decides to terminate early prior to dosing, then he visi should b considered the early termination visit and all early termination procedures should be performed.
[n] Subjects who developed exudation related to CNV prior to Mon h 20 of the a tecedent 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 det cted b the investigator.
[o] If pegcetacoplan is being injected bilaterally on the same day the study ey should be administered first.

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Table 13: 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
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

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Table 13: 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**	
FFA[h]												x	x
OCT-A[h]						x						x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x		
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 Trea ment w th Pegcetacoplan													
Fellow eye IOP measurement	To be completed prior to fellow eye p gcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR [h]	To be collected on the day o initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration [o]	Regimen per PI s discretion												
Fellow eye postinjection assessment [k]	To e complet d 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 autofluorescen e; FFA = fundus fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BC A = 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; 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.

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[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 subjects [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 subject 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 ac ve choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select subjects [those who had the assessment performed in the antecedent study]) images should 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 th 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. Wh n 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 sho ld 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 p rticipant 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 oranterior 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 sho ld b 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 nti-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 n the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) us d by t e participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments shoul be p rformed 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 he 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 e 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, he study eye should be administered first.

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Table 14: 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
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
IOP measurement [a,b]		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

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Table 14: 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**	
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
DCFP [a,b,k]		x						x	x
FFA [a,b,k]		x						x	x
OCT-A [a,b,k]		x			x			x	x
Pegcetacoplan administration [a,b,l,m]		x	x	x	x	x	x	x	
Follow-up call [n]		x	x	x					
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
Adverse events [a,b]		x	x	x	x	x	x	x	x
Schedule of Activities for Participants R ceiving 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; EXUDATIVE AMD = 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; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

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[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 ser m 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 dil ting the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select subjects [those who had the assessment performed in the antecedent study]) wi 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 uld be captured prior to dosing on dosing days. If a subject 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 is suspected, SD-OCT, FFA, and OCT-A (select subjects [those who had the assessment performed in the ant cedent 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 i 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 appr al 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 subjects will be contacted by study site staff with n 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 oc lar 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 fter 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 subject passes gross vision test, the subject may leave the site. If subject fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site If ssa y, antiglaucomatous medication can be given to lower the IOP. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the subject 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 treatm nt 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, pr scription a d over-the-counter medications) used by the subject throughout the subject's participation in the study.

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

[r] Subjects who developed exu ation related to exudative AMD 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 te hould be performed for women of childbearing potential. If positive, subject 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.

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Table 15: 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 antiPEG 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
IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (sele t 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

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Table 15: 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**	
FFA[h]						x	x
OCT-A[h]			x			x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	
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
Schedule of Activities for Participants Receiving Fellow Eye Treatme t with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fello eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on t day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[o]	Regi n per PI's discre ion						
Fellow eye postinjection assessment[k]	T be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = b st-correct d visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluores ein angiog aphy or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-correct d 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; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vas ular endothelial growth factor.

[a] Obtain prior to fluorescein angi graphy 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 subjects [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.

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[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 sessment 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 par cipantfails gross ision 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 r corded as a AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approxima ly 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 th 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 par icipan hroughout 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 hould 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 anteced t stu ies 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 th investigat r.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study ye sho ld be administered first.

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Table 16: Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ETm
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
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (se ect 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

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Table 16: Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ETm
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**	
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]			x			x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x		
Postinjection assessment[k]	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 pri r to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be co l ted 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 ompleted following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = bes 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 est-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; 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.

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[f] Microperimetry assessments (select subjects [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 occu s 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 pegce coplan 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 incl de 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. f a particip ntfails 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 ch mber (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 recor ed 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 inject 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 e 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 vis shou d 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 a tecedent 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 dete ted b the inv stigator.

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

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17.2. Protocol Changes to be followed during COVID-19 Restrictions

OVERVIEW

In response to the COVID-19 crisis, to ensure the safety of study subjects 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 subjects, and to poten ially mitigate missed IP administration, an extended IP administration window can e 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 day

During COVID-19 restrictions, the IP admin stration 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 d ys to +30 days for the first study year and –16 days to +30 days for the se ond study year

MINIMUM SCHEDULE OF ASSESSMENT

Where feasible, sites could continue to follow the full Schedule of Activities (based on their treatment group assignm nt). 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. Subjects 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.

Subjects 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 subjects should be instructed to phone call. The site must inform the sponsor of any subjects lost to follow-up.

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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.

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Table 17: 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	10	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
IOP measurement [a,b]		x	x	x	x	x	x	x	x	x	x	x	x	x	x
MNRead or Radner Reading Cha ts (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

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Table 17: 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	10	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	
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
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										
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	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 Recei ing 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 assessm nt [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; 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.

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[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 s ould be performed monocularly first, then binocularly.
[i] Microperimetry assessments (select subjects [those who had the assessment performed in the antecedent study]) will be performed post dilation.
[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 a ove 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 e captured p ior to dosing on dosing days. If a subject 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 visi . If new active choroidal neovascularization is suspected, SD-OCT, FFA and OCT-A (select subjects [those who had the assessment performed in the antecedent study]) image 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 medi l 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 subjects will be contacted by study site staff within 4 ± 2 days afte 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 symp ms in he 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 d sing by the phys cian or study staff and should include a gross assessment of vision (finger-counting, hand-motion, then light perception when applicable). If subject passes gross visio test, he subj ct may leave the site. If subject fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site. If necessary, antiglauc matous medication can be given to lower the IOP. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement unti the subject pa ses 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-coun er medications) used by the subject throughout the subject's participation in the study.
[q] For subjects who discontinue the study early, the early ination assessments should be performed after a minimum of 30 days have passed from the last dosing visit. If a subject reports for a scheduled visit and decides to terminate arly prior to dosing, then the visit should be considered the early termination visit and all early termination procedures should be performed.
[r] Subjects who developed exudation related to exu tive AMD 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 r -started if d sease activity is detected by the investigator.
[s] At screening, serum pregnancy test shou d be perfo med for women of childbearing potential. If positive, subject is not eligible to continue in the study.
[t] Beginning at Day 1, perform the urine preg ancy 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 injec d bilaterally on the same day, the study eye should be administered first.

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Table 18: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ETm
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
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

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Table 18: COVID-19 Schedule of Activities—Monthly Treatment Group (Year 2)

	Treatment												ETm
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**	
DCFP[h]												x	x
FFA[h]												x	x
OCT-A[h]						x						x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x	x	
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
Schedule of Activities for Participants Receiving Fellow Eye Treatment ith Pegcetacoplan													
Fellow eye IOP measurement	To be completed prio to fel w eye pegcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected the day of init ation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration[o]	Reg men per P 's discretion												
Fellow eye postinjection assessment[k]	To be ompleted 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 = fund s fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance bes ected 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; 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.

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[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 subjects [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 subject 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 ac ve choroidal neovascularization is suspected, SD-OCT, FFA and OCT-A (select in the study eye is suspected, SD-OCT, FFA and OCT-A (select subjects [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 th 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. Wh n 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 sh uld include a gross assessment of vision (finger-counting, handmotion, then light perception when applicable). If subject passes gross vision test, the subject may leave the site. If subject fail gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site. If necessary, antiAntiglaucomatous medication or glaucomatousanterior chamber (medication can be given to lower the IOP.AC) If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from tap can be used to l wer the previous measurement until the subject passes gross vision test and IOP is ≤30 mm Hg. Note: if to the study eye is treated with an antiappropriate range to allow for VEGF injection during the same visit as pegcetacoplan, pegcetacoplan injection or after the the pegcetacoplan injection if IOP is >30 mm Hg. If any treatment with anti-VEGF must is ecessary to lower the IOP, the increase in the IOP should be performed first. The pre- recorded as an AE and post-antimedication/AC tap should be recorded as a concomitant medication/co comitant procedure. VEGF If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the subject passes gro visio test and IOP is ≤30 mm Hg. Note: if the study eye is treated with an antiIOP VEGF injection during the same visit as pegcetacoplan, the treatment with anti-VEGF must b performed first. The pre- and post-antiVEGF IOP values must be measured and recorded on the eCRF.

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

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

[n] Subjects who developed exudation related to CNV prior to Mo th 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 de cted by the investigator.

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

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

	Treatment												ETm
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
IOP measurement	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

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

	Treatment												ETm
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**	
FFA[h]												x	x
OCT-A[h]						x						x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	x	x	x	x	x		
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 Trea ment w th Pegcetacoplan													
Fellow eye IOP measurement	To be completed prior to fellow eye p gcetacoplan administration												
Fellow eye FAF, SD-OCT, and NIR [h]	To be collected on the day o initiation of pegcetacoplan, then follow study eye schedule												
Fellow eye pegcetacoplan administration [o]	Regimen per PI s discretion												
Fellow eye postinjection assessment [k]	To e complet d 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 = fun us fluorescein angiography or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance be t 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; 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.

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[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 subjects [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 subject 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 ac ve choroidal neovascularization in the study eye is suspected, SD-OCT, FFA and OCT-A (select subjects [those who had the assessment performed in the antecedent study]) images should 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 th 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. Wh n 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 sho ld 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 p rticipant 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 oranterior 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 sho ld b 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 nti-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 n the eCRF.

[l] Record concomitant medications (ie, prescription and over-the-counter medications) us d by t e participant throughout the participant's participation in the study.

[m] For participants who discontinue the study early, the early termination assessments shoul be p rformed 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 he 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 e 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 udy eye should be administered first.

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Table 20: 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 (+ 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
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
IOP measurement [a,b]		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

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Table 20: 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 (+ or – days)	N/A [a,b]		16	16	16	16	16	16	
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
DCFP [a,b,k]		x						x	x
FFA [a,b,k]		x						x	x
OCT-A [a,b,k]		x			x			x	x
Pegcetacoplan administration [a,b,l,m]		x	x	x	x	x	x	x	
Follow-up call [n]		x	x	x					
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
Adverse events [a,b]		x	x	x	x	x	x	x	x
Schedule of Activities for Participants R ceiving 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; EXUDATIVE AMD = 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; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vascular endothelial growth factor.

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[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 ser m 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 dil ting the eyes. It should be performed monocularly first, then binocularly.

[i] Microperimetry assessments (select subjects [those who had the assessment performed in the antecedent study]) wi 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 uld be captured prior to dosing on dosing days. If a subject 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 is suspected, SD-OCT, FFA, and OCT-A (select subjects [those who had the assessment performed in the ant cedent 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 i 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 appr al 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 subjects will be contacted by study site staff with n 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 oc lar 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 fter 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 subject passes gross vision test, the subject may leave the site. If subject fails gross vision test, tonometry should be performed. IOP should be ≤30 mm Hg in order for the subject to leave the site If ssa y, antiglaucomatous medication can be given to lower the IOP. If IOP is >30 mm Hg, assessments will continue every approximately 30 minutes from the previous measurement until the subject 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 treatm nt 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, pr scription a d over-the-counter medications) used by the subject throughout the subject's participation in the study.

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

[r] Subjects who developed exu ation related to exudative AMD 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 te hould be performed for women of childbearing potential. If positive, subject 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.

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Table 21: 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 (+ 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 antiPEG 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
IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (sele t 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

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Table 21: 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 (+ or – days)	**16**	**16**	**16**	**16**	**16**	**16**	
FFA[h]						x	x
OCT-A[h]			x			x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x	x	
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
Schedule of Activities for Participants Receiving Fellow Eye Treatme t with Pegcetacoplan							
Fellow eye IOP measurement	To be completed prior to fello eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be collected on t day of initiation of pegcetacoplan, then follow study eye schedule						
Fellow eye pegcetacoplan administration[o]	Regi n per PI's discre ion						
Fellow eye postinjection assessment[k]	T be completed following fellow eye pegcetacoplan administration						

Abbreviations: Ab = antibody; BCVA = b st-correct d visual acuity; CNV = choroidal neovascularization; DCFP = digital color fundus photography; ET = early termination; FAF = fundus autofluorescence; FFA = fundus fluores ein angiog aphy or fluorescein angiography; FRI = Functional Reading Independence Index; IOP = intraocular pressure; labs = laboratory tests; LL-BCVA = low-luminance best-correct d 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; SD-OCT = spectral domain optical coherence tomography; SE = study eye; VEGF = vas ular endothelial growth factor.

[a] Obtain prior to fluorescein angi graphy 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 subjects [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.

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[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 sessment 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 par cipantfails gross ision 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 r corded as a AE and medication/AC tap should be recorded as a concomitant medication/concomitant procedure. If IOP is >30 mm Hg, assessments will continue every approxima ly 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 th 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 par icipan hroughout 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 hould 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 anteced t stu ies 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 th investigat r.

[o] If pegcetacoplan is being injected bilaterally on the same day, the study ye sho ld be administered first.

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Table 22: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ETm
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
Dilated indirect ophthalmoscopy	x	x	x	x	x	x	x
IOP measurement	x	x	x	x	x	x	x
MNRead or Radner Reading Charts (sele t 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

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Table 22: COVID-19 Schedule of Activities—Every-Other-Month Treatment Group (Year 3)

	Treatment						ETm
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**	
DCFP[h]						x	x
FFA[h]						x	x
OCT-A[h]			x			x	x
Pegcetacoplan administration[i,j]	x	x	x	x	x		
Postinjection assessment[k]	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 w th Pegcetacoplan							
Fellow eye IOP measurement	To be completed prio to fellow eye pegcetacoplan administration						
Fellow eye FAF, SD-OCT, and NIR[h]	To be o l ted 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 = be 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 est-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; 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.

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[f] Microperimetry assessments (select subjects [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 occu s 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 pegce coplan 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 incl de 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. f a particip ntfails 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 ch mber (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 recor ed 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 inject 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.

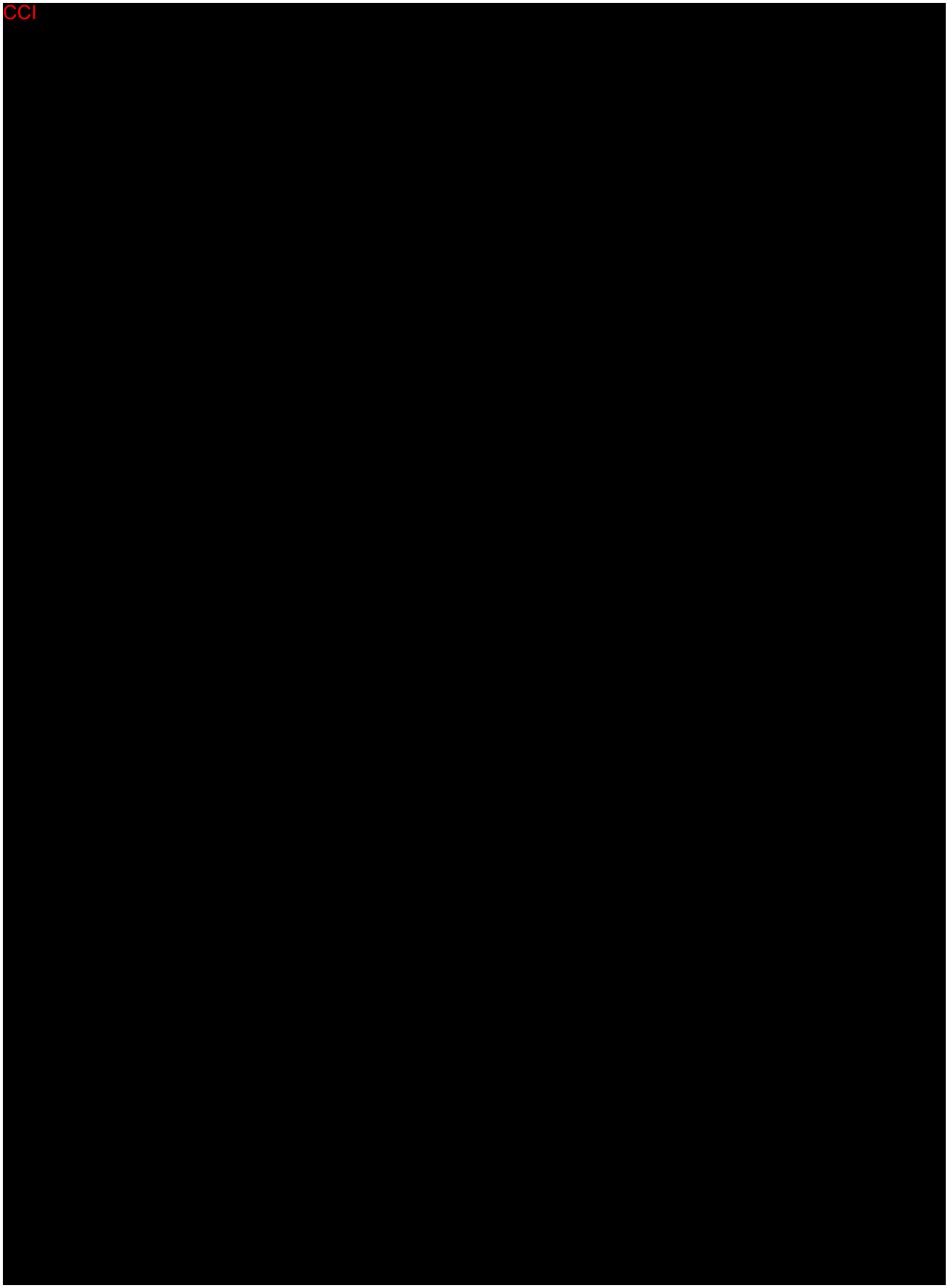
[m] For participants who discontinue the study early, the early termination assessments should e performed after a minimum of 30 days have passed from the last dosing visit. If a participant reports for a scheduled visit and decides to terminate early prior to dosing, then the vis shou d be considered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

