SAMSUNG BIOEPIS

Clinical Study Protocol

# An open-label, single group, single-dose clinical study to evaluate the usability of the pre-filled syringe (PFS) of SB11 in subjects with Neovascular Age-Related Macular Degeneration (AMD) or Macular Oedema Secondary to Retinal Vein Occlusion (RVO)

| | |
|---|---|
| **Product** | SB11 (proposed ranibizumab biosimilar) |
| **EudraCT Number** | 2021-003566-12 |
| **US IND Number (if applicable)** | NA |
| **Protocol Number** | SB11-2001 |
| **Study Phase** | II |
| **Version and Effective Date** | Version 1.0 Jul 05, 2021 |
| **Sponsor** | Samsung Bioepis Co., Ltd.<br>76, Songdogyoyuk-ro, Yeonsu-gu,<br>Incheon, 21987<br>Republic of Korea |

# SYNOPSIS

| | | |
|---|---|---|
| **Name of Sponsor/Company:** | Samsung Bioepis Co., Ltd. | |
| **Name of Finished Product:** | SB11 (proposed ranibizumab biosimilar) | |
| **Name of Active Ingredient:** | Ranibizumab | |
| **Title of Study:** An open-label, single group, single-dose clinical study to evaluate the usability of the pre-filled syringe (PFS) of SB11 in subjects with Neovascular Age-Related Macular Degeneration (AMD) or Macular Oedema Secondary to Retinal Vein Occlusion (RVO) | | |
| **Protocol No:** | SB11-2001 | **Phase:** II |

**Planned Study Period:**

Approximately 7 days (except screening period)
Screening period will be up to 14 days.

**Objectives:**

Primary objective

To assess the ability of Healthcare Professionals (HCPs) to follow the instructions for use (IFU) to prepare and administer SB11 PFS intravitreal (ITV) injection to subjects

Secondary objective

To evaluate the safety of SB11 PFS in subjects with neovascular AMD or macular oedema secondary to RVO

**Study Design:**

This is an open-label, single group, single-dose clinical study to evaluate the usability of the PFS of SB11 in patients with neovascular AMD or macular oedema secondary to RVO. HCPs will prepare and administer ITV injections of SB11 0.5 mg delivered via PFS to subjects (1 injection to each subject) on Day 1 (baseline), and safety follow-up will be assessed until Day 7.

**Number of Subjects:**

Approximately 30 subjects will participate in the study.

**Target Population:**

Patients with neovascular AMD or macula oedema secondary to RVO

**Main Eligibility Criteria:**

Only one eye will be selected as the study eye. For subjects who meet eligibility criteria in both eyes, study eye is selected at the discretion of the Investigator.

Inclusion criteria

Subjects must meet all of the following criteria to be eligible for the study:

1. Neovascular AMD or macular oedema secondary to RVO in the study eye
2. Study eye deemed to be indicated for ranibizumab ITV therapy at the discretion of the ophthalmologist (e.g., retina specialist)
3. Aged 18 years and older at the time of signing the informed consent form (ICF)
4. Written ICF must be obtained from the subject prior to any study-related procedure (if the subject cannot read ICF, an impartial witness will be present during the entire informed consent discussion)

5. Willingness and ability to undertake all scheduled visits and assessments
6. Non-childbearing potential female (e.g., permanently sterilized, postmenopausal [defined as 12 months with no menses without an alternative medical cause prior to Screening]), OR Childbearing potential female subjects or male subjects with their (respectively male or female) partners who agree to use at least 2 forms of appropriate contraception method (e.g., established use of oral, injected, intravaginal, transdermal or implanted hormonal contraceptive, placement of an intrauterine device or intrauterine hormone-releasing system, bilateral tubal occlusion, vasectomized partner or physical barrier [Note: Female condom and male condom should not be used together]) or 1 highly effective contraception method (e.g., sexual abstinence) from Screening until 3 months after the ITV injection of investigational product (IP) to achieve a failure rate of less than 1% per year. Vasectomy will be allowed for male subjects and female subjects of childbearing potential with a sole vasectomised male partner. Vasectomised subjects or partners should be medically confirmed for sterilisation. True abstinence alone will be allowed if this is in line with the preferred and usual lifestyle of the subject, or for subjects who do not have a partner. Periodic abstinence (e.g., calendar, ovulation, symptothermal post-ovulation methods) and withdrawal are not acceptable methods of contraception. Contraceptive methods do not apply for subjects whose partner is on the same gender.

