STATISTICAL ANALYSIS PLAN

PROTOCOL NUMBER: UBX1325-02

A Phase 2a, Prospective, Multicenter, Randomized, Double-Masked, Sham-Controlled Study to Assess the Safety, Tolerability and Evidence of Activity of a Single Intravitreal Injection of UBX1325 in Patients with Diabetic Macular Edema

PHASE 2a

Version 1.0
Date: July 22, 2022

Prepared by:

BioStat Solutions LLC
5280 Corporate Drive, Suite C200
Frederick, MD 21703
(301) 829 4001

Statistical Analysis Plan (SAP) Approval Form

Author Signature

This signature indicates that appropriate and accurate information has been included in this SAP.

Typed Name/Title	Signature	Date
Jennifer Schroeder/Senior Manager, Statistics	Jennifer Schroeder Digitally signed by Jennifer Schroeder Date: 2022.07.22 19:20:58 -04'00'	

Peer Reviewer Signature

This signature indicates that the information contained in this SAP has been reviewed and is accurate.

Typed Name/Title	Signature	Date
Joshua Rathmell/Senior Manager, Statistics	Esigned by: Joshua Rathmell 2022.07.23 11:10:29 -0400 I approve this document Joshua Rathmell Pharmalex	07/23/2022

Quality Assurance Signature

This signature indicates that the information contained in this SAP has been reviewed and is accurate.

Typed Name/Title	Signature	Date
Daniel Natividad/Quality Assurance Manager	Esigned by: Daniel Natividad 2022.07.23 20:43:16 +0800 I approve this document Daniel Natividad Pharmalex	07/23/2022

Management Signature

This signature indicates that the information contained in this SAP has been reviewed and is accurate.

Typed Name/Title	Signature	Date
Lin Li/Chief Executive Officer	Esigned by: Lin Li 2022.07.22 23:15:02 -0400 I approve this document Lin Li BioStat Solutions, LLC	07/22/2022

Unity Reviewer Signatures

This signature indicates that the information contained in this SAP has been reviewed and is accurate.

Typed Name/Title	Signature	Date
Jamie Dananberg/Chief Medical Officer	Esigned by: Jamie Dananberg 2022.07.22 14:32:07 -0700 I approve this document Jamie Dananberg Chief Medical Officer, UNITY Biotechnology	07/22/2022
Ben Xie/Senior Director, Biostatistics	Esigned by: Ben Xie 2022.07.22 14:46:29 -0700 I approve this document Ben Xie UNITY Biotechnology	07/22/2022

Revision History

Version	Date	Summary of Revision
1.0	22 July, 2022	Final Version

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List of Abbreviations

Abbreviation	Definition
AAO	American Academy of Ophthalmology
AE	Adverse event
AR	Adverse reaction
ATC4	Anatomical Therapeutic Chemical level 4
AUC	Area under the curve
BCVA	Best corrected visual acuity
BMI	Body mass index
CFBL	Change from baseline
CFP	Color fundus photography
CI	Confidence interval
CNV	Choroidal neovascularization
CST	Central Subfield Thickness
DME	Diabetic macular edema
DR	Diabetic retinopathy
DRSS	Diabetic retinopathy severity scale
ECG	Electrocardiogram
ETDRS	Early Treatment Diabetic Retinopathy Study
FA	Fluorescein angiography
Hg	Mercury
IOP	Intraocular pressure
IVT	Intravitreal
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed model for repeated measures
OCT-A	Optical coherence tomography angiography
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD-OCT	Spectral domain optical coherence tomography
SLE	Split lamp exam
SOC	System organ class
TEAE	Treatment-emergent adverse event
TFL	Tables, figures, and listings
UBX1325	Investigational product
VEGF	Vascular endothelial growth factor
WHO	World Health Organization

1. Introduction

The statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of data collected in study UBX1325-02. This SAP is based on the Protocol Version 5.0 Amendment 4 dated 14 February 2022. Specifications for tables, figures, and listings will be provided in a separate document.