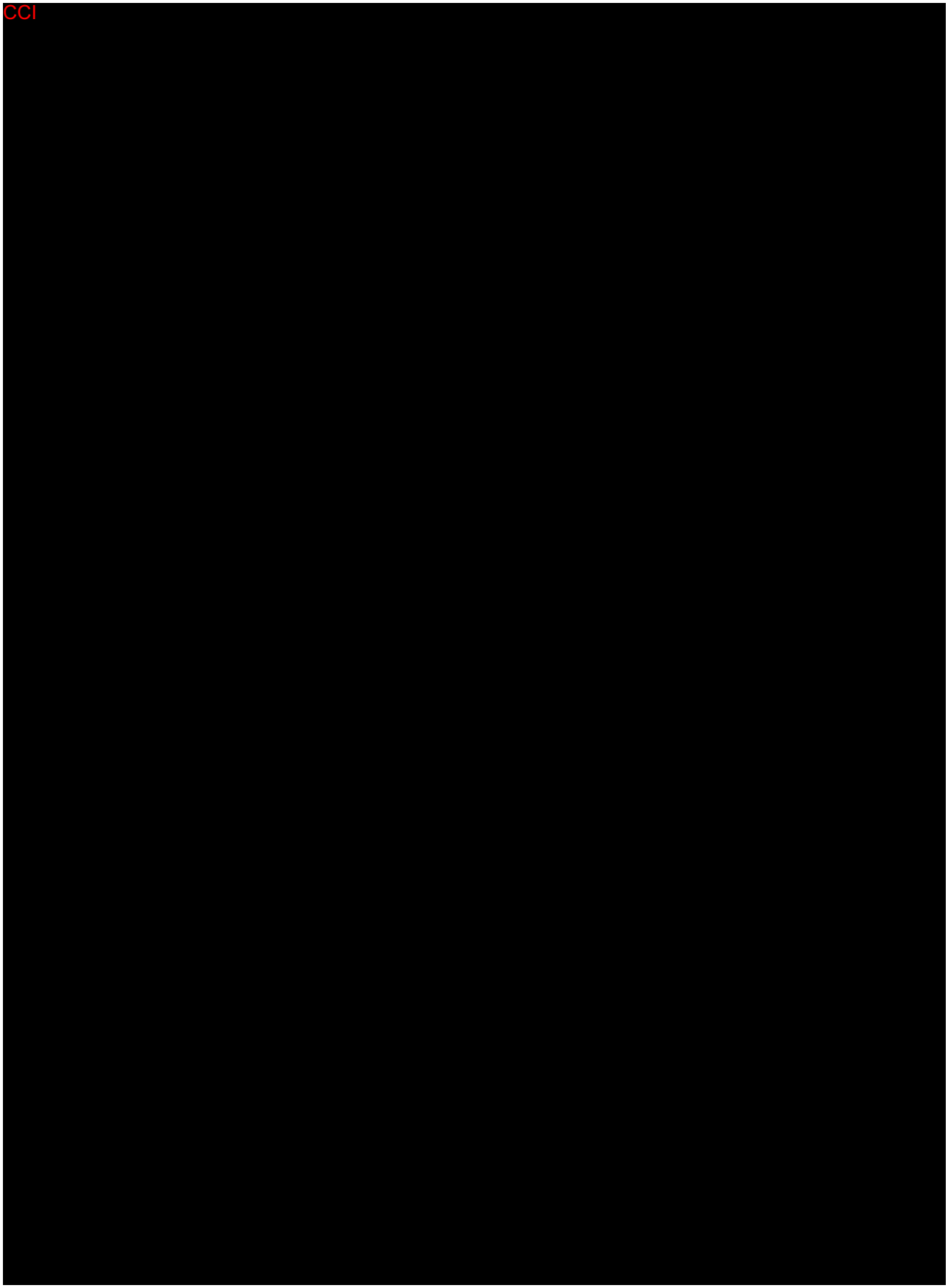
[n] Participants who developed exudation related to CNV prior to month 20 of the a tecedent studies must be assessed by monthly OCTs in this study starting at baseline, and treatment with anti-VEGF therapy must only be restarted if disease activity is dete ted b the inv stigator.

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

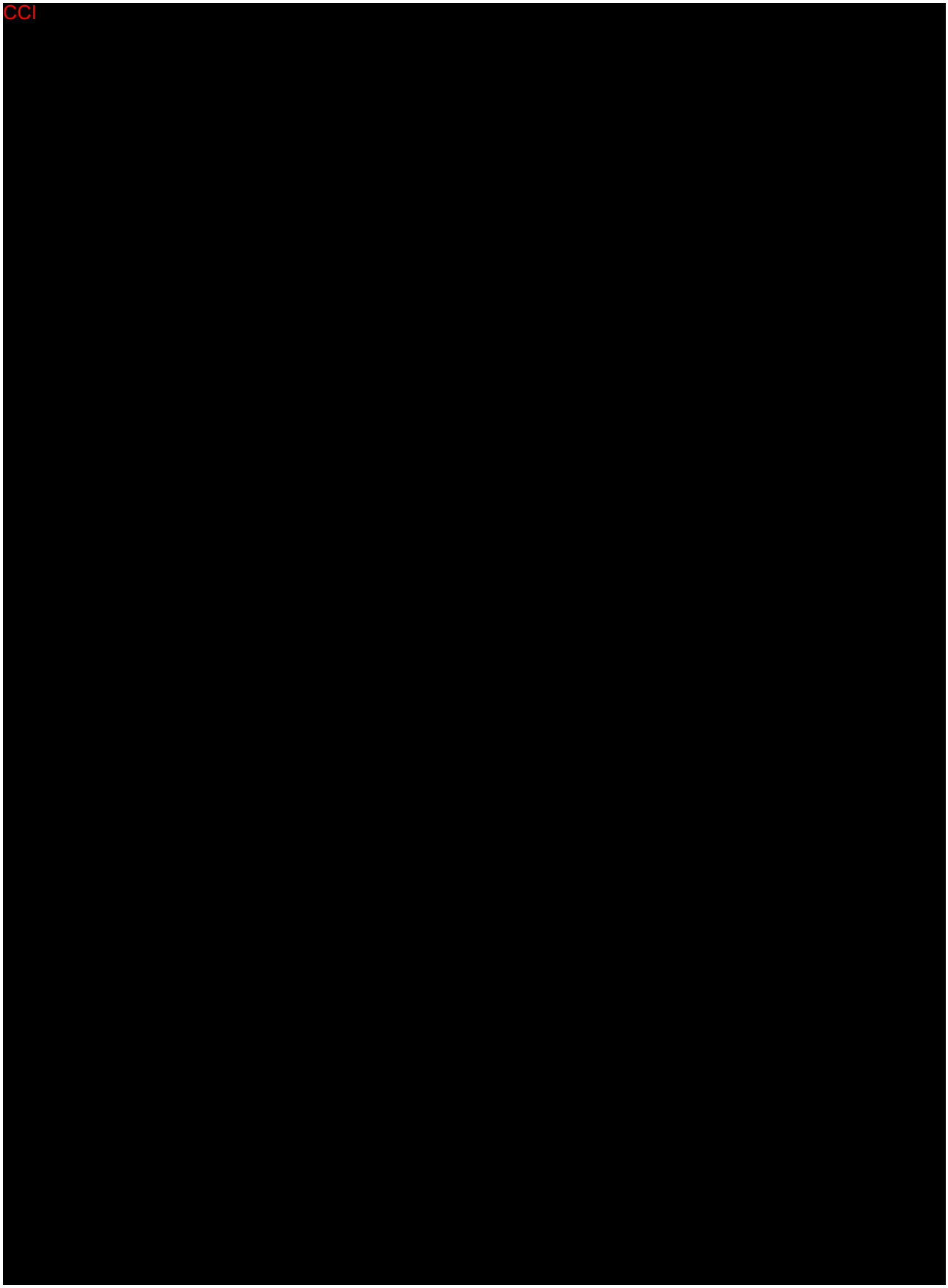
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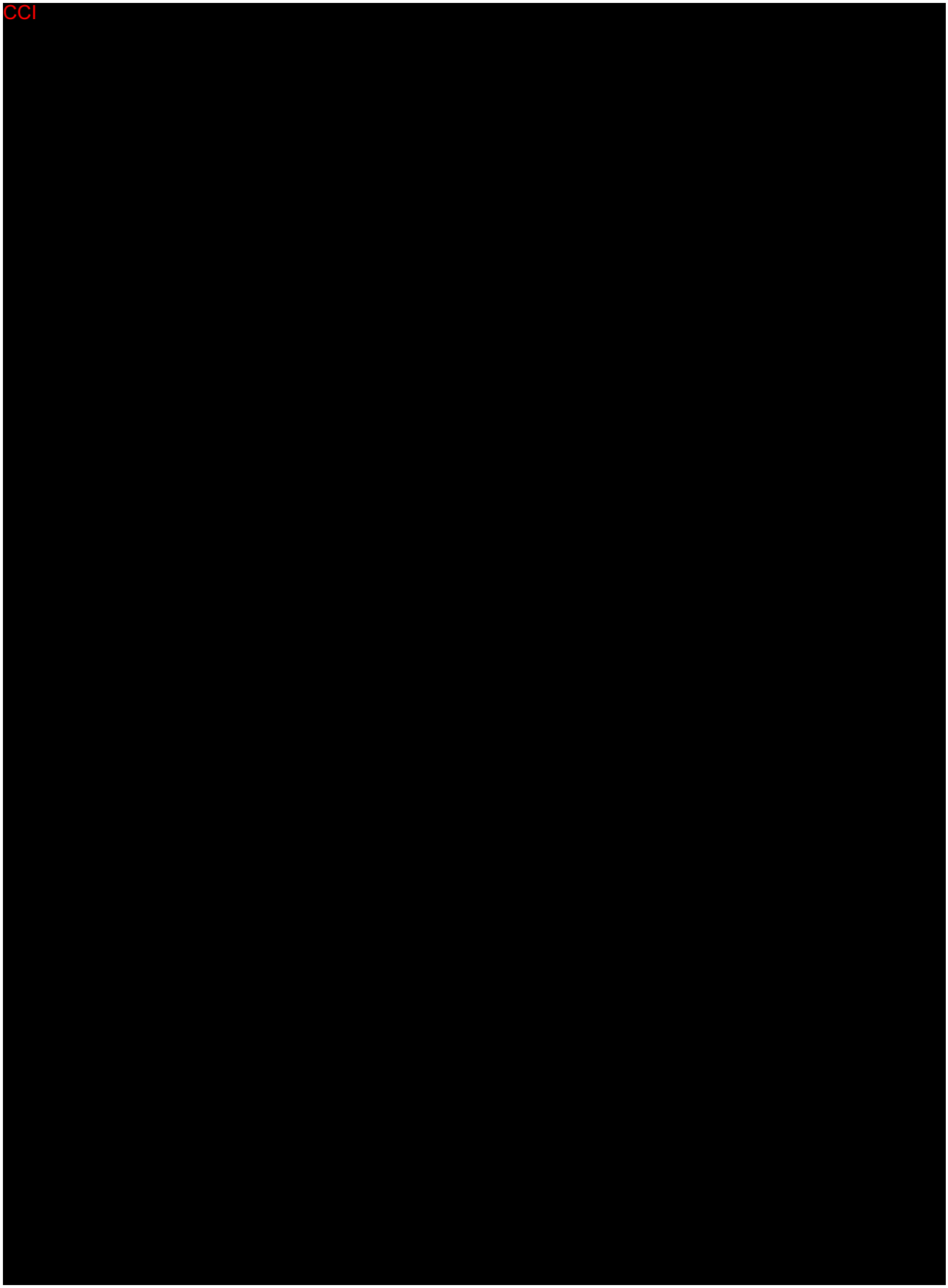


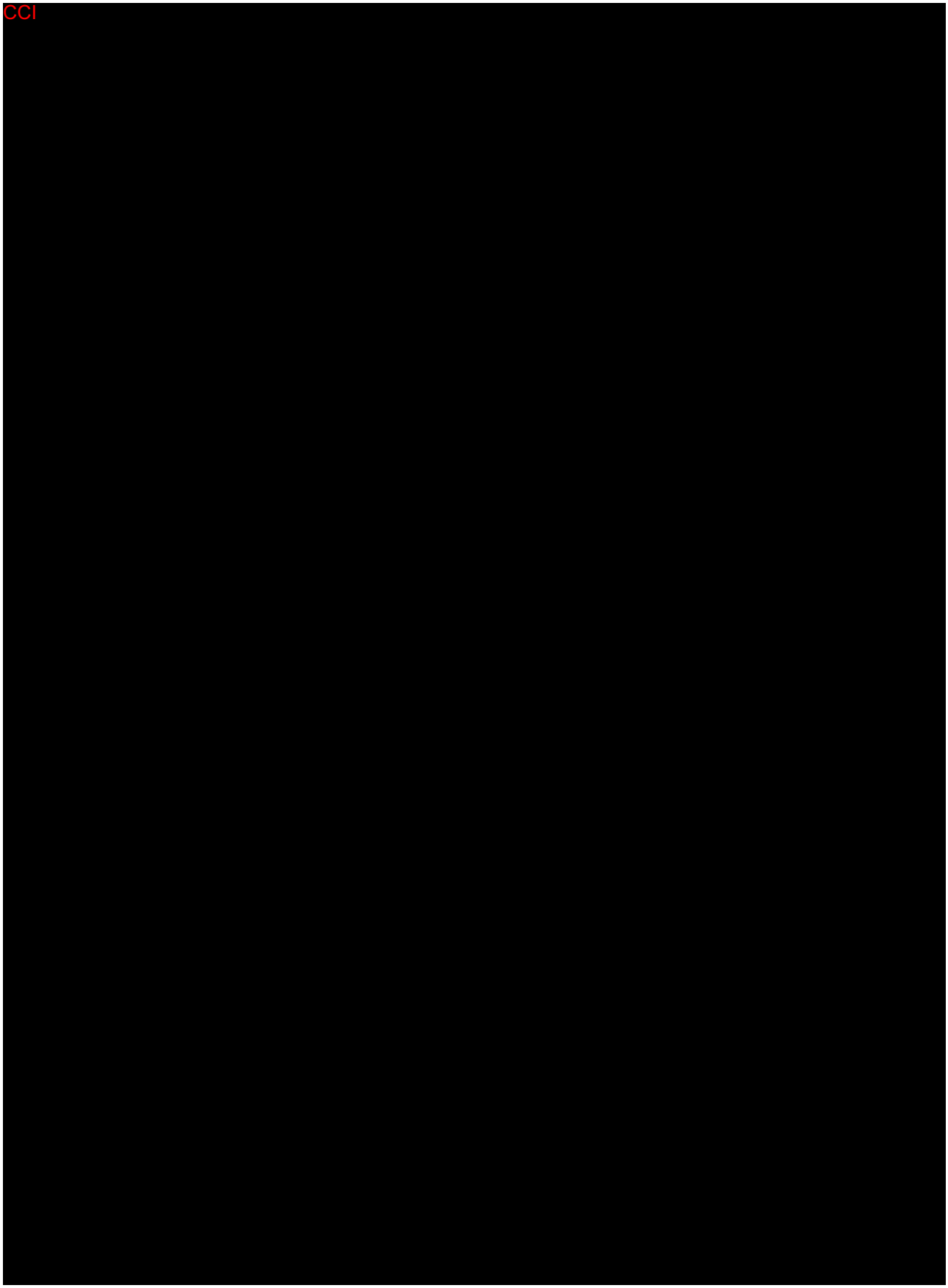

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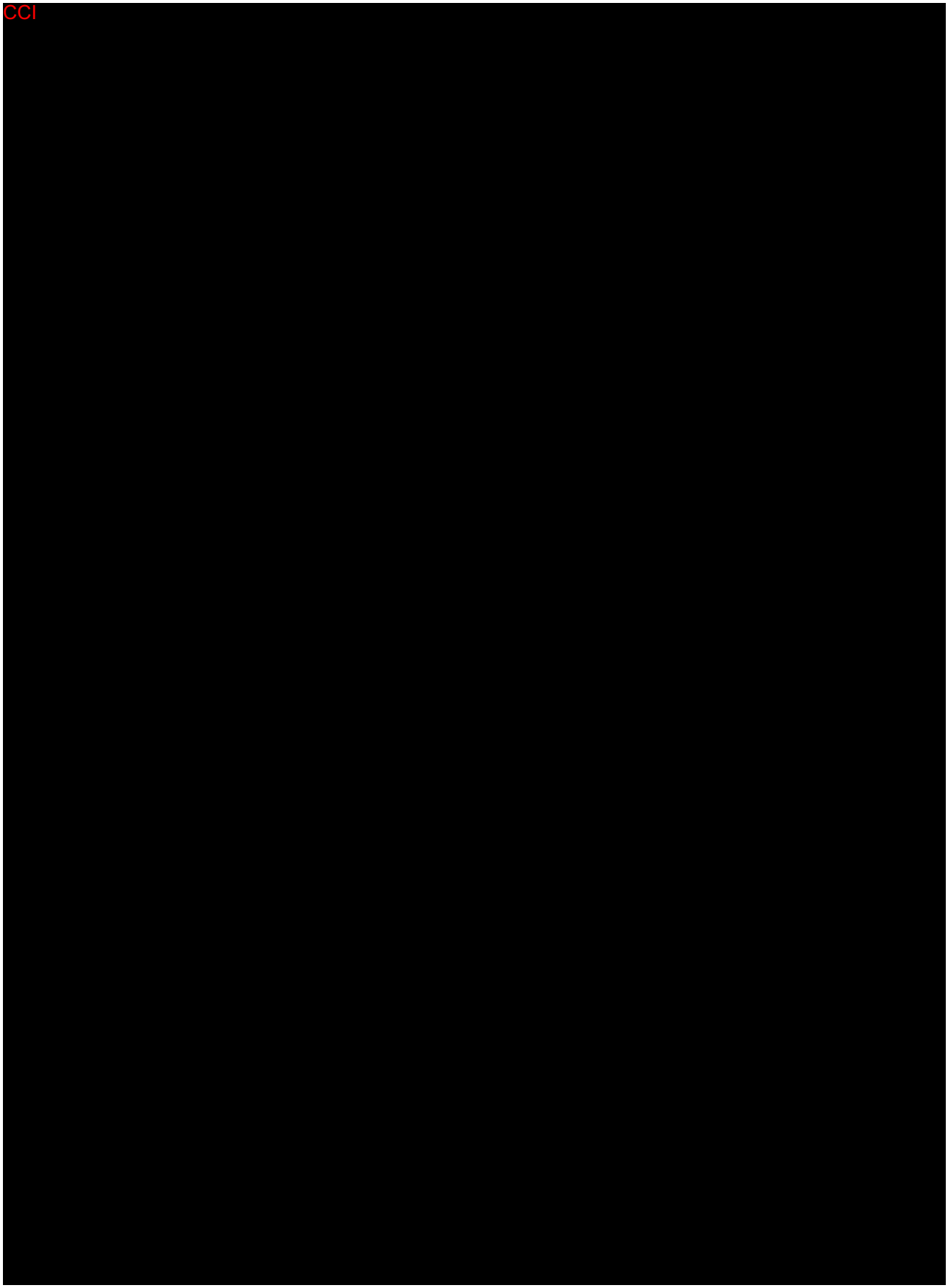