Exclusion criteria

Subjects meeting any of the following criteria are not eligible for the study:

1. Best Corrected Visual Acuity (BCVA) of the level of Finger Count or worse [i.e., 0 letter reading using Early Treatment Diabetic Retinopathy Study (ETDRS) chart] in one or both eyes at Screening or at Day 1
2. History of and/or current intraocular inflammation (any grading from trace and greater is excluded), including non-infectious uveitis, infectious uveitis, or scleritis, or history of sterile inflammatory reaction after the past ITV injections with any agent in either eye
3. Active or suspected infectious disease, or active disorder that preclude safe use of IP at the discretion of the Investigator, in either eye or adnexa of either eye at Screening or at Day 1
4. History of excessive bleeding and recurrent haemorrhages, including any prior excessive intraocular bleeding or haemorrhages after ITV injection or intraocular procedures in either eye
5. History of massive subconjunctival haemorrhages of concern reported by the subject after an ITV injection in either eye
6. Uncontrolled intraocular pressure (IOP) greater than (≥) 25 mmHg in the study eye at Screening or at Day 1
7. Treatment with any ITV injection within the 30 days prior to Day 1 in the study eye
8. History of treatment with ITV injection of brolucizumab (approved or investigational) in either eye
9. Any invasive ocular surgery including retinal detachment surgery, long-acting ocular therapeutic agent/implant including corticosteroid, or ocular drug release device implant (approved or investigational) in the study eye within 90 days prior to Day 1 or planned intraocular surgery within next 28 days after Day 1
10. Ocular laser surgery in study eye at any time within the past 30 days prior to Day 1
11. Treatment with any ocular IP in either eye within 90 days prior to Day 1
12. Treatment with systemic anti-Vascular Endothelial Growth Factor (anti-VEGF) within 180 days prior to Day 1
13. Receipt of any systemic (non-ocular) IP within 180 days prior to Day 1
14. Use of therapies that are known to be toxic to ocular tissue within the 180 days prior to Day 1, including, but not limited to, deferoxamine, chloroquine/hydroxychloroquine, tamoxifen, phenothiazines, vigabatrin, or ethambutol

15. Current systemic coagulation or bleeding disorders, or history of recurrent haemorrhages
16. Known ocular or non-ocular conditions that per the ophthalmologist (e.g., retina specialist) represent a contraindication to ranibizumab use in the patient or may represent an unwarranted patient risk
17. Uncontrolled hypertension (defined as systolic blood pressure >160 mmHg and/or diastolic blood pressure >100 mmHg while sitting confirmed after repeated measurement) at Screening or Day 1
18. Current systemic infectious disease or therapy for active infectious disease
19. History of hypersensitivity to the active substance or any of the excipients
20. Known history of intolerance, reaction, or anti-drug antibody (ADA) formation to prior biological therapies
21. Pregnant or lactating women at Screening or at Day 1
22. Have had a positive test result for Coronavirus disease 2019 (COVID-19) within 8 weeks prior to ICF-signed date, or any suggestive sign and/or symptom of COVID-19 (e.g., fever, dry cough, dyspnoea, sore throat, or fatigue) at Screening or at Day 1. Subjects will adhere to local/national requirements (e.g., testing, isolation) for reduction of the public Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

**Investigational Products:**

- Name: SB11 (proposed ranibizumab biosimilar)
- Formulation: SB11 0.5 mg (1 ml contains 10 mg ranibizumab)
- Route of administration: ITV injection via PFS
- Dose regimen: 1 injection to each subject via PFS at Day 1

**Main Criteria for Evaluation**

Primary Endpoint

- Percentage of successful task completions (Day 1)

**Table 1. Task to be Evaluated in the Usability Study**

| Sequence | Task | Critical Task | Essential Task |
|---|---|---|---|
| 1 | Open the carton | - | O |
| 2 | Remove contents | - | O |
| 3 | Peel the lid off the blister pack | - | O |
| 4 | Carefully remove the PFS from the blister using aseptic technique | - | O |
| 5 | Remove the syringe cap | - | O |
| 6 | Attach a needle | O | - |
| 7 | Remove the needle cap | O | - |
| 8 | Set the dose | O | - |
| 9 | Insert the needle into the injection site | O | - |
| 10 | Press the plunger down to inject the medication | O | - |
| 11 | Remove the needle from the injection site | - | O |
| 12 | Dispose product | O | - |