1.1. Design overview

This study is a Phase 2a, proof-of-concept placebo-controlled study to assess the safety, tolerability, and evidence of activity of a single intravitreal (IVT) injection of UBX1325 for treatment of Diabetic Macular Edema (DME). Approximately 62 patients will be enrolled and randomized 1:1 into either UBX1325 or sham study arms to assess study objectives. This is a multi-site clinical trial, expected to have approximately 32 sites in the U.S. Subjects will participate for up to approximately 24 months, including start-up.

1.2. Study objectives

1.2.1 Primary objective

- Assess local and systemic safety and tolerability of UBX1325 following a single-dose IVT injection compared to sham procedure in patients with DME

1.2.2 Secondary objectives

- Assess biological activity following a single UBX1325 injection in patients with DME
- Assess efficacy parameters and retinal structure improvement of patients receiving a single IVT injection of UBX1325 compared to sham procedure

1.2.3 Exploratory objective

- Assess efficacy parameters and retinal structure improvement of patients following a single IVT injection of UBX1325 compared to sham procedure

1.3 Study endpoints

1.3.1 Primary endpoint

- Ocular and systemic safety and tolerability of a single IVT injection of UBX1325 evaluated by treatment emergent adverse events (TEAEs)

1.3.2 Secondary endpoints

- Change in Best corrected visual acuity (BCVA) from Baseline to Weeks 12, 24, and 48
- Proportion of patients who require 2 or more anti-VEGF rescue over 12, 24, and 48 Weeks
- Change in CST from Baseline to each study visit as assessed by spectral domain optical coherence tomography (SD-OCT) and read by a Reading Center
- Area under the curve (AUC) of change from baseline of CST for each study visit

- Area under the curve (AUC) of change from baseline of BCVA for each study visit
- Proportion of patients without macular fluid at Weeks 12, 24, and 48 as assessed by SD-OCT

1.3.3 Exploratory endpoints

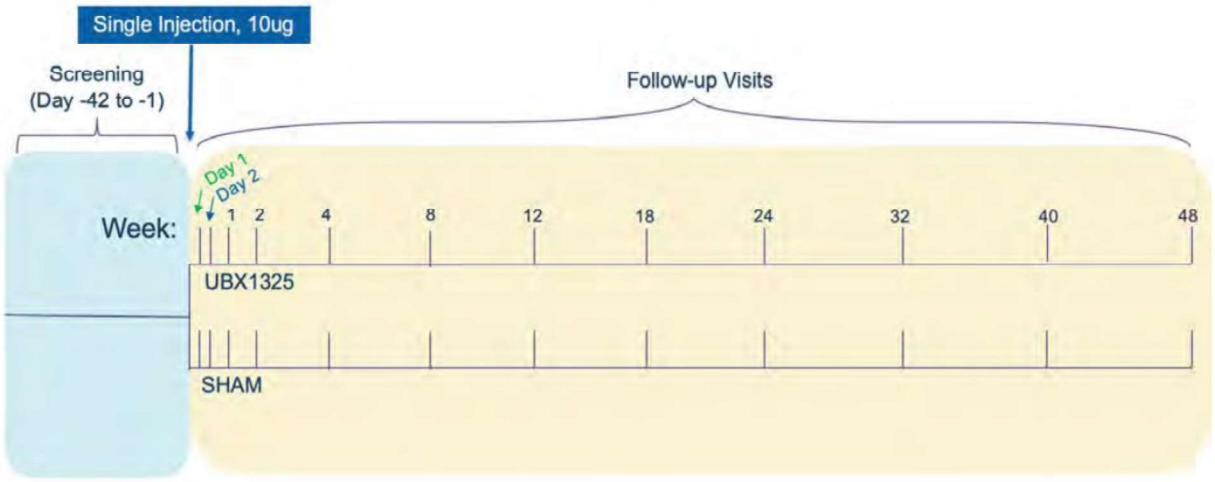
- Change from Baseline in Diabetic Retinopathy Severity Scale (DRSS) score at Weeks 24 and 48
- Change in capillary perfusion from Baseline to Weeks 12, 24, and 48 as assessed by Optical Coherence Tomography Angiography (OCT-A) and Fluorescein Angiography (FA)