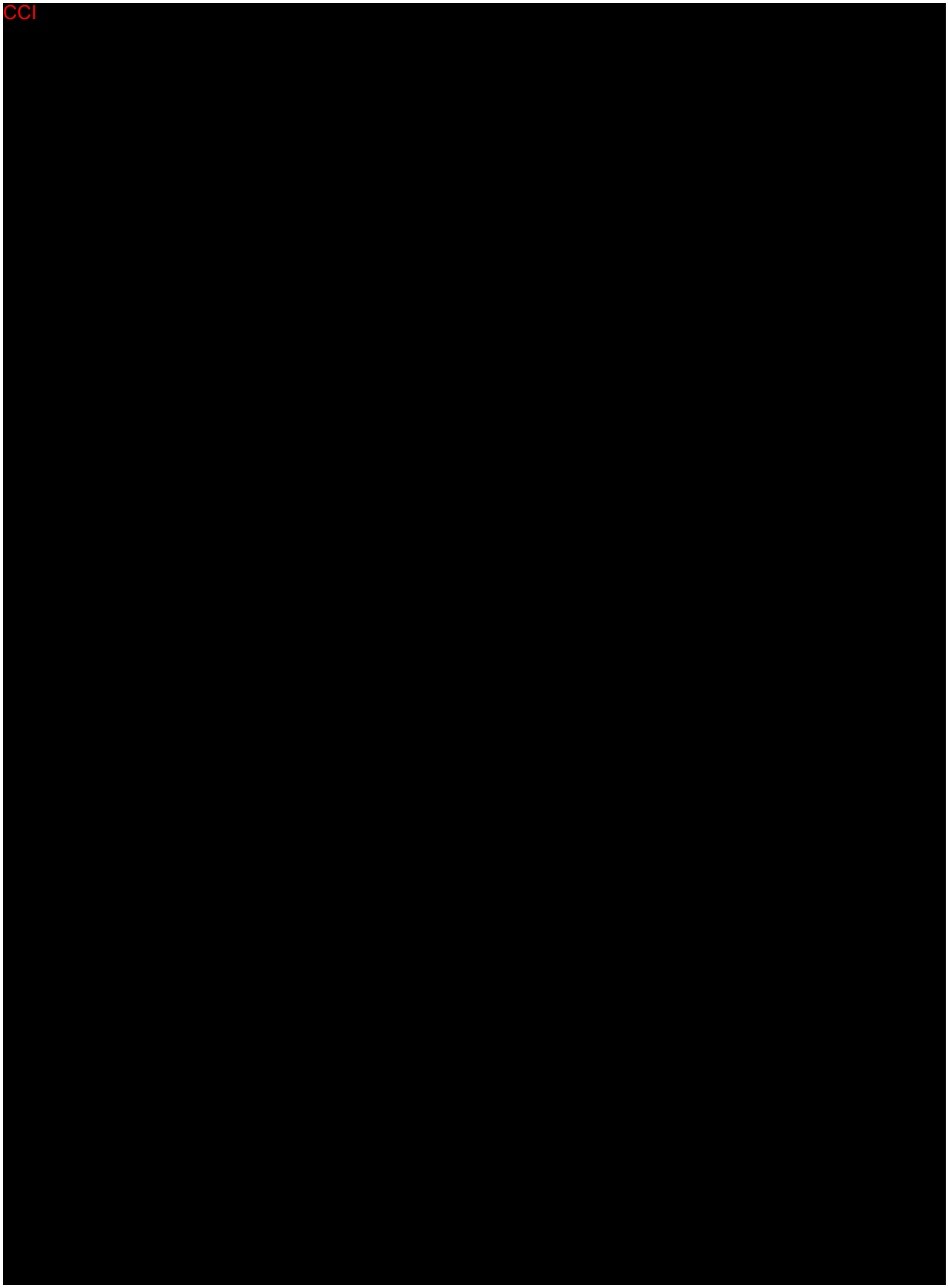
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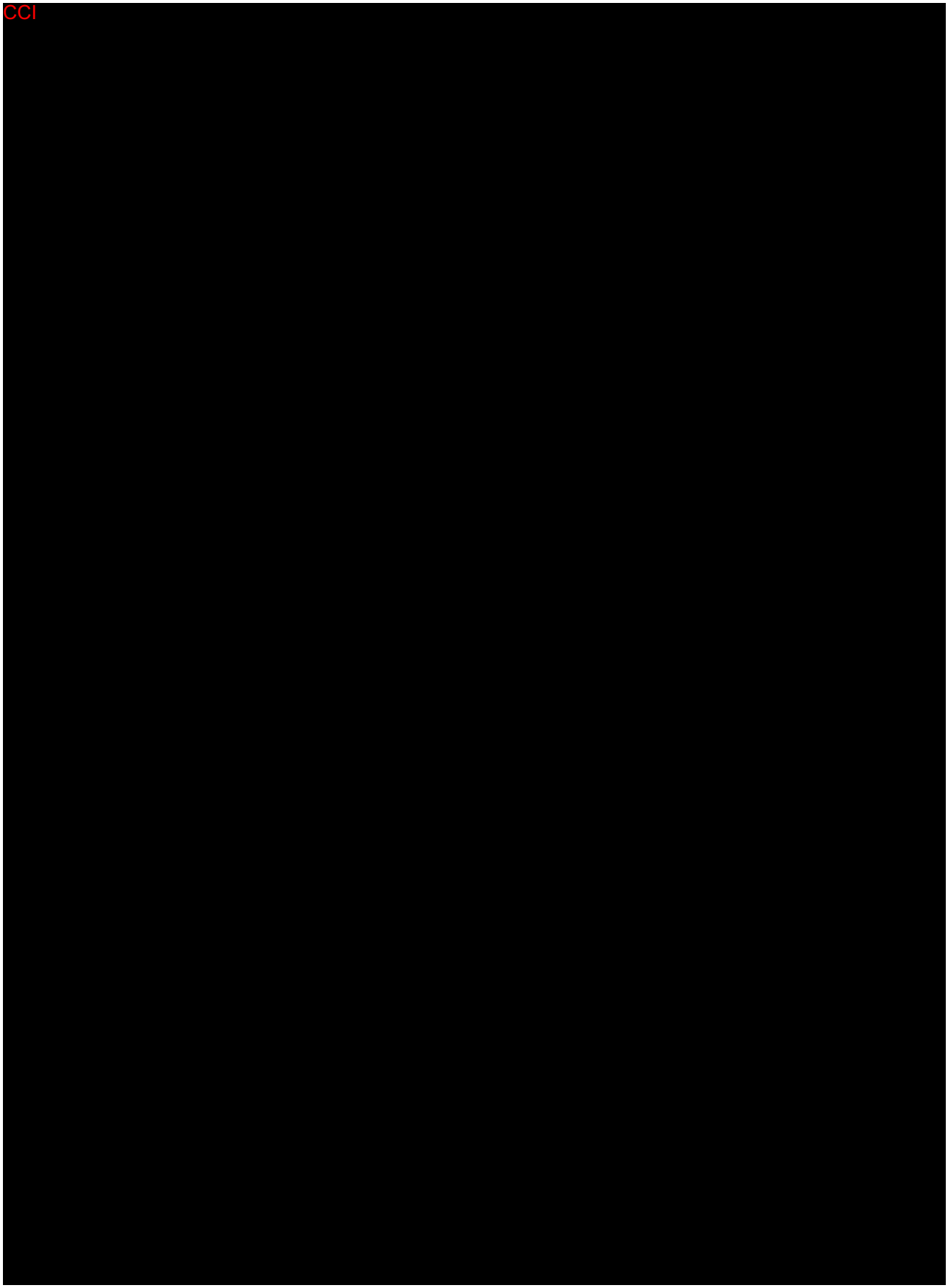



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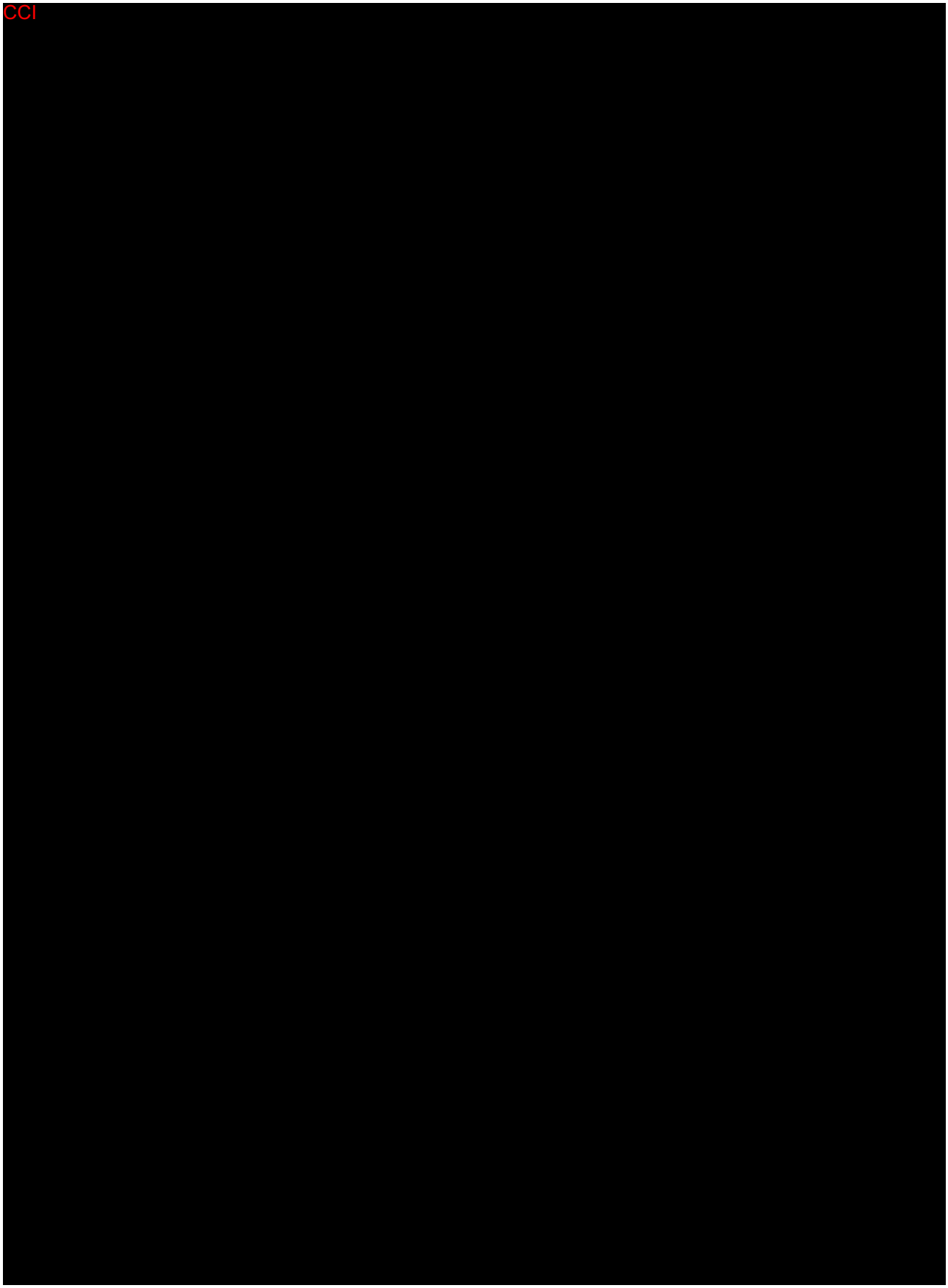
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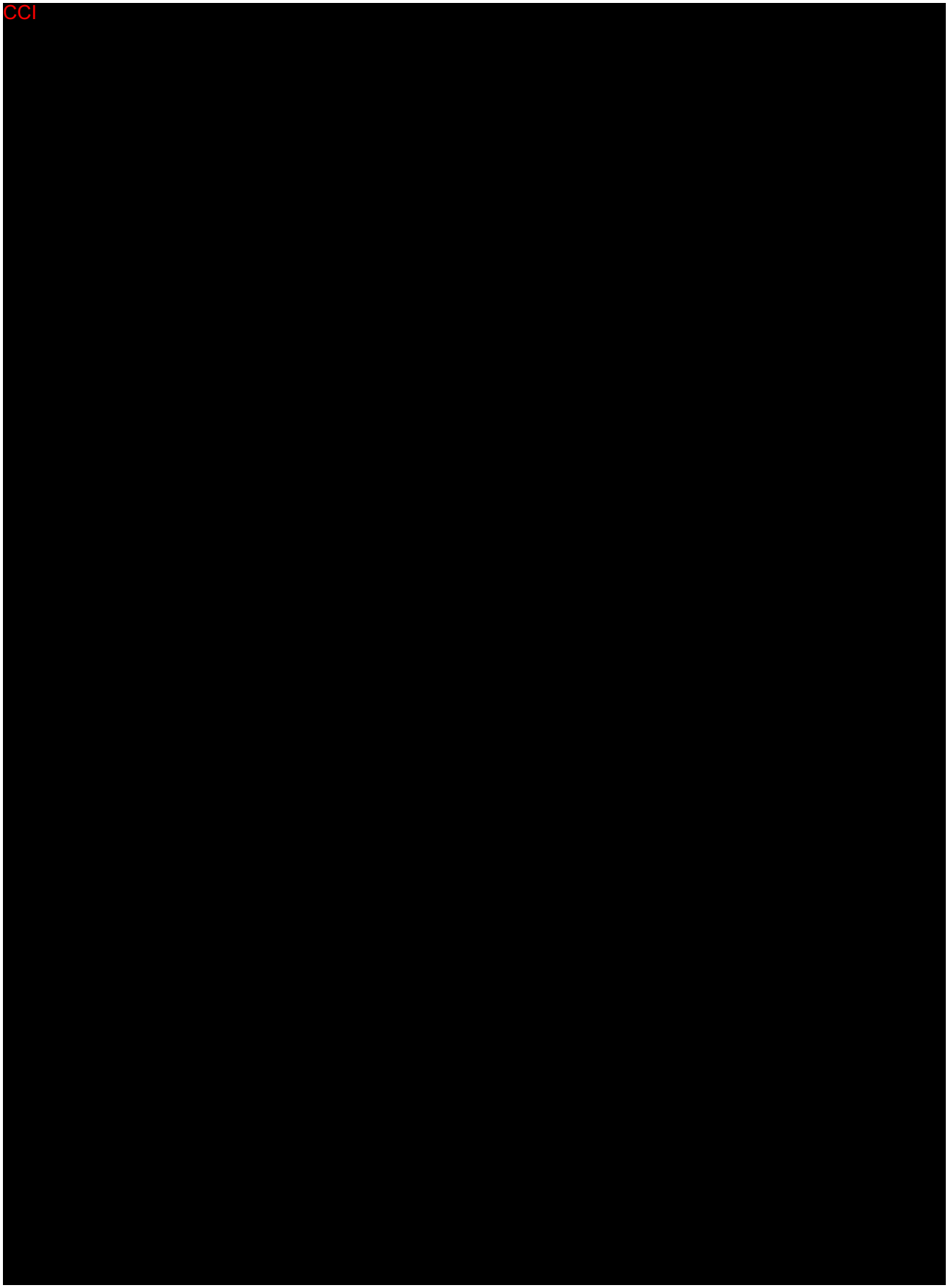