Secondary Endpoints

- Percentage of successful completion on critical tasks (Day 1)

| |
|---|
| • Percentage of successful completion on essential tasks (Day 1)<br><br>Safety Endpoint<br><br>• Incidence of adverse events (AEs) and serious adverse events (SAEs) from Day 1 to Day 7 |
| **Statistical Methods**<br><br>No formal statistical analysis will be performed. All endpoints will be summarized descriptively with appropriate statistics. |

# GRAPHICAL STUDY DESIGN AND SCHEDULE OF ACTIVITIES

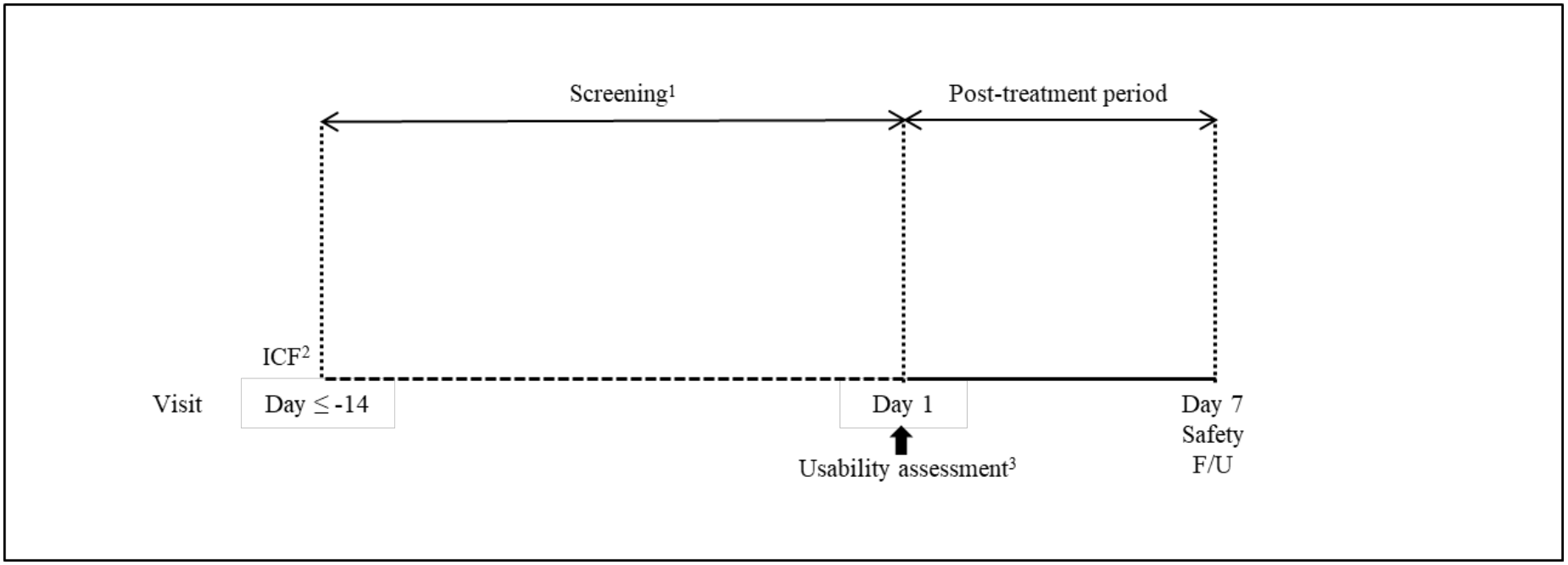


**Figure 1. Graphical Study Design**

F/U = Follow-up; ICF = Informed Consent Form; Post-treatment period = safety follow-up period after IP administration; ⬆ = Investigational Product (IP) administration

[1] Screening must be done within 14 days prior to IP administration. Screening and Day 1 visits can be performed on the same day.

[2] Informed consent should be obtained prior to any study-related procedures.

[3] Healthcare Professionals will prepare and administer intravitreal injection of SB11 via pre-filled syringe (PFS). Usability of the PFS will be assessed on the same day of treatment.