2. Study Methods

2.1 Trial design

This is a Phase 2a, prospective, randomized, double-masked sham-controlled two-arm clinical trial. Patients will be randomized in a 1:1 ratio to UBX1325 or sham arm, stratified by most recent anti-VEGF treatment that patients received prior to Day 1. There will be two strata: 1) aflibercept vs 2) ranibizumab or bevacizumab. Each patient will be administered a single 50 µL UBX1325 IVT injection or sham procedure on Day 1 and be followed for up to 54 weeks (6-week screening period + 1 dose day + 24-week follow-up period + 24-week extended follow-up period). This is a multicenter trial that plans to enroll patients at approximately 32 sites in the U.S. and Canada. A study schematic is shown below (Figure 1 from the study protocol). Schedule of visits and assessments is presented in Appendix A.

Figure 1 Schematic of Phase 2a Proof-of-Concept Study



2.2 Study population

This study will enroll patients ≥18 years of age with DME and best corrected visual acuity (BCVA) between 70 to 20 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (equivalent to 20/40 to 20/400 on the Snellen chart) at Screening and at Day 1. Additionally, patients are

required to have had at least one of 3 anti-VEGF agents: aflibercept, bevacizumab or ranibizumab in the preceding 6 months prior to Day 1, with the last anti-VEGF given between 3 and 6 weeks prior to Day 1.

2.3 Randomization and masking

Randomization personnel of the Sponsor or designee will generate the randomization schedule prior to the start of the study. An interactive web response system will be used for subject randomization. All randomization information will be stored in a secured area, accessible only by authorized personnel.

This study will be double-masked, so patients and Investigators are masked to the treatment assigned, while certain roles at the site and at the Sponsor are unmasked. Sites will have a qualified injector who is unmasked in order to perform the study treatment injection or sham procedure, as well as certain post-injection assessments on Day 1 only. Specifically, the unmasked injector will do the anterior and posterior segment exams, intraocular pressure (IOP) and adverse event (AE) assessment. Other supporting activities such as study drug preparation, study drug accountability, as well as screening assessments as needed, will be performed by designated unmasked personnel. Unmasked personnel should not be involved in any other study procedures outside of those on Day 1. Subsequent visits (Day 2 and onward) should be conducted by masked staff. It is important the randomization code is not revealed to anyone in order to maintain the integrity of the double-masking.

In addition to the patients and Investigators being masked, any Sponsor or designee team members who are actively engaged with the site will be masked. There will be no planned unmasking. If there is an unplanned or unintentional unmasking, the randomization system will be used to manage the roles and permissions with respect to the ability to break the masking. The Investigator must contact the Medical Monitor to discuss any need to unmask, unless medical emergency dictates otherwise. The randomization code and records related to the unmasking will be filed as essential study documents. A patient who has unplanned or unintentional unmasking during the study will be asked to continue in the study through Week 24 for safety follow-up (AE and concomitant medication reporting, vital signs, physical examinations, and laboratory testing).

2.4 Determination of sample size

Assuming the difference of change from Baseline in BCVA between UBX1325 and sham is 8 letters, the standard deviation is 13 letters, and the drop-out rate is 5%, a sample size of 62 subjects (31 per group) would provide 80% power to detect the difference at a two-sided significance level of 0.15.

3. General Methods

3.1 General considerations

All study parameters will be listed, and a selected list of parameters will be summarized descriptively by study arm and overall. The descriptive statistics will include number of subjects, mean, standard deviation, median, minimum, and maximum for continuous parameters, and frequency and percent for categorical parameters.