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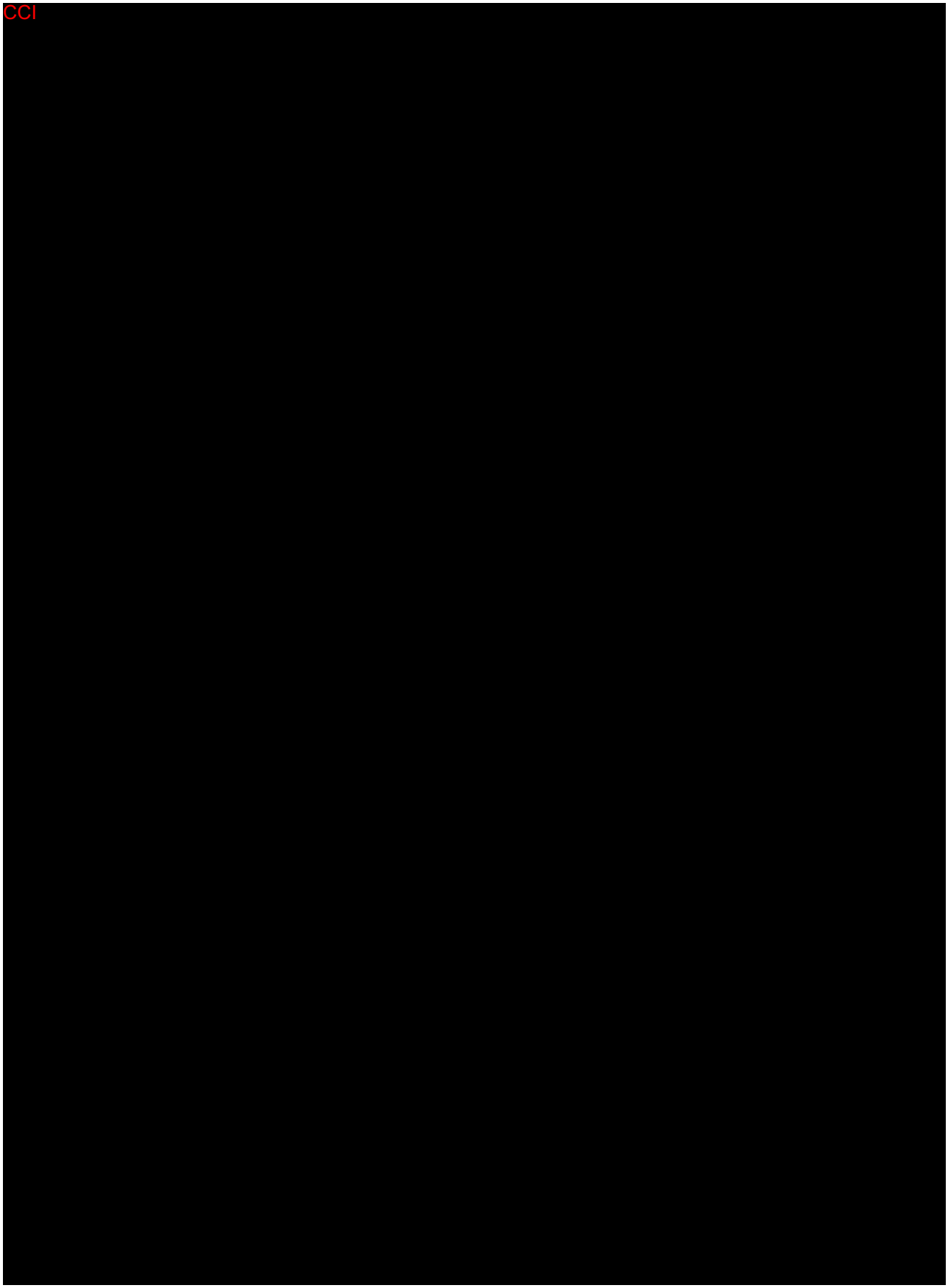

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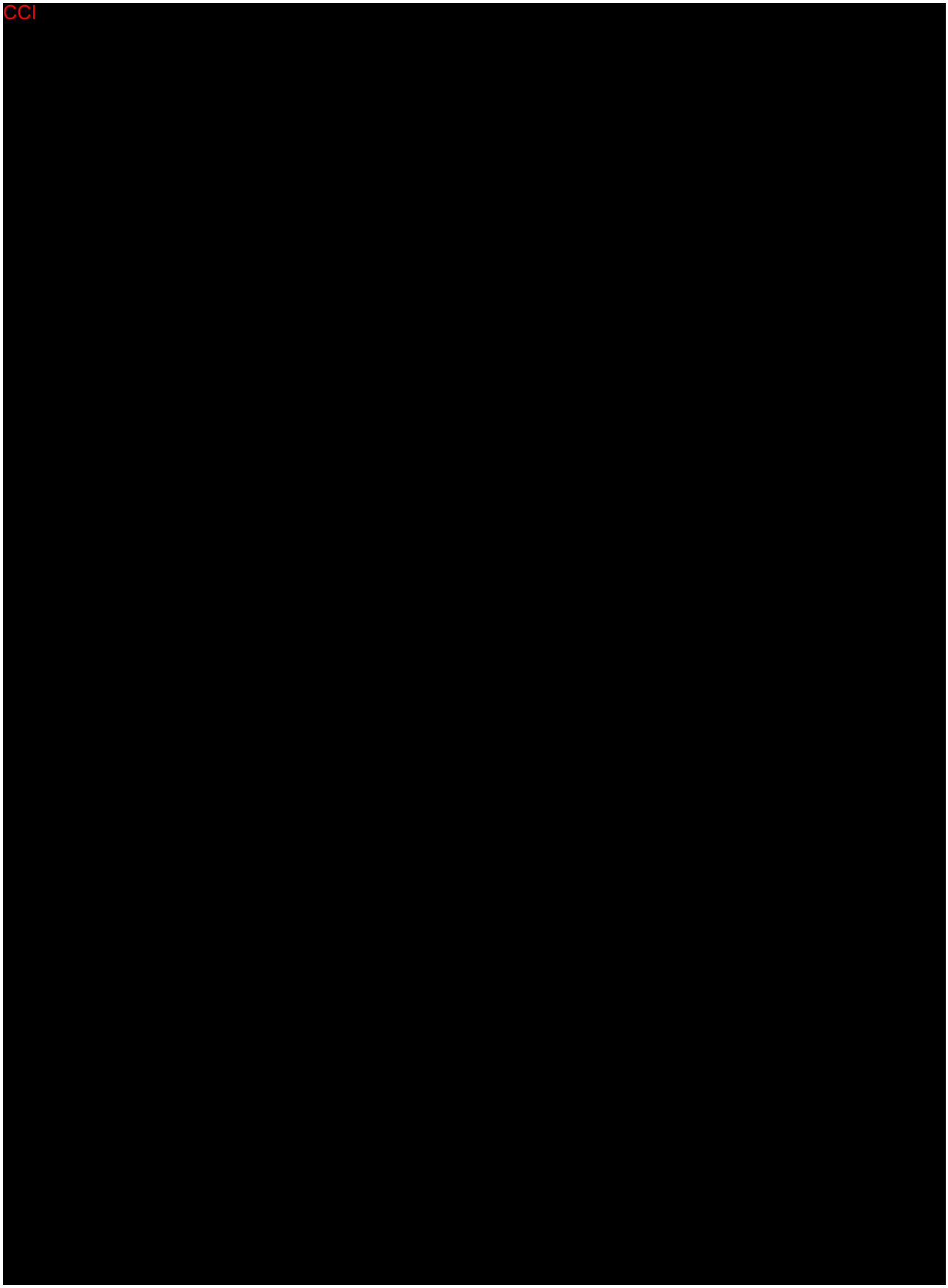
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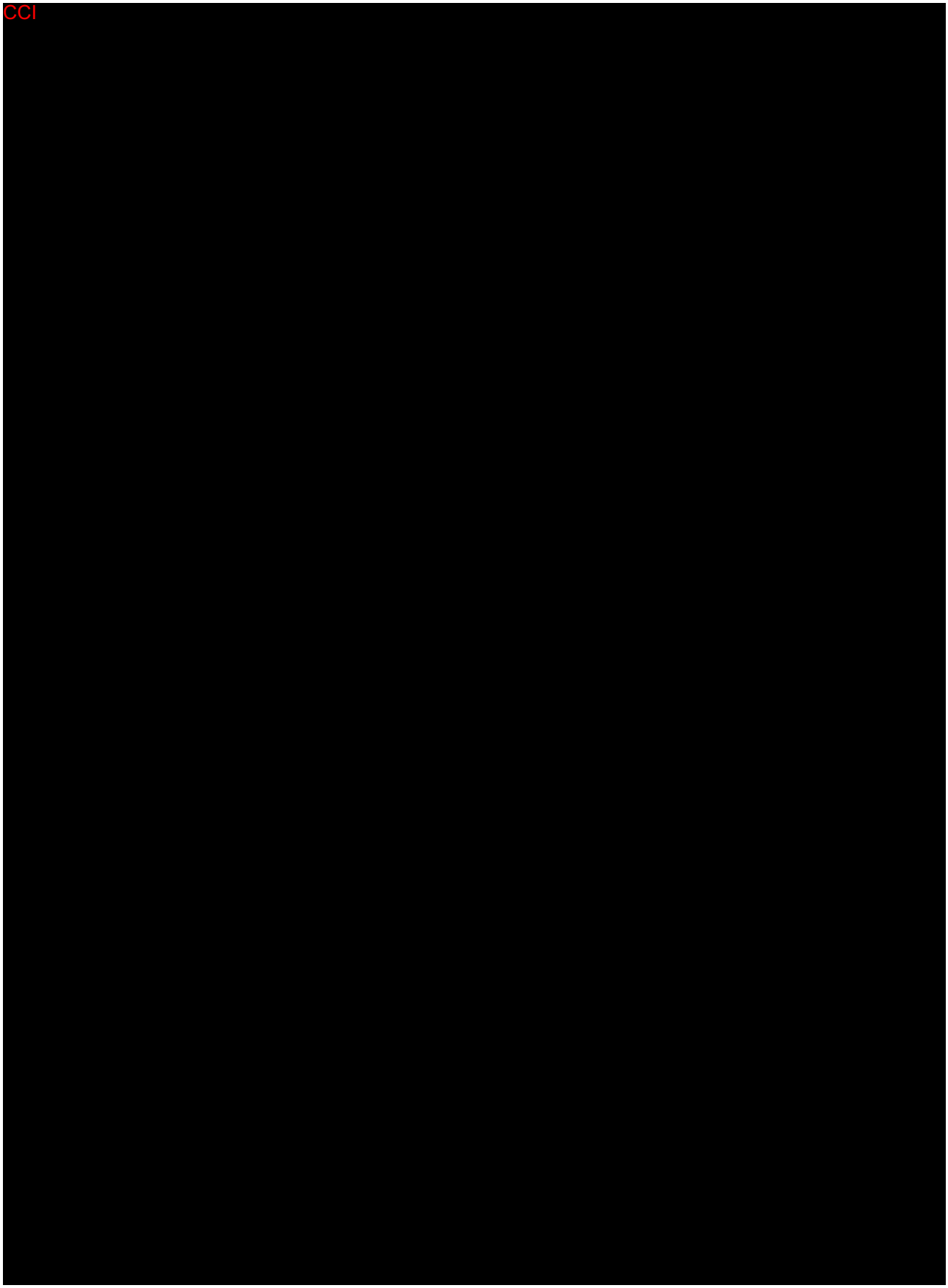


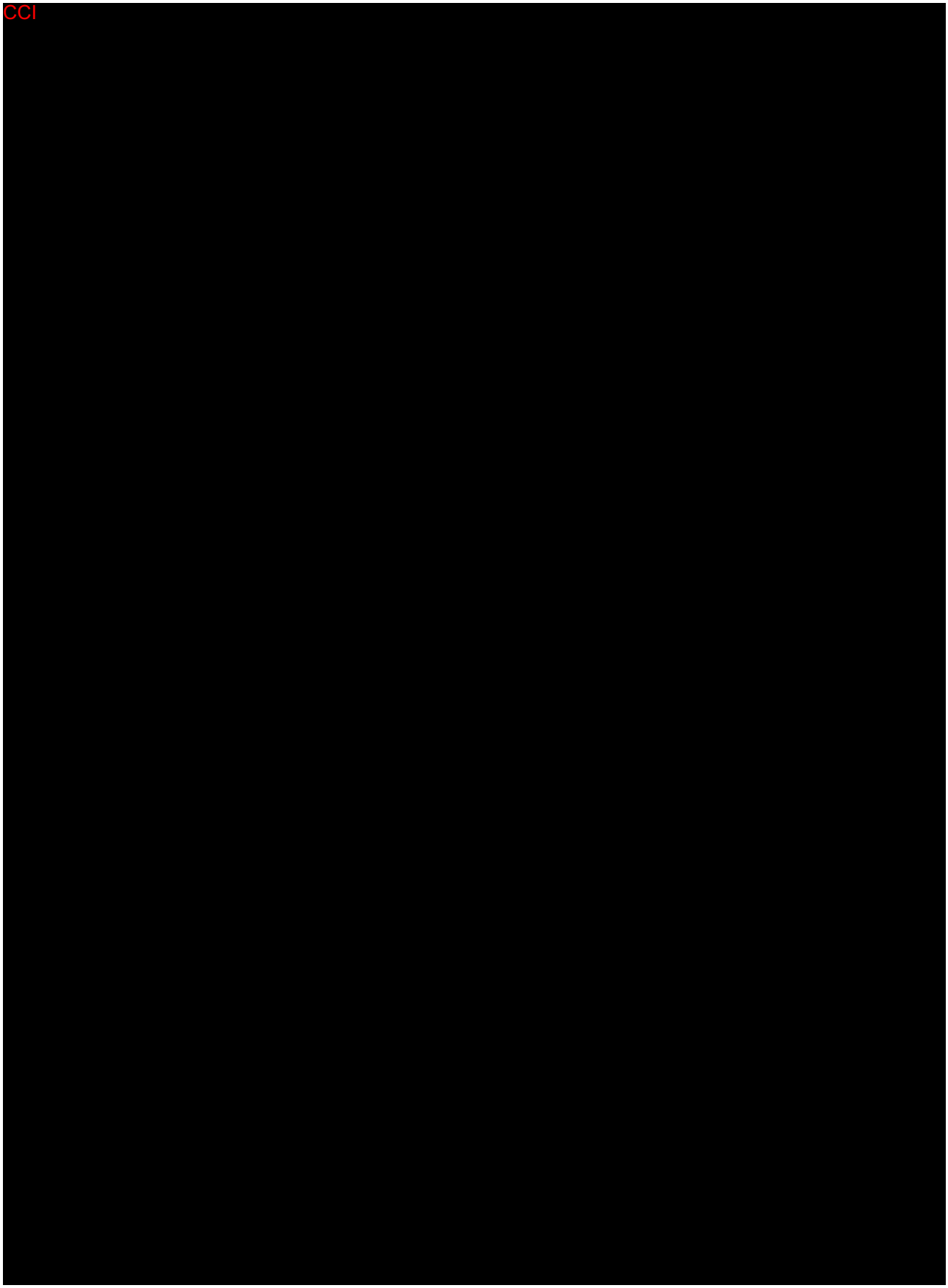

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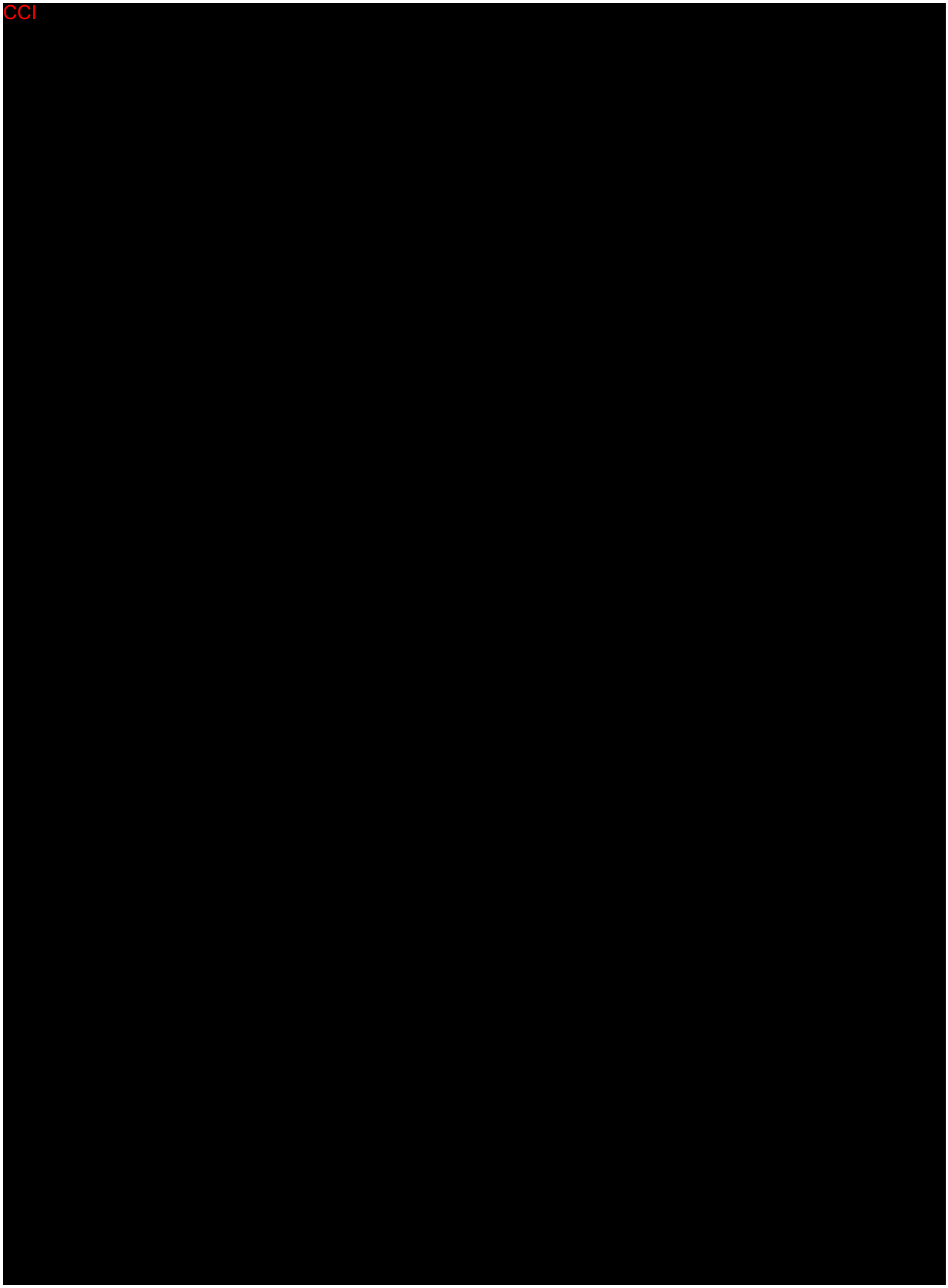