**Table 2. Schedule of Activities**

| **Procedures** | **Study Period** | | |
|---|---|---|---|
| **Period** | **Screening[1]** | **Open Label Treatment[1]** | **Post-Treatment Follow up /EOS/ET** |
| **D: Day (± visit window)** | **D-14 to D-1** | **D1** | **D7 (+2)** |
| **V: Visit** | **V1** | **V2 (Baseline)** | **V3** |
| **Screening/Baseline** | | | |
| Written informed consent[3] | X | | |
| Inclusion/exclusion criteria[4] | X | X[2] | |
| Demographic data[5] | X | | |
| Medical/Surgical history | X | | |
| Physical examination | X | | |
| Pregnancy test[6] | X | (X)[2] | (X) |
| Vital signs | X | X[2] | X |
| **Ophthalmic Examination** | | | |
| BCVA examination[7] | X | X[2] | X |
| Slit lamp examination[8] | X | X[2] | X |
| IOP[9] (pre- and post-dose) | X | X[2] | X |
| Indirect ophthalmoscopy[10] (pre- and post-dose) | X | X[2] | X |
| OCT[11] | X | X[2] | X |
| **Treatment** | | | |
| IP administration[12] | | X | |
| **Usability Assessment** | | | |
| Assessment of task completion[13] | | X | |
| **Safety assessment** | | | |
| AE monitoring[14] | Continuously | | |
| Prior or concomitant medication or therapy[15] | Continuously | | |

AE = Adverse event; BCVA = Best Corrected Visual Acuity; EOS = End of Study; ET = Early Termination; IOP = Intraocular pressure, IP = Investigational product; OCT = Optical Coherence Tomography

1. Screening and Day 1 visits can be performed on the same day.
2. If Screening and Day 1 visits are performed on the same day, the procedures (e.g., ophthalmic examinations) which should be performed both at Screening and Day 1 will be performed once.
3. Written informed consent must be obtained from the subject prior to any study-related procedures.
4. All subjects' eligibility must be confirmed by Investigator.
5. Demographic data will include year of birth, gender, race, and ethnicity.
6. **For women of childbearing potential**, pregnancy (serum or urine) test must be performed at Screening. If necessary, additional pregnancy test (serum or urine) can be performed at the Investigator's discretion during the study period [e.g., Day 1 or Day 7 (EOS visit)]. All pregnancies must be followed up until 6-8 weeks after the outcome of the pregnancy becomes available.
7. Visual acuity (VA) will be assessed in both the study eye and fellow (non-study) eye at Screening and prior to ITV injection of IP at Day 1. VA will be assessed in the study eye at any time at Day 7 (EOS visit) or ET visit. Subject will use either original series ETDRS charts or 2702 series number charts (at a starting distance of 4 meters and then repeated at a distance of 1 meter, if necessary) consistently from Screening to Day 7 (EOS visit) or ET visit. VA testing must be performed before dilation of pupils and other ophthalmic procedures such as OCT assessment.
8. Slit lamp examination will be performed in both the study eye and fellow (non-study) eye at Screening and prior to ITV injection of IP at Day 1. Slit lamp examination will also be performed in both eyes at Day 7 (EOS visit) or ET visit.
9. IOP will be measured at Screening, prior to ITV injection of IP and 30-60 minutes after ITV injection of IP at Day 1 on the study eye. IOP will also be measured at any time during the visit at Day 7 (EOS visit) or ET visit on the study eye. The same device and method of IOP measurement should be used in each subject from Screening to Day 7 (EOS visit) or ET visit.
10. Indirect ophthalmoscopy using a standard way (i.e., usually using a head-mounted light source and a 20-30 dioptre lens) will be performed on the study eye at Screening and prior to ITV injection of IP and within 15 minutes after ITV injection of IP at Day 1. Indirect ophthalmoscopy will also be performed on the study eye at any time during the visit at Day 7 (EOS visit) or ET visit.
11. OCT will be performed on the study eye at Screening and prior to ITV injection of IP at Day 1 (baseline visit). OCT will be performed on the study eye at Day 7 (EOS visit) or ET visit. The same OCT device should be used from Screening to Day 7 (EOS visit) or ET visit.
12. The ITV injection of IP will be performed on Day 1. Qualified HCPs will be given enough time to read the instructions for use (IFU) prior to IP administration and then perform preparation and administration of ITV injection using SB11 PFS.
13. During IP administration, HCPs' task completion using SB11 PFS will be assessed by the observer(s) through a questionnaire (APPENDIX 1). During a follow-up session, HCP will self-assess the successful completion of her/his own task through a questionnaire (APPENDIX 2). After completion of HCP's self-assessment, the observer may ask and record the reason why use failure occurs, when applicable.
14. AEs will be recorded after the written informed consent is obtained from the subject until Day 7 (EOS visit) or ET visit.
15. Any medication including prescription drug, non-prescription drugs, or any therapy received locally [in the study eye and/or fellow (non-study) eye] or systemically within 6 months prior to Day 1 until Day 7 (EOS visit) or ET visit will be recorded.

# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADA | Anti-drug Antibody |
| AE | Adverse Event |
| AESI | Adverse Events of Special Interest |
| AMD | Age-related Macular Degeneration |
| BCVA | Best Corrected Visual Acuity |
| CNV | Choroidal Neovascularisation |
| COVID-19 | Coronavirus Disease 2019 |
| CPT | Centre Point Thickness |
| CRLT | Central Retinal Lesion Thickness |
| CRO | Contract Research Organisation |
| CSR | Clinical Study Report |
| CST | Central Subfield Thickness |
| DME | Diabetic Macular Oedema |
| DR | Diabetic Retinopathy |
| eCRF | Electronic Case Report Form |
| EMA | European Medicines Agency |
| ENR | Enrolled Set |
| EOS | End of Study |
| ET | Early Termination |
| ETDRS | Early Treatment Diabetic Retinopathy Study |
| EU | European Union |
| FA | Fluorescein Angiography |
| FAS | Full Analysis Set |
| FDA | Food and Drug Administration |

| | |
|---|---|
| FP | Fundus Photography |
| GCP | Good Clinical Practice |
| HCP | Healthcare Professional |
| IB | Investigator's Brochure |
| ICF | Informed Consent Form |
| ICH | International Council for Harmonisation |
| IEC | Independent Ethics Committee |
| IFU | Instructions For Use |
| IOP | Intraocular Pressure |
| IP | Investigational Product |
| IRB | Institutional Review Board |
| ITV | Intravitreal |
| MedDRA | Medical Dictionary for Regulatory Activities |
| NAb | Neutralising Antibody |
| OCT | Optical Coherence Tomography |
| PD | Protocol Deviation |
| PFS | Pre-filled Syringe |
| PK | Pharmacokinetics |
| PPS | Per-protocol Set |
| PT | Preferred Term |
| RPE | Retinal Pigment Epithelium |
| RVO | Retinal Vein Occlusion |
| SAE | Serious Adverse Event |
| SAF | Safety Set |
| SAP | Statistical Analysis Plan |

| | |
|---|---|
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |
| SOC | System Organ Class |
| SOP | Standard Operation Procedure |
| US | United States |
| VA | Visual Acuity |
| VEGF | Vascular Endothelial Growth Factor |
| WHO | World Health Organisation |
| WOCBP | Women of Child Bearing Potential |

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# LIST OF STUDY STAFF

| | |
|---|---|
| **SPONSOR:** | **Samsung Bioepis Co., Ltd.**<br>76, Songdogyoyuk-ro, Yeonsu-gu,<br>Incheon, 21987<br>Republic of Korea<br>Tel: +82 (32) 455 6114 |
| Clinical Project Manager | PPD |
| Clinical Development Lead/<br>Clinical Research Physician | |
| Clinical Research Scientist | |
| Statistician | |
| Safety Physician | |
| Project Safety Lead | |

# 1. Introduction

## 1.1. Background

Age-related Macular Degeneration (AMD), left untreated, is a leading cause of adult blindness in the developed world. Most of severe visual loss of AMD occurs from Choroidal Neovascularisation (CNV) or the neovascular form of AMD. CNV can be associated with fibrous replacement of the retinal photoreceptors and Retinal Pigment Epithelium (RPE), as well as atrophy of these portions of the retina in the macula, leading to severe visual decline with loss of reading vision, driving vision, and the ability to recognise faces. Vascular Endothelial Growth Factor (VEGF), a protein growth factor that both stimulates angiogenesis and increases vascular permeability, is a major pathogenic factor in CNV due to AMD. Counteracting these effects of VEGF can provide significant therapeutic benefit to subjects suffering from this disorder.

SB11 is a proposed similar biological medicinal product (hereafter 'biosimilar') of Lucentis® having ranibizumab as the active substance. Ranibizumab, a humanized monoclonal antibody (Fab) fragment which selectively binds to VEGF-A (hereafter referred to as 'VEGF'), thereby preventing the interaction of VEGF with its receptors VEGFR-1 and VEGFR-2 on the surface of endothelial cells. Binding of VEGF to its receptors leads to endothelial cell proliferation and neovascularization and vascular leakage. Increased level of VEGF expression has been implicated in the pathogenesis of neovascular AMD, CNV, and visual impairment caused by either diabetic macular oedema (DME) or macular oedema following retinal vein occlusion (RVO) [1].