The following reporting conventions will be implemented:

- All statistical tests will be conducted as 2-sided tests unless otherwise specified.
- Confidence intervals (CIs) will be presented as 2-sided 95% CIs unless otherwise specified.
- All mean and median values will be formatted to one more decimal place than the measured value. Standard deviation values will be formatted to two more decimal places than the measured value.
- All percentages will be rounded to one decimal place. The number and percentage of responses will be presented in the form xx (xx.x), where the percentage is in the parentheses. The percentage will be omitted when the numerator is zero. In the case the numerator is equal to the denominator, the percentage should be presented as (100) instead of (100.0).
- All analysis and summary tables will have the analysis population sample size (*i.e.*, number of participants) wherever applicable.

3.2. Study Day and Baseline

Study Day 1 is defined as the day UBX1325 injection or sham procedure is administered. Subsequent days are numbered consecutively (*i.e.,* Day 2, Day 3) and are calculated as: visit date - dosing date + 1. Before Day 1, study days are numbered sequentially with negative values (*i.e.,* Day -1, Day -2) and are calculated as: visit date - dosing date. There is no Day 0.

Baseline value will be the last measurement taken on or before the date of UBX1325 injection or sham procedure administration. It will be taken from the pre-dose assessment on Day 1 unless otherwise noted.

3.3 Analysis visit window

Analysis visit windowing rule will be applied to all ocular parameter data (including BCVA and CST) to choose value at each visit. The rules are described in appendix B.

3.4 Timing of analyses

Analyses to evaluate safety, tolerability, efficacy, and exploratory outcomes will utilize data from baseline through Week 48 of follow-up. The analyses of 12-week, 24-week and 48-week data will be performed.

3.5 Early termination

Patients who drop out of the study prematurely will have study data collected at the Early Termination Visit (see Appendix A). The numbers and proportions of participants who terminate study participation prematurely, by arm and overall, will be tabulated (see section 5).

3.6 Interim analysis

A formal interim analysis will be performed through Week 12 in all randomized patients. If week 12 data raise questions on durability of effect, data from week 18 and/or week 24 may be evaluated using all available data.

3.7 Multiple testing and error control

No formal adjustment for multiple comparisons is planned.

4. Analysis Populations

Full Analysis Set

The Full Analysis Set will include all randomized subjects who received a single IVT treatment of UBX1325 or sham, have a baseline BCVA assessment, and at least one post-baseline BCVA assessment. The Full Analysis Set will be the primary population for evaluating all efficacy variables. For analysis, subjects will be grouped by randomized treatment arm.

Safety Analysis Set

The Safety Analysis Set includes all patients who received a single IVT treatment of UBX1325 or sham. The Safety Analysis Set will be the primary population for evaluating all safety variables and subject characteristics. For analysis, subjects will be grouped by actual treatment received.

5. Subject Disposition

The number of patients screened, screen failed and the reasons that patients did not qualify for this study will be summarized for the study as a whole. The following data will be summarized for each treatment arm and overall, for all screened subjects:

- Randomized
- Treatment administered
- Completed study
- Did not complete study and reason
- Patients in each analysis population (Full, Safety) randomized

A protocol deviation listing will be provided that includes the start/end date of the deviation and the deviation description. A listing of subject disposition data will also be provided.

6. Demographics and Baseline Characteristics

Demographics and baseline characteristics, including medical history, prior and concomitant medications, will be summarized using the Safety Analysis Set. These data will be listed and summarized for the study overall, as well as for each treatment arm.

6.1 Demographics and baseline characteristics

Demographic and baseline characteristics include age, sex, race, ethnicity, weight, height, and other parameters as appropriate. Body Mass Index (BMI) will be calculated using the following formula: BMI (kg/m^2) = Weight(kg)/(Height(m)]^2.

6.2 Medical history

Medical history will be coded using the latest version of Medical Dictionary for Regulatory Activities (MedDRA) and summarized by system organ class (SOC) and preferred term (PT) by treatment arm and total. A patient will be counted only once for multiple events within each SOC/PT. Medical History, including a detailed ophthalmic history reported prior to dosing, will be listed by patient.