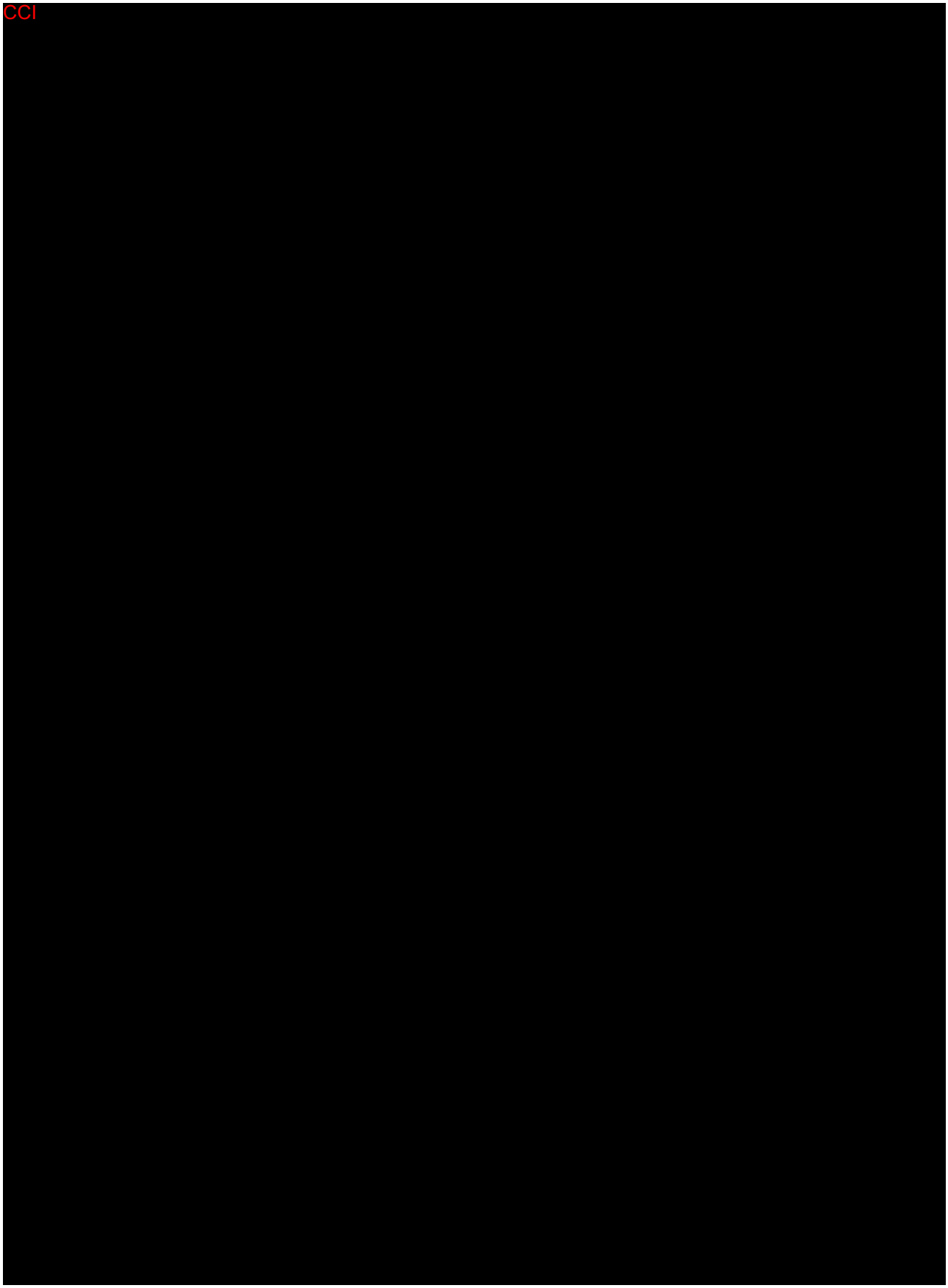

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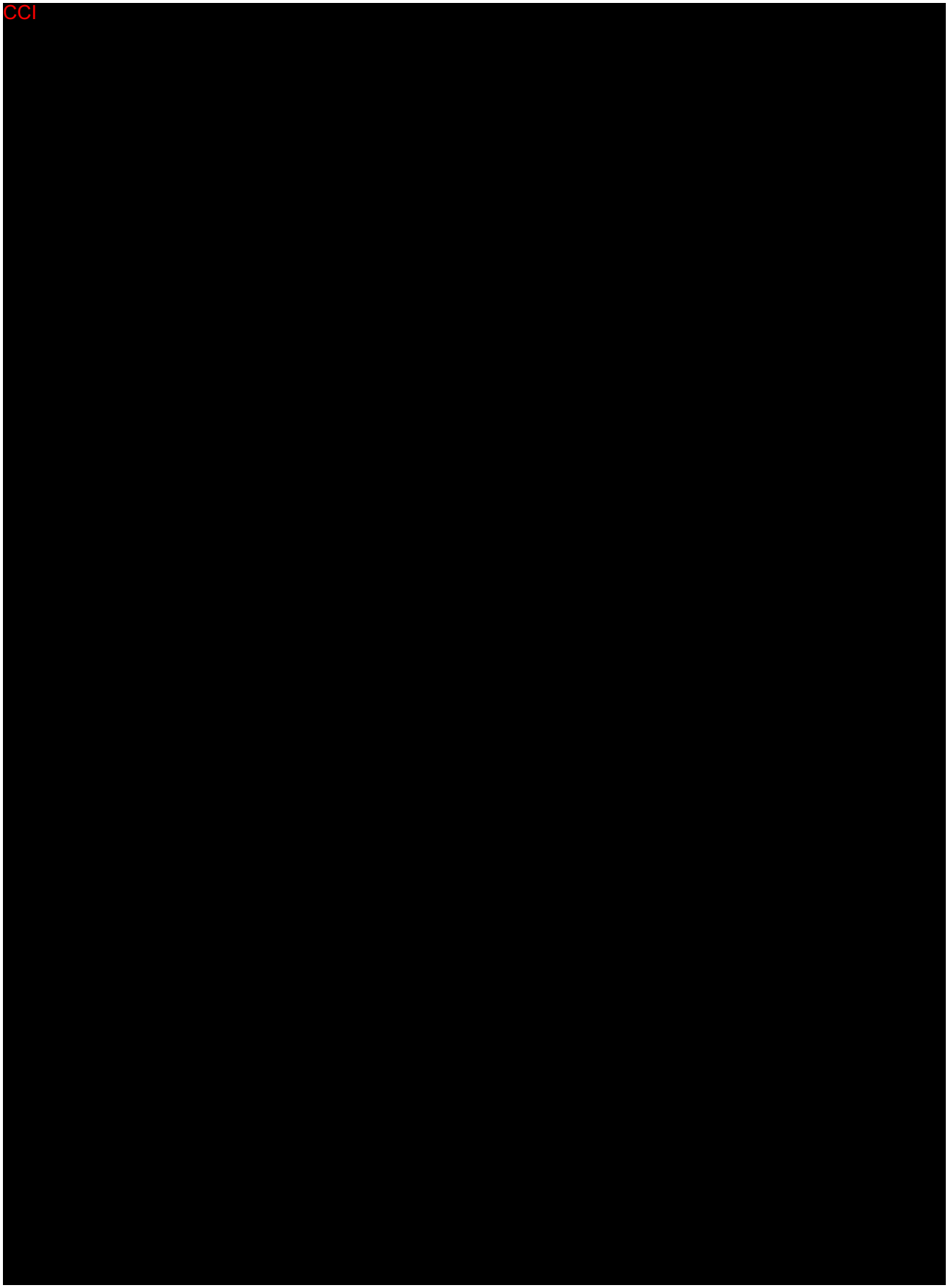

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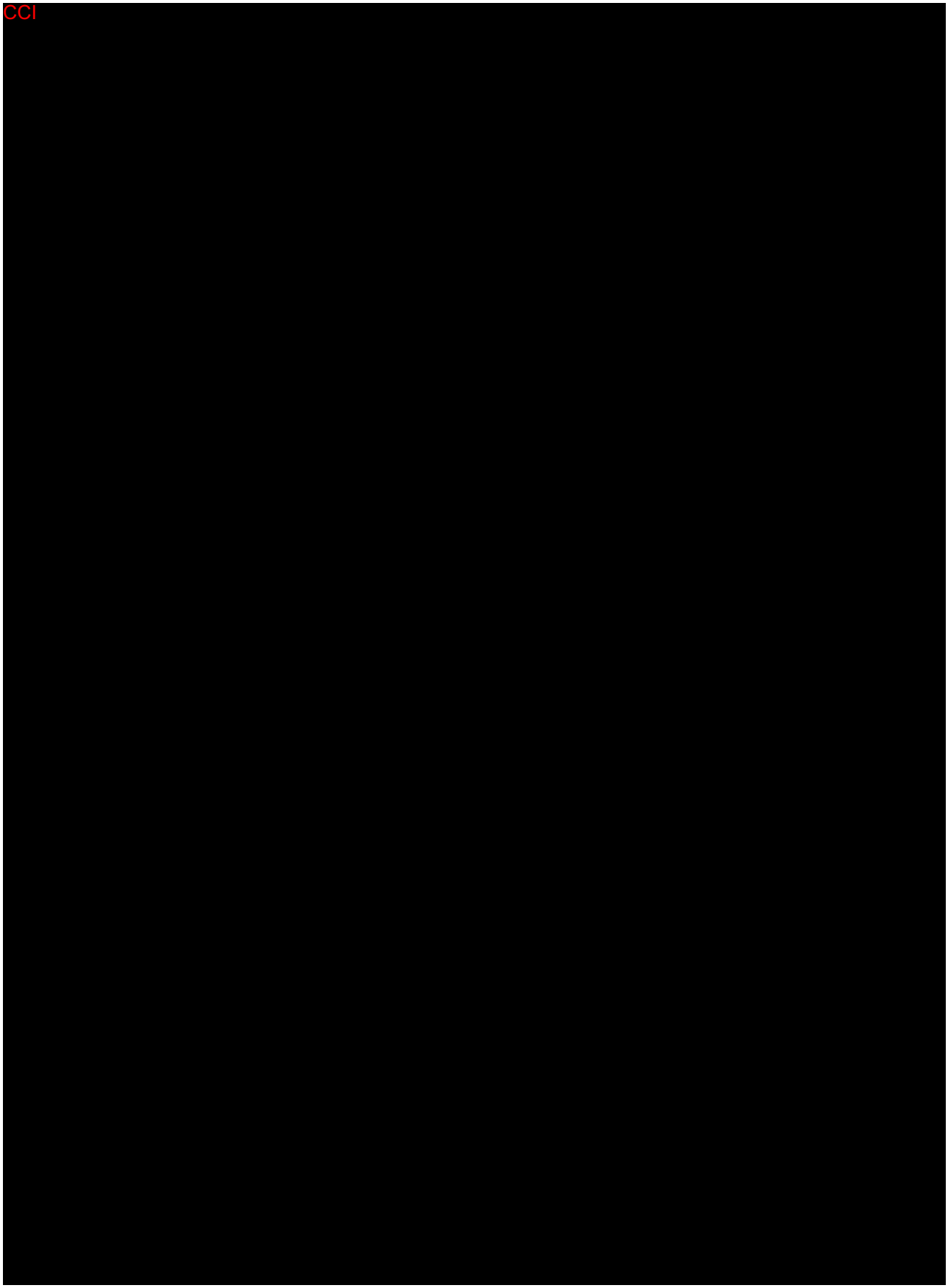
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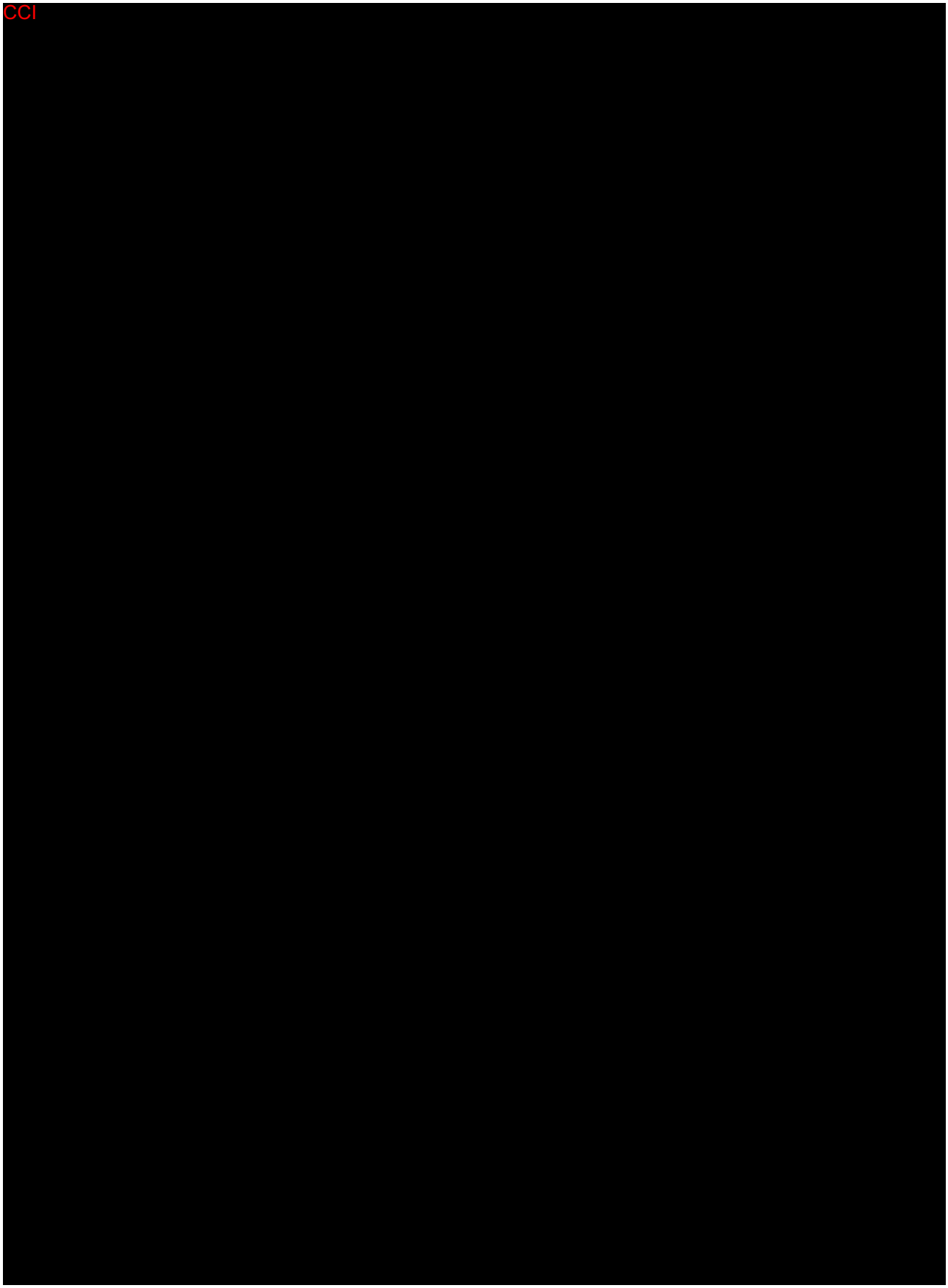


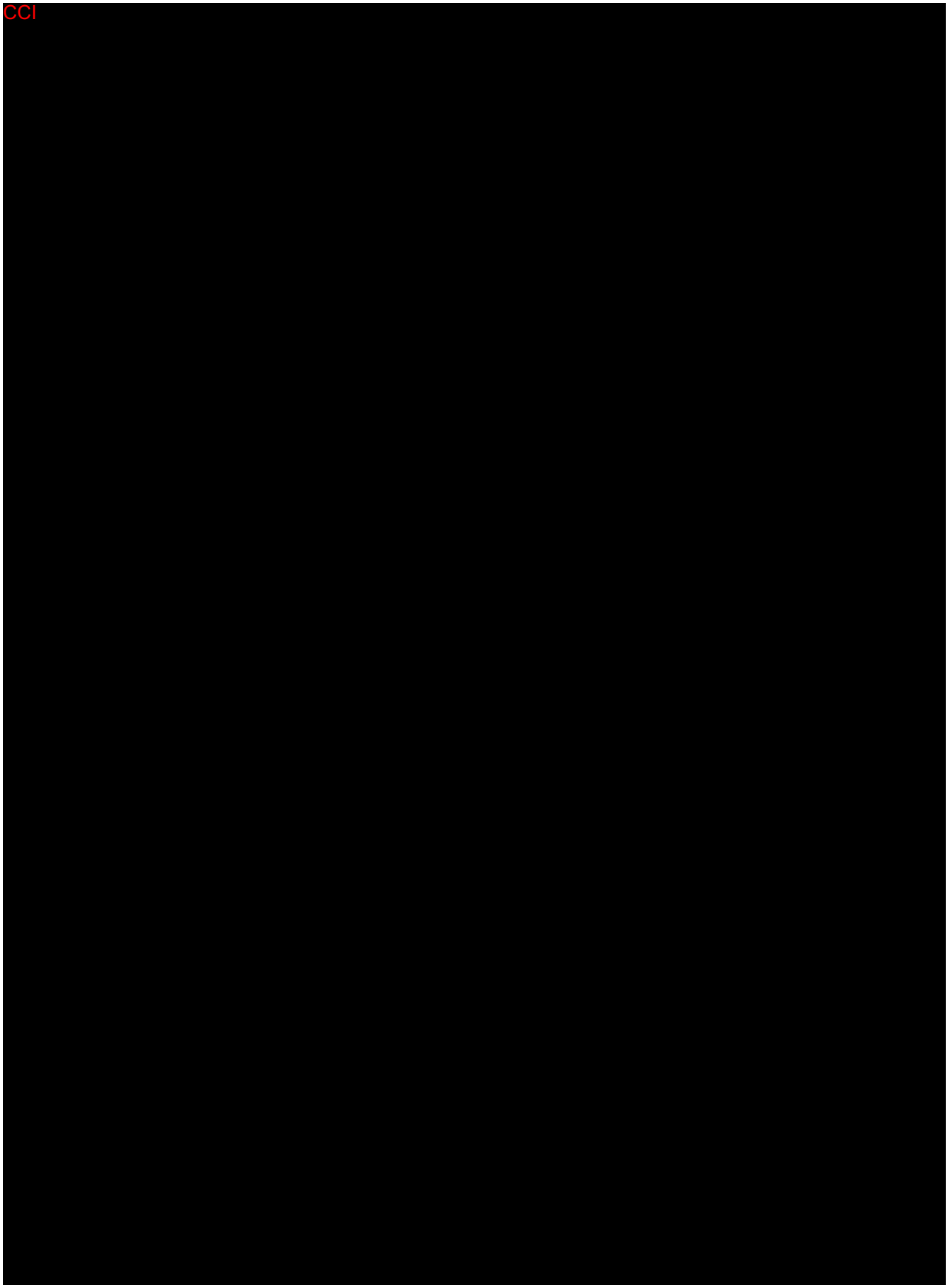

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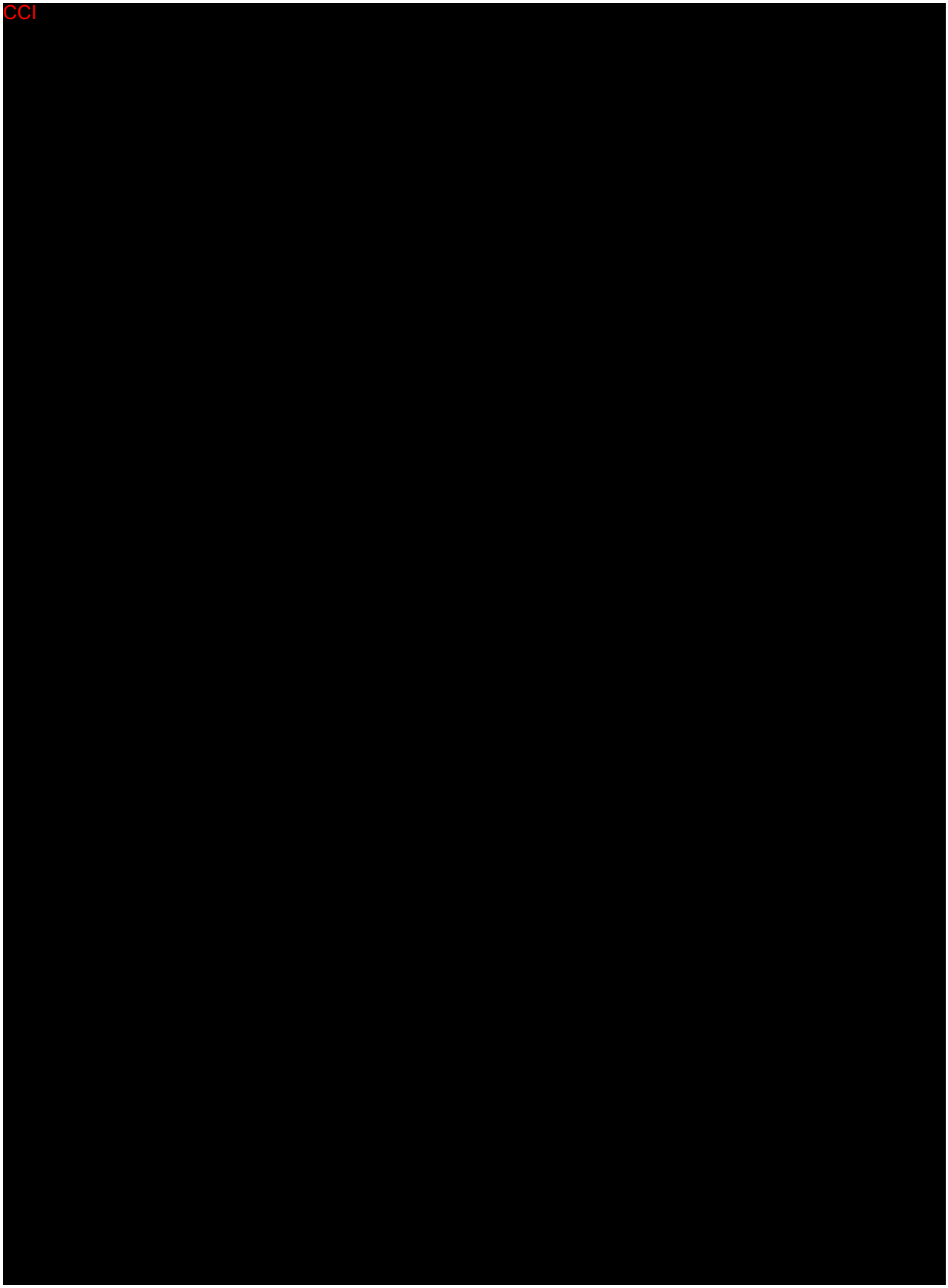



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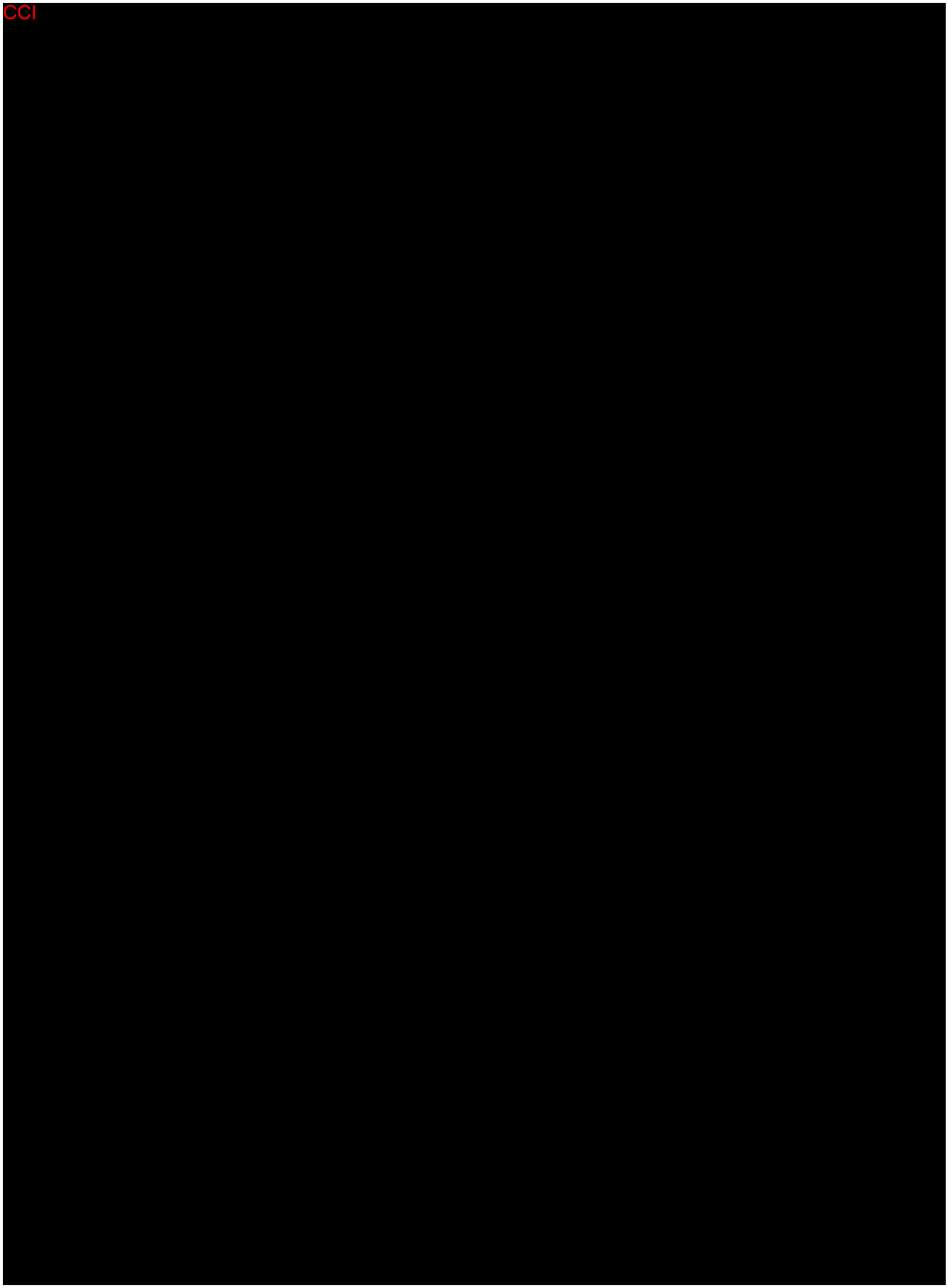
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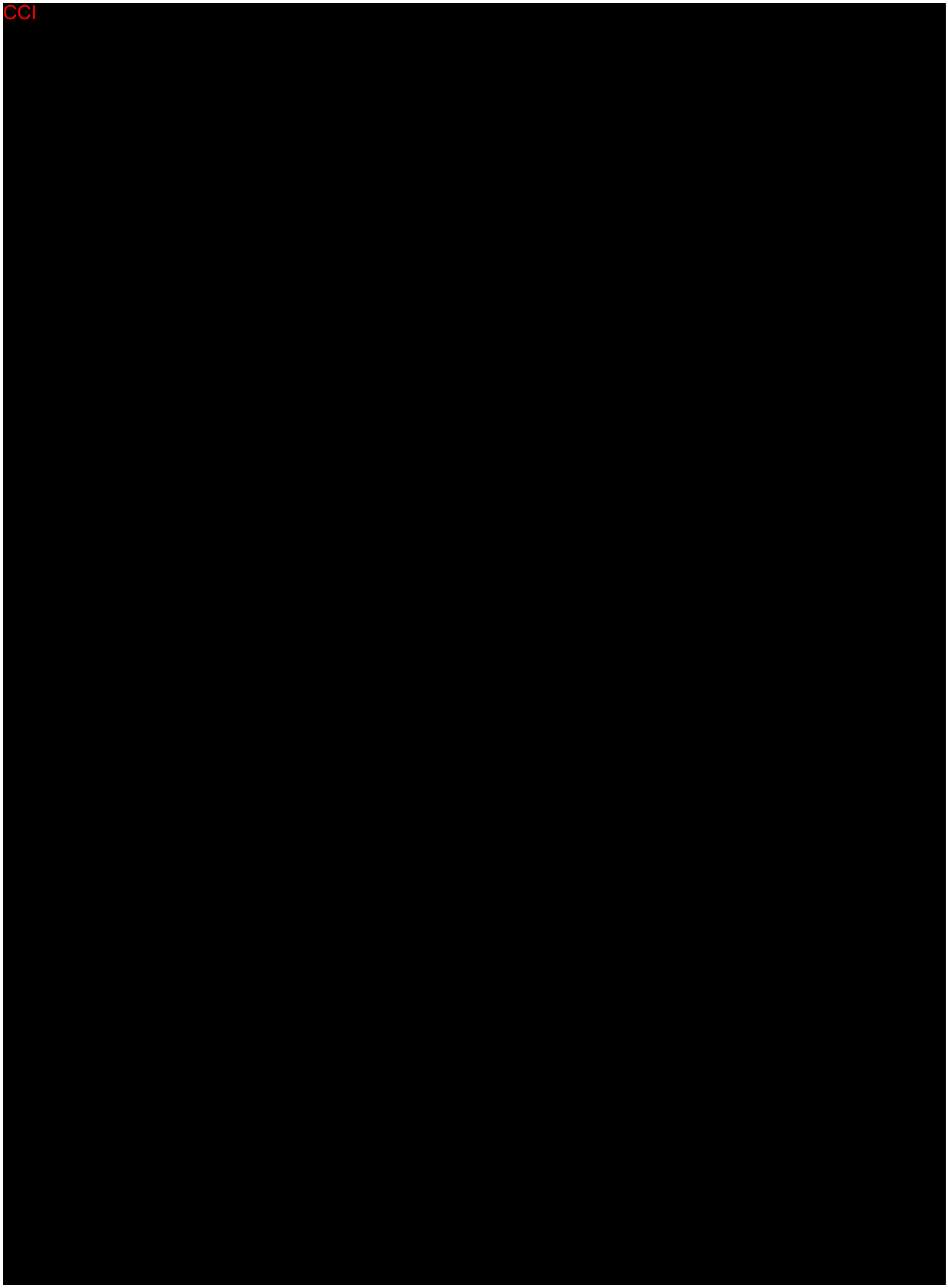


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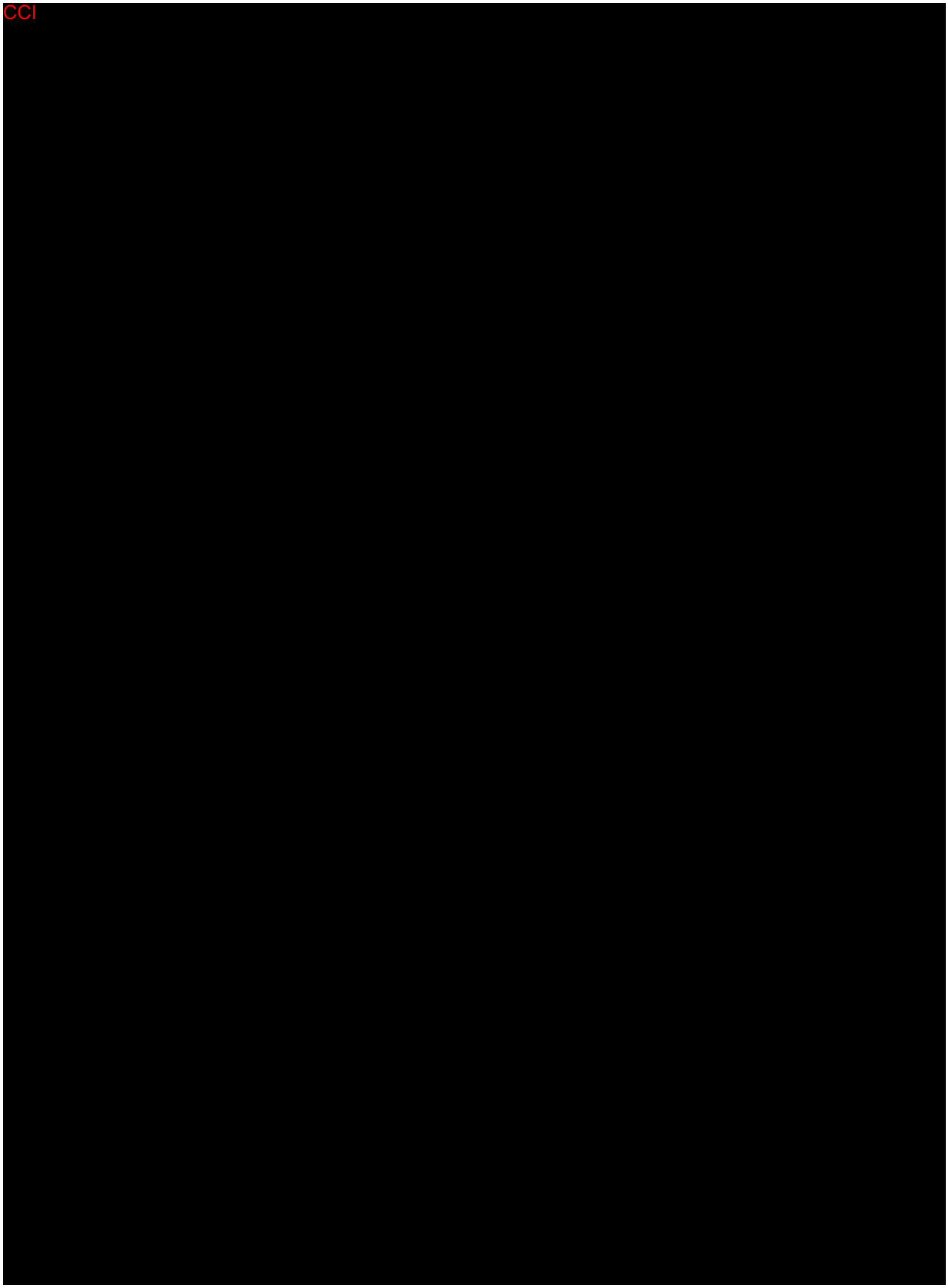
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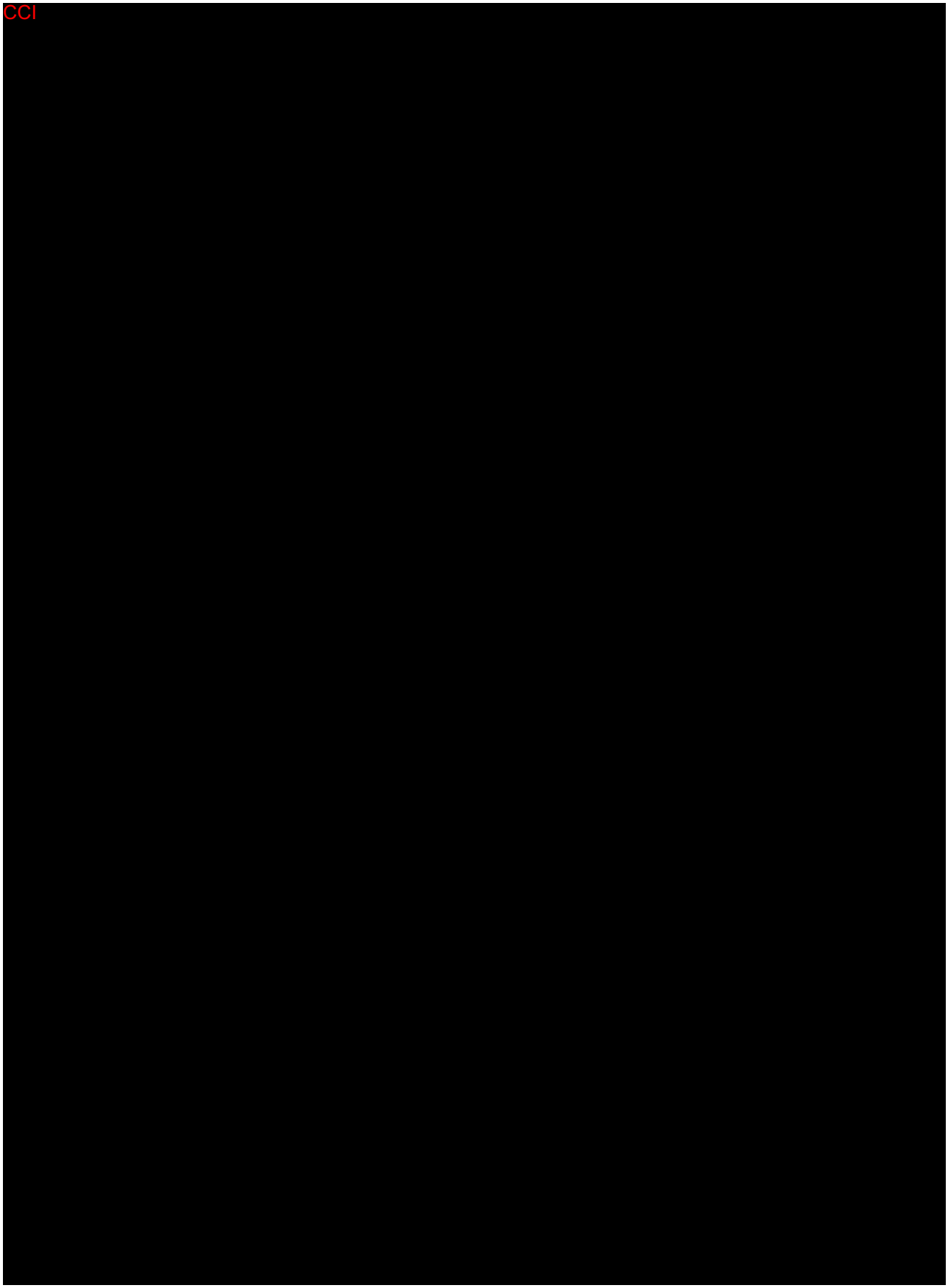
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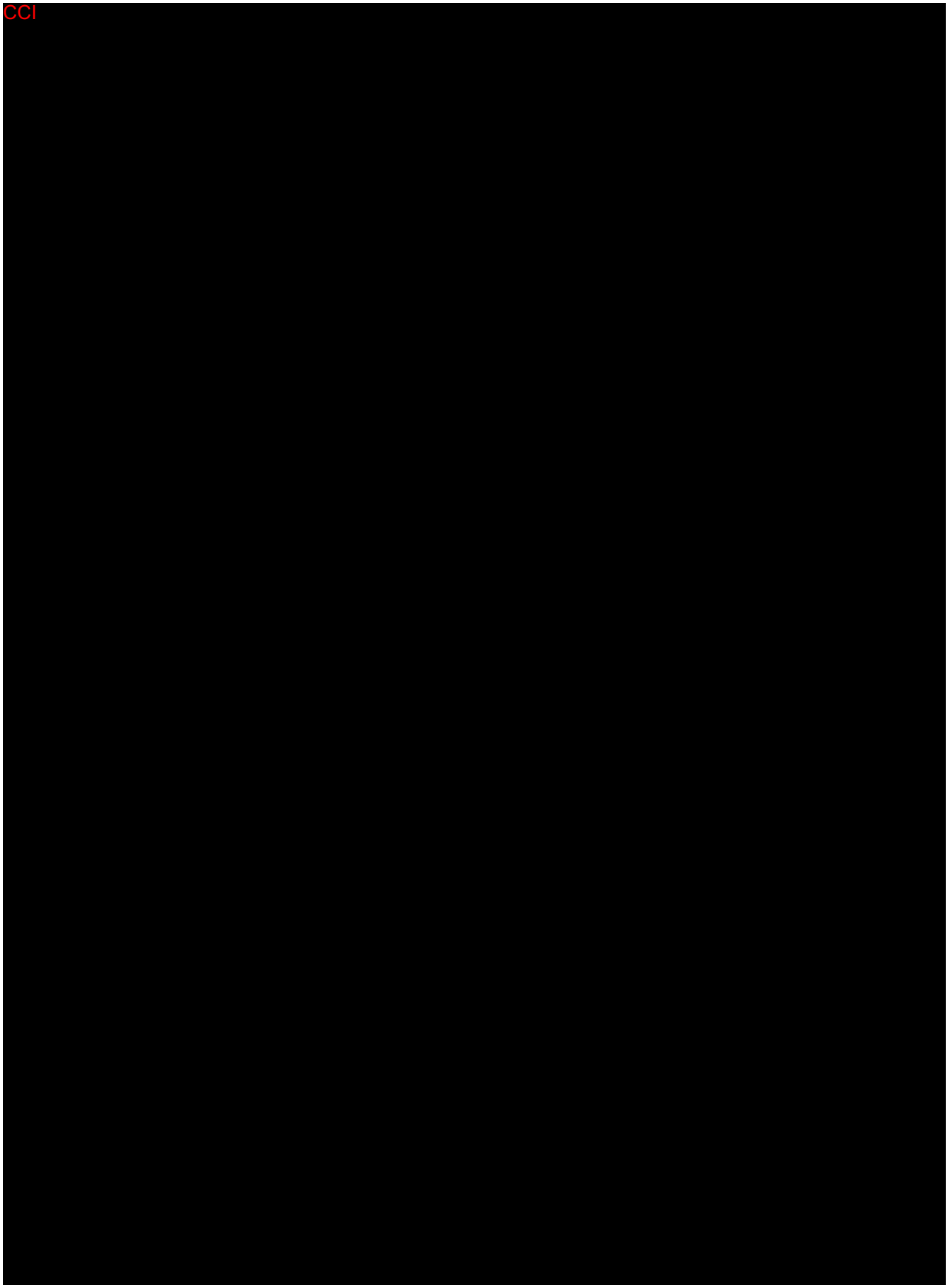