6.3 Prior and concomitant medications

Prior medication is the medication that patient stopped taking prior to screening visit. Concomitant medication is the medication that patient continued taking or took from screening visit through end of study. Prior and concomitant medications will be coded using the latest version of World Health Organization (WHO) Drug Dictionary and summarized by Anatomical Therapeutic Chemical level 4 (ATC4) and preferred term (PT) by study arm and total. A patient will be counted only once for multiple events within each ATC4 and PT. Prior and concomitant medications will be summarized in table form. Listings of prior and concomitant medications will also be provided.

7. Efficacy Analysis

7.1 Secondary endpoints

The following continuous secondary efficacy endpoints will be analyzed using mixed models for repeated measures (MMRM):

- Change in BCVA from Baseline to Weeks 12, 24, and 48
- Change in CST from Baseline to each study visit as assessed by SD-OCT and read by a Reading Center
- Area under the curve (AUC) of change from baseline of CST for each study visit
- Area under the curve (AUC) of change from baseline of BCVA for each study visit

The MMRM will be used for the primary analysis of the change from baseline in BCVA, which is based on the ETDRS VA chart assessed at a starting distance of four meters. The model will include the change from baseline at Day 2, Week 1 to Week 48 as the dependent variable, and the independent variables will include continuous BCVA baseline, categorical treatment arm

(active or sham), categorical study visit, and arm-by-visit interaction. Within-subject correlation will be modeled using subject-specific random intercepts. The model will assume a compound symmetry covariance structure. If there are convergence problems with this model, then other covariance structure may be fitted. The primary analysis will be limited to data collected prior to or on the rescue date. A supportive analysis will be performed for all data collected, regardless of rescue therapy. Subjects who violated major inclusion or exclusion criteria will be excluded from the primary and supportive analyses.

When BCVA outliers occur, a sensitivity analysis excluding the outliers will be performed. If deemed appropriate, other sensitivity analyses may also be considered to assess the impact of outliers.

The change from baseline in CST, as assessed by SD-OCT and read by a Reading Center, AUC of change from baseline in BCVA and CST, will be analyzed using MMRM, same as the analysis of BCVA.

The following binary secondary efficacy endpoints will be summarized:

- Proportion of patients who require 2 or more, or 1 or more anti-VEGF rescue over 12, 24, and 48 Weeks
- Proportion of patients without macular fluid at Weeks 12, 24, and 48 as assessed by SD-OCT

Proportion of patients who require 2 or more, or 1 or more anti-VEGF rescue over 12, 24, and 48 Weeks will be summarized for each treatment group. Confidence intervals of difference in proportions between treatment groups will be calculated using an exact method (Chan and Zhang, 1999) implemented in the SAS procedure Freq. Criteria for rescue therapy are worsening of CST by 75 µm relative to Baseline and/or a 10-letter decrease in BCVA compared to peak BCVA from Baseline. Patients who meet rescue criteria can be rescued with anti-VEGF treatment. Rescued patients will continue with study visits per protocol. Proportion of patients without macular fluid at Weeks 12, 24, and 48 as assessed by SD-OCT will be analyzed using same method.

BCVA and SD-OCT data will be listed.

7.2 Exploratory endpoints

Exploratory endpoints include

- Change from Baseline in Diabetic Retinopathy Severity Scale (DRSS) score at Weeks 24 and 48
- Change in capillary perfusion from Baseline to Weeks 12, 24, and 48 as assessed by Optical Coherence Tomography Angiography (OCT-A) and Fluorescein Angiography (FA)

Change from Baseline in DRSS score will be presented as the proportion of patients with a $\geq$ 2-step improvement in diabetic retinopathy (DR) severity from baseline on the ETDRS DRSS at Weeks 24 and 48. The proportion of patients with a $\geq$ 2-step improvement in diabetic retinopathy

(DR) severity from baseline will be analyzed using the analysis method following those for the binary secondary efficacy endpoints.