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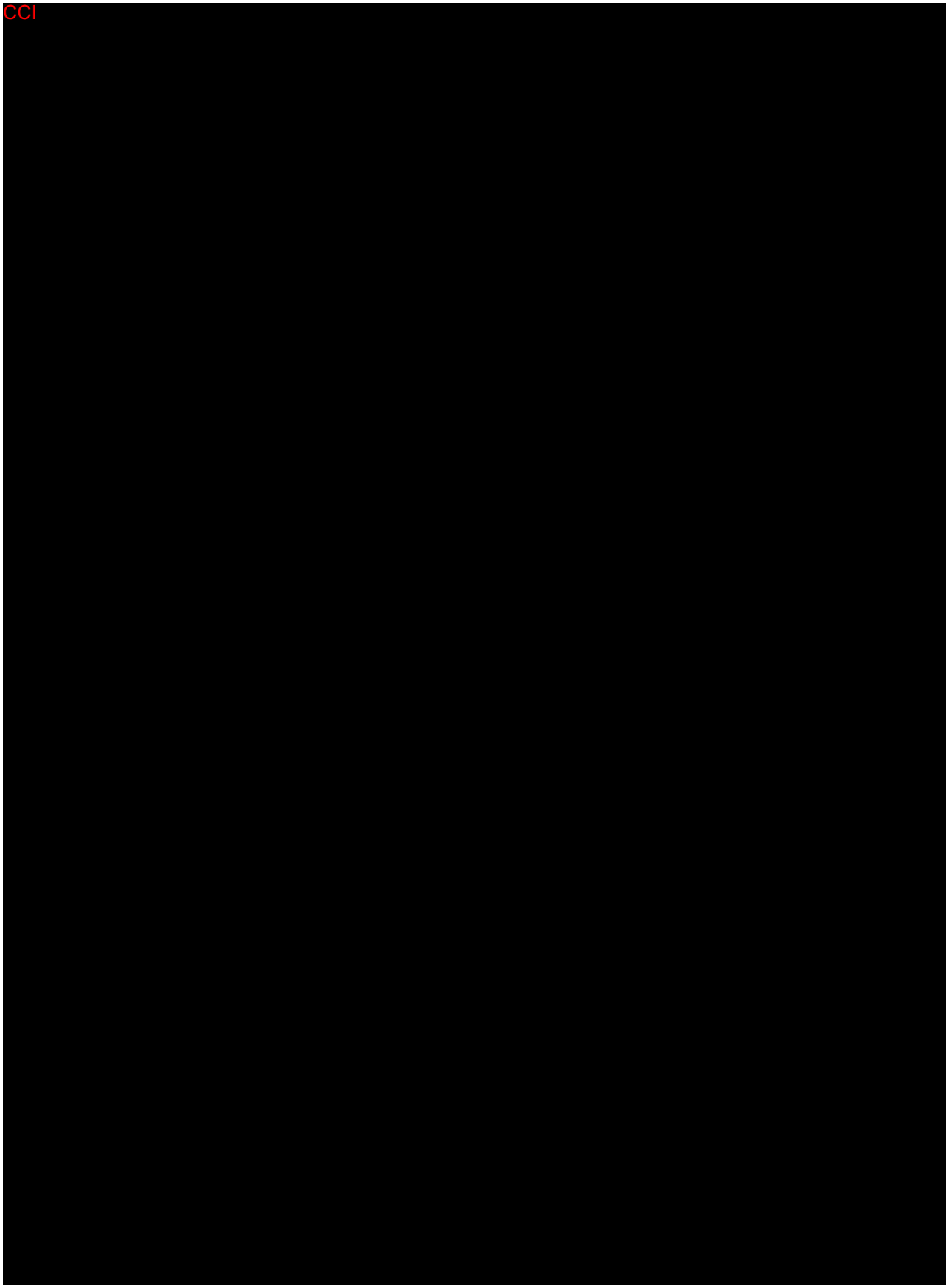
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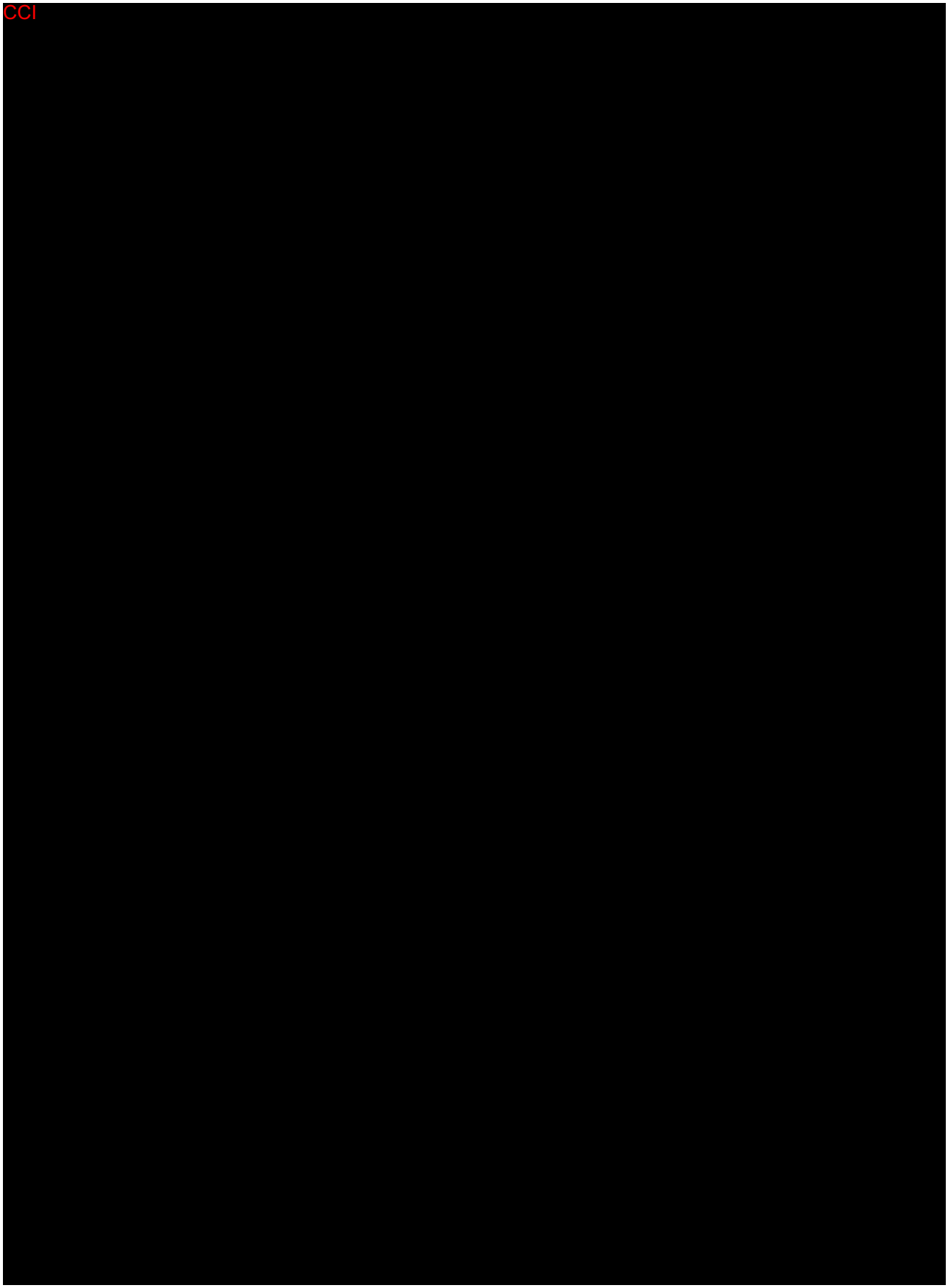


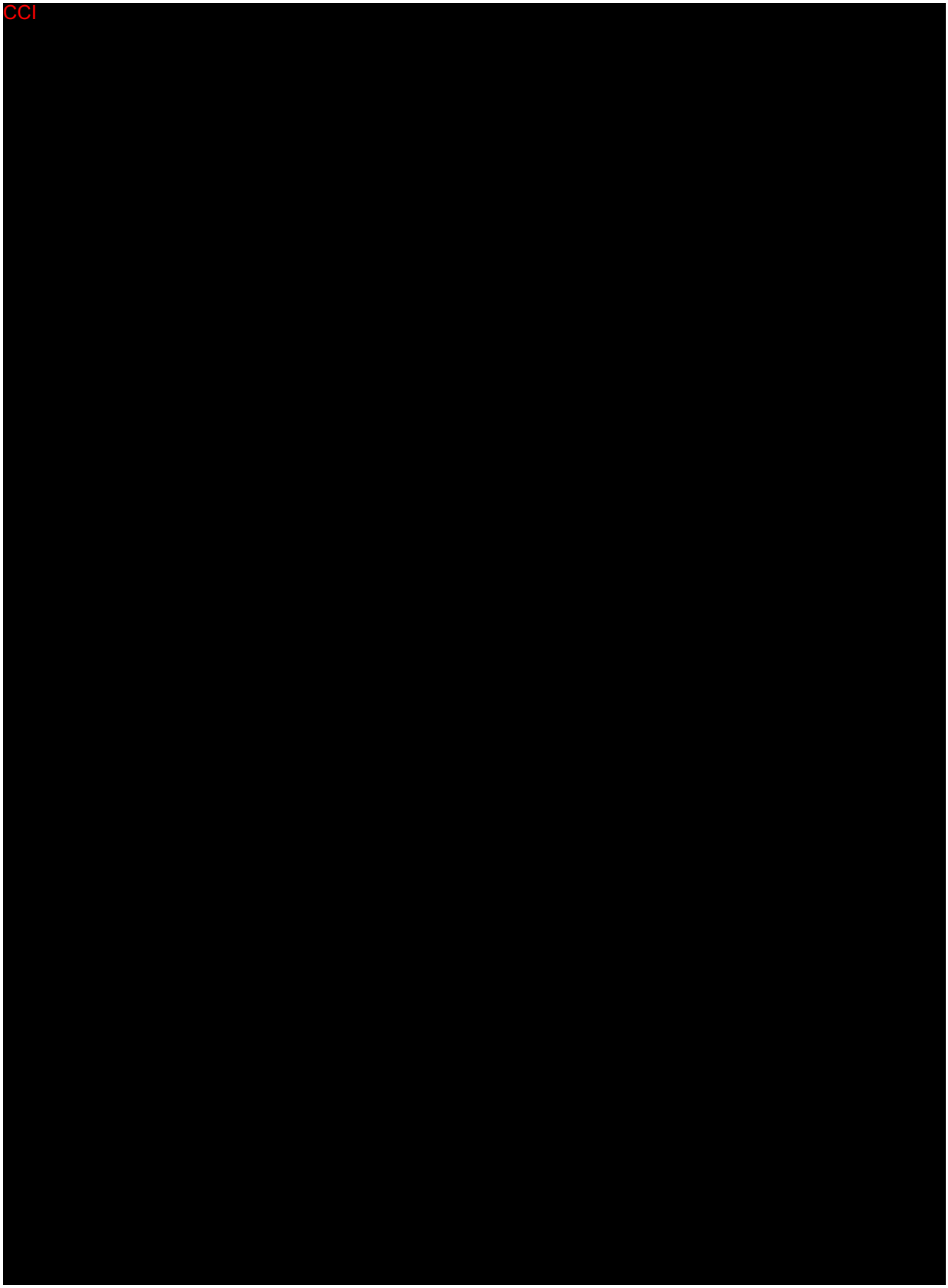

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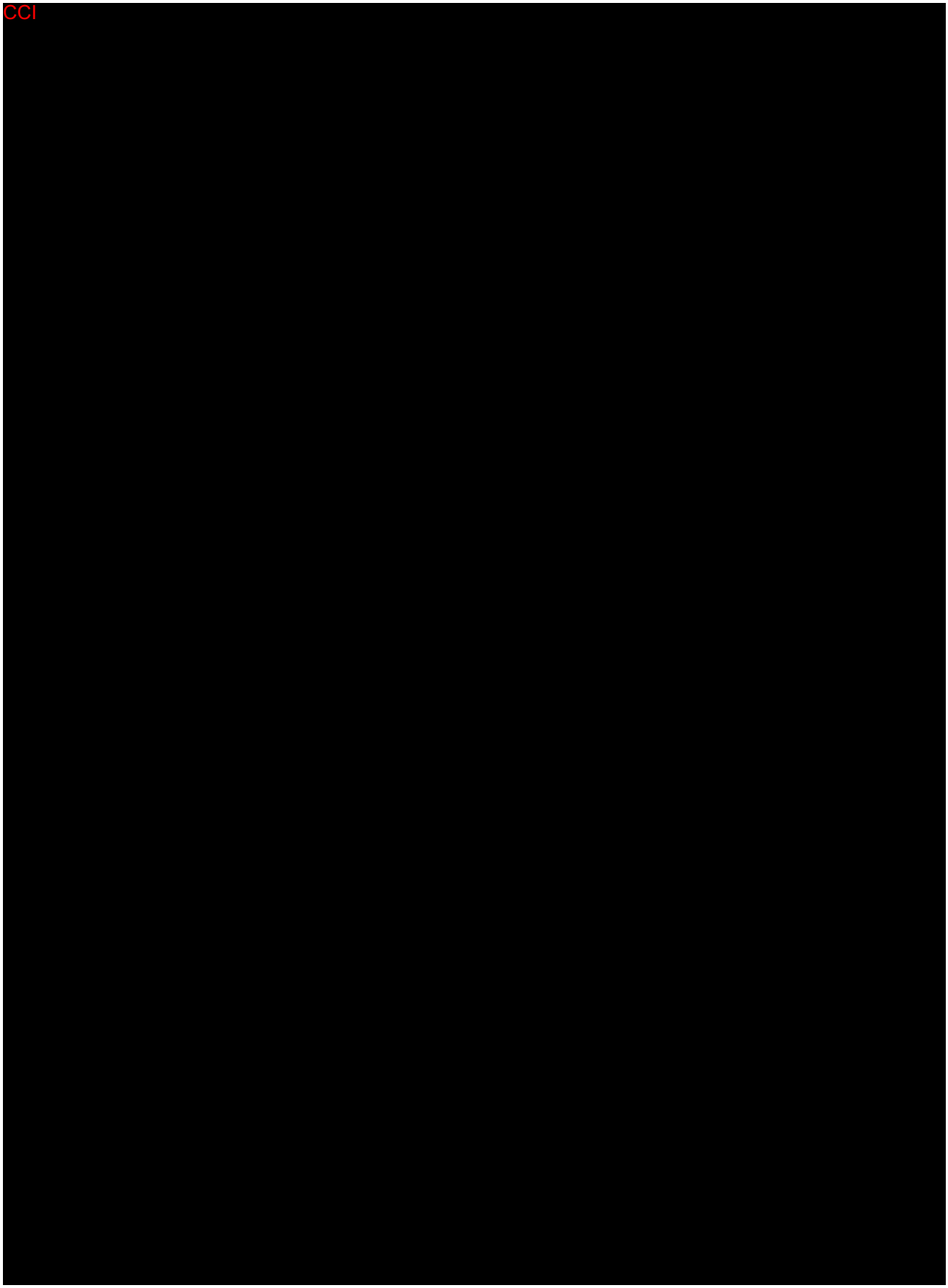

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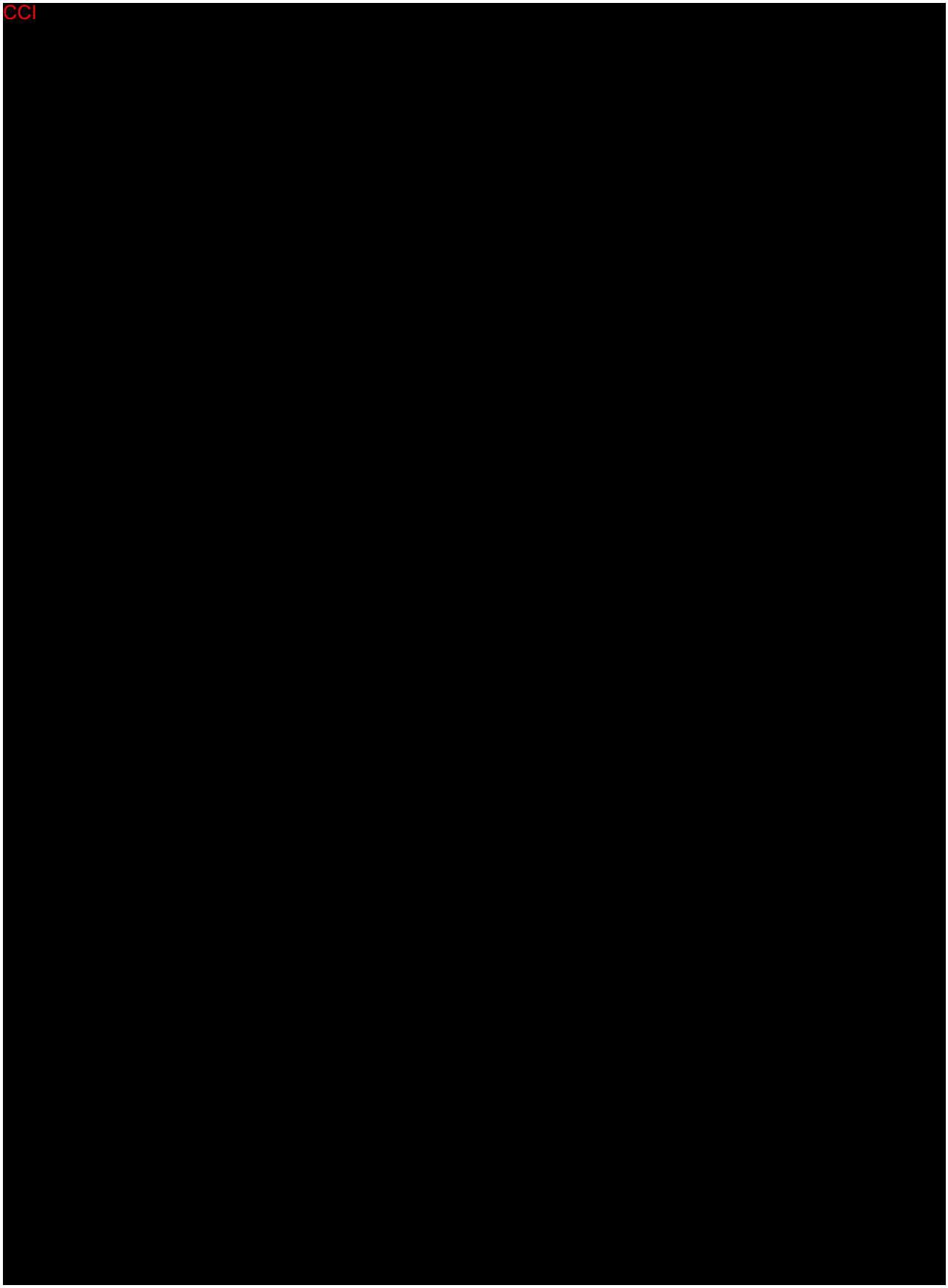
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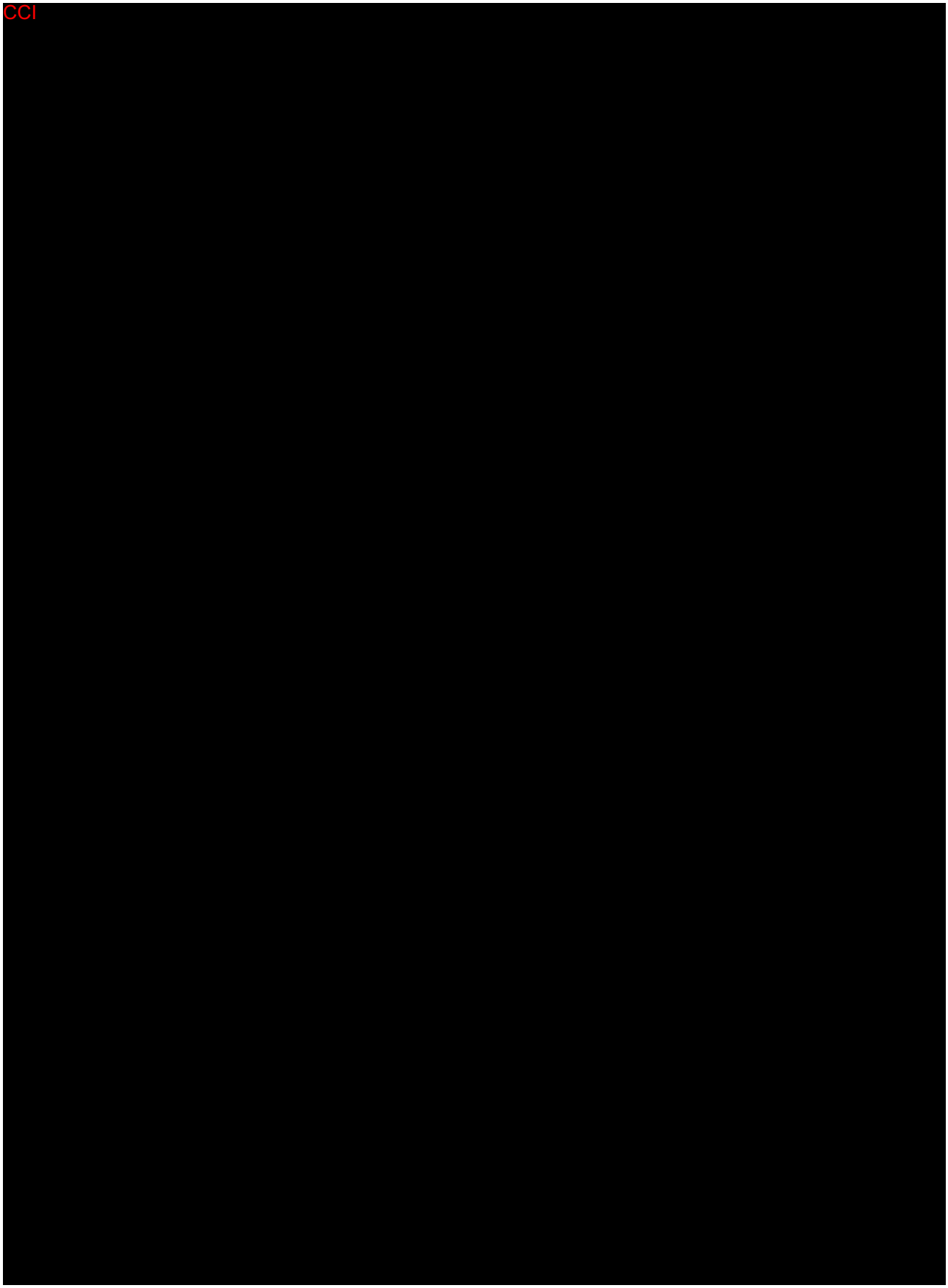


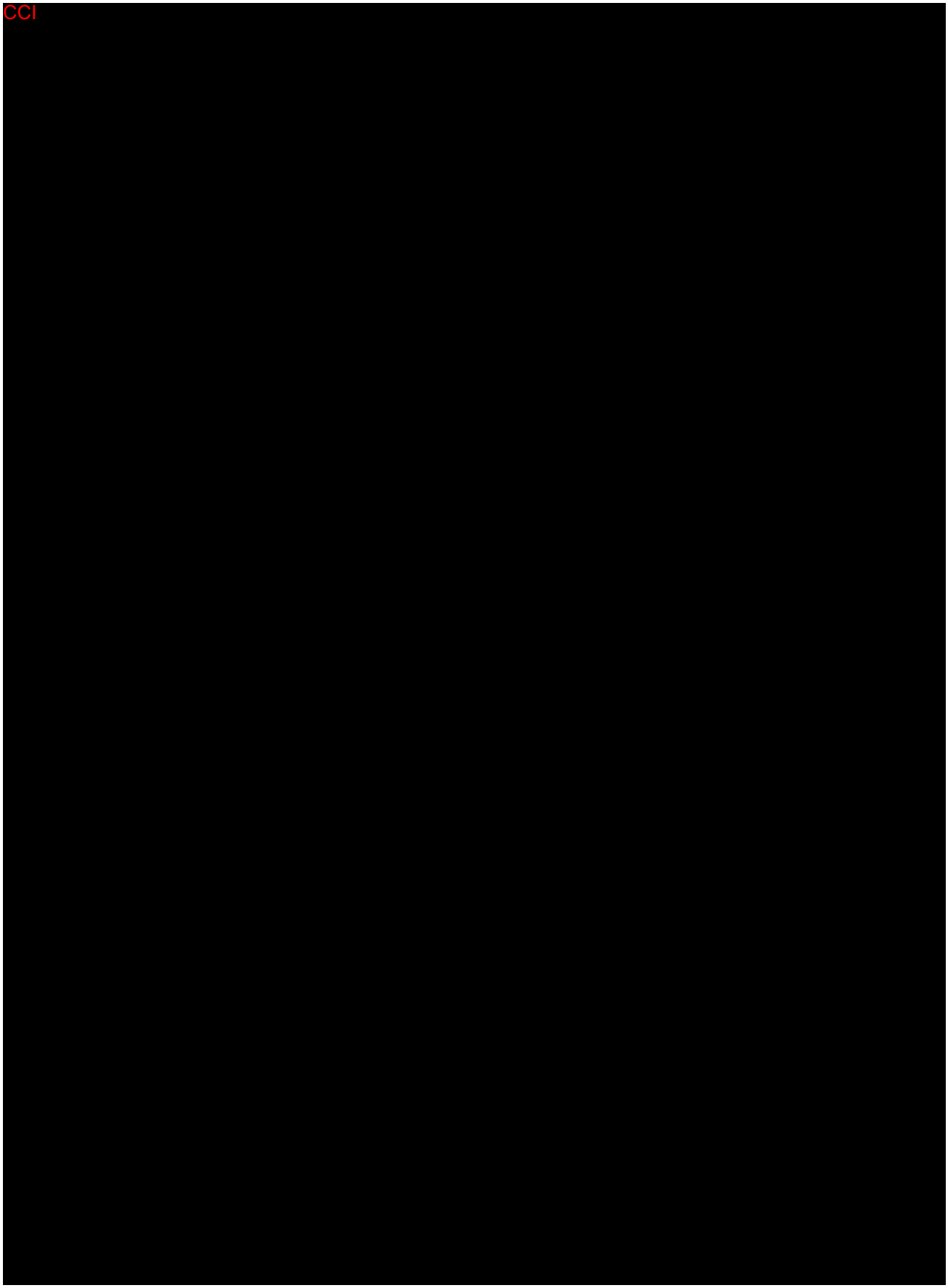

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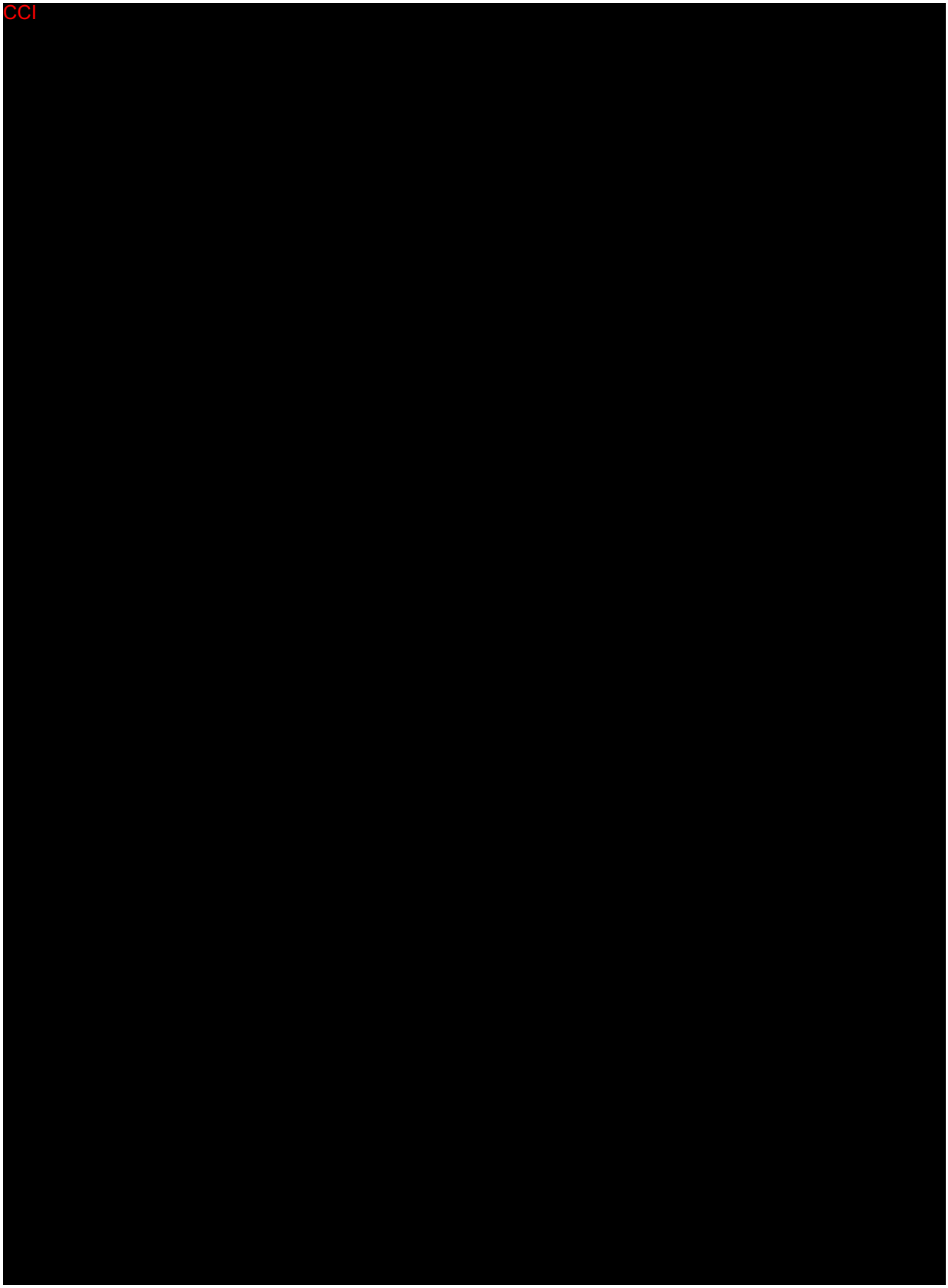

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