For change in capillary perfusion from Baseline to Weeks 12, 24, and 48, the analysis method will follow those for the continuous secondary efficacy endpoints.

Key parameters of OCT-A and FA will be summarized, and all OCT-A, FA and CFP data will be listed.

7.3 Subgroup Analyses

The following subgroups will be analyzed with respect to two secondary efficacy endpoints: change in BCVA from Baseline to Weeks 12, 24, and 48, and change in CST from Baseline to each study visit.

- Baseline BCVA (≤60 letters and >60 letters)
- Baseline CST (≤400 µm and >400 µm)
- Baseline DR severity (<47, ≥47 DRSS score)
- Baseline HbA1c (≤7% and >7%)

The analysis method will be the same as specified above for each respective endpoint. The subgroup categories may be adjusted if there is not enough representation of a specific subpopulation or treatment group. Additional analysis of BCVA and CST with the subgroup as covariate may be performed if clinically significant subgroup difference is observed in the subgroup analysis.

8. Safety Analysis

8.1 Adverse events

Ocular and systemic safety and tolerability of a single IVT injection of UBX1325 will be evaluated by treatment-emergent adverse events (TEAEs). A TEAE is an adverse event that occurs after the initiation of the study treatment (*i.e.,* the onset date is the same as or after Day 1), or an adverse event with onset prior to the study treatment that worsens in severity or becomes serious after the initiation of the study treatment. Summary tables will include only TEAEs, and listings will include all adverse events reported in the clinical database.

The following summaries of TEAE data will be performed by study arm and overall:

- Overall summary of TEAEs
- TEAEs by SOC, PT, and severity
- Ocular TEAEs in the study eye by PT
- Treatment-related ocular TEAEs in the study eye by PT, severity
- Treatment-emergent serious adverse events by PT

Overall summary of TEAEs will include the number and percentage of patients experiencing at least one TEAE, related TEAE, grade >=3 TEAE, serious TEAE, and TEAE leading to death.

For summaries by SOC and PT, a patient will only be counted once for each PT and once for the overall count for a SOC. However, patients may be included in more than one PT category within a SOC. For summaries which also include severity, a patient who experiences the same event more than once will have the event with the worst severity counted in the summary. Summaries by SOC and PT will be presented by SOC alphabetically then by descending frequency of PT within SOC based on the overall column.

8.2 Intraocular Pressure

Intraocular Pressure (IOP) will be measured using Goldmann applanation tonometry or equivalent tonometer in both eyes at all scheduled visits. Tonometry should be performed prior to pupillary dilation or as per site's standard procedures. IOP will be summarized for each eye by visit and by dose using descriptive statistics. The number and percentage of patients with the following at any post-baseline visit will also be summarized:
Change from baseline in IOP by visit and treatment group

- IOP ≥ 25, ≥30 and ≥35 mmHg
- IOP increase from baseline ≥ 10 mmHg
- IOP increase from baseline ≥ 20 mmHg

Intraocular pressure data will be listed for both eyes at each visit.

8.3 Laboratory data

Laboratory safety parameters are measures of hematology and serum chemistry. These measures will be obtained at Screening, Weeks 24 and 48, and ET (if applicable). Actual values and CFBL will be summarized for each treatment arm, and a 95% confidence interval will be calculated for the mean CFBL for each treatment arm. Shift tables of the changes from baseline to Week 24/ET and Week 48/ET will also be presented.

Analysis visit windowing rules will be applied to laboratory data before analysis, according to the rules described in appendix B.

8.4 Electrocardiogram (ECG)

ECG will be performed at Screening, Weeks 24 and 48, and ET (if applicable). ECG results (normal / abnormal) will be summarized for each treatment arm.

8.5 Vital signs

Vital signs will be taken at all study visits. Actual values and CFBL for each vital signs parameter will be summarized for each treatment arm.

8.6 Physical examinations

A complete physical examination will be performed at Screening, Weeks 24 and 48, and ET (if applicable). The physical examination data will be listed.

9. Quality Assurance

9.1 Software and programming specifications

All statistical programs written to generate TFLs and perform statistical analyses will use either SAS version 9.4 or higher, or R version 4.0 or higher. Every statistical program will be developed and validated for correctness according to the four-stage process outlined in the BSSI Control and Execution of Statistical Analysis Programming SOP (SOP-OP-010).

9.2 File management and data security

Data and program files will be managed according to BSSI SOP-OP-002, Folder and File Structure Management. Electronic file security and integrity will be protected by procedures outlined in BSSI SOP-IT-002, Data Security.

10. Changes in the Statistical Analysis Plan from the Protocol Analysis Plan

The definition of the Full Analysis Set has changed from the protocol to be based on BCVA instead of CST. The area under the curve (AUC) of change from baseline of BCVA for each study visit has been added as a secondary efficacy endpoint.

11. References

AAO PPP DME Guidelines (2019) available at https://www.aaojournal.org/article/S0161-6420(19)32092-5/pdf

Bandello F, Battaglio Parodi M, Lanzetta P, Loewenstein A, Massin P, Menchini F, Veritti D (2017) Diabetic Macular Edema. *Developments in Ophthalmology*, 102-138.

Chan, I. S. F., and Zhang, Z. (1999). Test-Based Exact Confidence Intervals for the Difference of Two Binomial Proportions. *Biometrics* 55:1202–1209.

Coney JM. (2019) Addressing unmet needs in diabetic retinopathy. *American Journal of Managed Care* 25:S0.

12. Appendices

12.1 Appendix A – Schedule of Events (Protocol Table 1)

Table 1 Schedule of Events

Test/Procedure	Screening Day -42 to Day -1	Visit 1 Week 0 Day 1	Visit 2 24 ± 4 hours Observation[a] Day 2	Visit 3 Week 1 Day 8 ±1	Visit 4 Week 2 Day 15 ±2	Visit 5 Week 4 Day 29 ±7	Visit 6 Week 8 Day 57 ±7	Visit 7 Week 12 Day 85 ±7	Visit 8 Week 18 Day 127 ±7	Visit 9 Week 24 Day 169 ±7
Informed Consent	X									
Demographics	X									
Medical/ Ophthalmic History	X	X	X	X	X	X	X	X	X	X
Medication History/ Concomitant Medications	X	X	X	X	X	X	X	X	X	X
Physical Examination	X									X
Vital Signs and Weight	X[b]	X	X	X	X	X	X	X	X	X
Laboratory Tests: Hematology and Chemistry	X									X
Pregnancy Test	X (serum)	X (urine)[c]								X (urine)[c]
12-Lead ECG	X									X
BCVA	X	X	X	X	X	X	X	X	X	X
Anterior Segment Evaluation	X	X[d]	X	X	X	X	X	X		X
Posterior Segment Evaluation	X	X[d]	X	X	X	X	X	X		X
IOP	X	X[d]	X	X	X	X	X	X		X
SD-OCT[e]	X	X		X	X	X	X	X	X	X
OCT-A[e]	X							X		X
FA[e]	X					X		X		X

Test/Procedure	Screening Day -42 to Day -1	Visit 1 Week 0 Day 1	Visit 2 24 ± 4 hours Observation[a] Day 2	Visit 3 Week 1 Day 8 ±1	Visit 4 Week 2 Day 15 ±2	Visit 5 Week 4 Day 29 ±7	Visit 6 Week 8 Day 57 ±7	Visit 7 Week 12 Day 85 ±7	Visit 8 Week 18 Day 127 ±7	Visit 9 Week 24 Day 169 ±7
CFP[e]	X							X		X
DRSS score	X							X		X
Eligibility Criteria	X	X								
Study Drug Administration[g]		X								
AE assessment		X	X	X	X	X	X	X	X	X

Table 1 Schedule of Events (Continued)

Test/Procedure	Visit 10 Week 32 Day 225 ± 7	Visit 11 Week 40 Day 281 ± 7	Visit 12 Week 48 Day 337 ± 7	Unscheduled Visit/ET
Medical/Ophthalmic History	X	X	X	X
Medication History/Concomitant Medications	X	X	X	X
Physical Examination			X	X
Vital Signs and Weight	X	X	X	X
Laboratory Tests: Hematology and Chemistry			X	X
Pregnancy Test			X (urine)	
12-Lead ECG			X	X
BCVA	X	X	X	X
Anterior Segment Evaluation	X	X	X	X
Posterior Segment Evaluation	X	X	X	X
IOP	X	X	X	X
SD-OCT	X	X	X	X
OCT-A			X	X
FA			X	X[f]
CFP			X	X
DRSS score			X	X
AE assessment	X	X	X	X

AE = adverse event; BCVA = best corrected visual acuity; CFP = color fundus photography; DRSS = diabetic retinopathy severity scores; ECG = electrocardiogram; ET = early termination; FA = fluorescein angiography; IOP = intraocular pressure; OCT-A = optical coherence tomography angiography; SD-OCT = spectral domain optical coherence tomography; rescue treatment administered if needed

[a] Procedures to be performed at the end of the ~24 hours (± 4 hours) of observation.

[b] Height should also be measured at Screening.

[c] Pre-dose urine dipstick for females of childbearing potential. Urine dipstick should also be done at the last study visit, Visit 9 Week 24.

[d] Procedure to be performed both pre-dose and post-dose. Post-dose procedures will be done in the study eye only by the unmasked injector, 30 minutes ± 15 minutes post dose.

[e] CFP, FA, SD-OCT, and OCT-A images should be transmitted to the Central Reading Center at each applicable visit. Screening images should be transmitted to Central Reading Center for eligibility verification. OCT-A to be conducted at sites with the proper equipment available.

[f] To be completed only if assessment has not been performed within the preceding 30 days.

[g] After all other study procedures have been completed. Optional post-injection prophylactic antibiotics may be administered. Sites should follow their standard practice and document all medication given.

12.2 Appendix B – Analysis Visit Windowing Rules

To address unscheduled and early termination visits, analysis visit windowing rules will be applied to ocular parameters, laboratory, and vital sign data. Within each window defined below, a single visit will be chosen as the analysis visit (for each eye for ocular parameters and for each subject for other parameters). Note that the assignment of the baseline visit is handled by a separate algorithm for this study, not by the visit windowing rules.

Table B.1: Analysis Windows for ocular and vital sign parameters

Planned Visit Day	Lower Limit	Upper Limit	Visit	Visit Number
	-200	-1	Screening	0
1	1	1	Visit 1 (Baseline)	1
2	2	4	Visit 2	2
8	5	11	Visit 3	3
15	12	22	Visit 4	4
29	23	42	Visit 5	5
57	43	70	Visit 6	6
85	71	105	Visit 7	7
127	106	147	Visit 8	8
169	148	196	Visit 9	9
225	197	252	Visit 10	10
281	253	308	Visit 11	11
337	309	519	Visit 12	12

Table B.2: Analysis Windows for laboratory parameters (other than urine pregnancy test, which is day 1 only)

Planned Visit Day	Lower Limit	Upper Limit	Visit	Visit Number
	-200	-1	Screening	0
169	1	252	Visit 9	9
253	309	519	Visit 12	12

Rules

1. If there is one visit in a window, assign that visit to be the analysis visit.
2. If there is more than one visit in a window, then calculate the absolute difference (in days) from the planned visit day to each visit.
    - If a single visit has the smallest absolute difference, then assign that visit as the analysis visit.
    - If multiple visits are tied for the smallest absolute difference, then do the following:
        - If there is a single planned visit, set it to be the analysis visit.
        - Else if there are multiple planned visits in a tie, take the latest visit as the analysis visit.
            - Exception: take the day 1 pre-dose visit instead of the post-dose visit, if applicable.
        - Else if there are no planned visits (*i.e.*, only unscheduled or early termination), then take the latest visit.