Lucentis® is indicated in adults for the treatment of patients with neovascular AMD, DME, proliferative diabetic retinopathy, macular oedema secondary to RVO (branched RVO or central RVO), CNV and it is indicated in preterm infants for the treatment of retinopathy of prematurity with zone I (stage 1+, 2+, 3 or 3+), zone II (stage 3+) or aggressive posterior retinopathy of prematurity disease in European Union (EU) [1]. It is indicated for the treatments of patients with neovascular AMD, DME, RVO, diabetic retinopathy (DR) and myopic CNV in the United States (US) [2].

### 1.1.1. Background to Coronavirus Disease-2019

There is currently an outbreak of respiratory disease, Coronavirus Disease 2019 (COVID-19), caused by a novel virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first detected in Wuhan City, Hubei Province, China in 2019. This new virus has rapidly spread across the globe, causing the World Health Organisation (WHO) to declare a pandemic situation on March 12, 2020. The countermeasures initiated by national and local governments worldwide and the recommendations issued by the health authorities have impacted current and new clinical studies. As the threat of pandemic burden, including new outbreaks, locally or globally, will impact the further conduct of clinical studies, appropriate risk assessments and mitigation measures will need to be taken into consideration in all clinical studies to protect subjects, site staff, and society as a whole.

Both the European Medicines Agency (EMA) [3] and the US Food and Drug Administration (FDA) [4], as well as national health authorities in Europe, have issued new guidelines that aim to provide recommendations for actions for conduct of clinical studies of medical products during COVID-19 pandemic. Since the pandemic situation is evolving, guidelines, recommendations, national laws, and local restrictions may change at a high pace. Given the circumstances of a potentially relapsing pandemic or epidemic situation with regard to the spread of COVID-19 in the future, special attention will be paid to protect subjects participating in the study and site staff involved in the investigations against infection with SARS-CoV-2 in accordance to such guidance.

## 1.2. Overview of SB11

### 1.2.1. Non-Clinical Studies of SB11

SB11 is a humanized monoclonal antibody (Fab) fragment, which has a molecular weight of approximately 48 kDa and is produced by an *E. coli* expression system in a nutrient medium containing the antibiotic tetracycline. Tetracycline is not detectable in the final product. Vial presentation of SB11 0.5 mg (0.05 ml of 10 mg/mL) has been developed as a proposed biosimilar to Lucentis®, and is currently under the Agencies' review.

According to the guideline International Council of Harmonisation (ICH) Q6B, characterisation of a biological therapeutic must involve its physicochemical properties, biological activities, purity, impurities, and quantity. The characterisation study will employ the 'state-of-the-art' analytical methods in order to investigate the primary, secondary, higher-order structures, and the post-translational modifications associated the structural heterogeneity, the charge variants, the purity, and the biological activities.

As outlined in the "Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues" [5], a risk-based approach was taken to the non-clinical evaluation of SB11. A series of *in vitro* biologic activity studies including binding and cell-based assays have been performed in order to demonstrate non-clinical similarity between SB11 and Lucentis®. As a result, observation from above studies has established non-clinical evidence of similarity between SB11 and Lucentis®, *in vivo* studies were thought to be not performed in line with the guideline. Also, non-clinical safety pharmacology, reproductive, and carcinogenicity studies were not performed, as they are not required for non-clinical testing of biosimilars as outlined in the guideline [5]. However, an *in vivo* toxicity study using non-human primates was conducted to demonstrate similarity in *in vivo* toxicological profiles between SB11 and US Lucentis® in support of country-specific regulatory requirements.

### 1.2.2. Clinical Pharmacology of SB11

Since SB11 has been developed as a proposed biosimilar to Lucentis®, the clinical pharmacology program for SB11 was designed to investigate and compare pharmacokinetics (PK) profiles between SB11 and Lucentis®. A clinical Phase I PK study was not conducted since it is considered not meaningful to determine the biosimilarity based on the PK comparison of systemic exposure of SB11 and Lucentis®. To support the overall assessment of the systemic exposure of SB11 relative to Lucentis®, the PK profiles of SB11 and US Lucentis® were evaluated in a subset of patients with neovascular AMD, which is considered the most representative and relevant patient population in the clinical Phase III comparative study (SB11-G31-AMD). Given the large variability observed in both treatment groups, the PK results showed that the concentrations including post-dose concentrations were generally comparable across all timepoints up to Week 52 between the SB11 and US Lucentis® treatment groups.

### 1.2.3. Clinical Safety and Efficacy of SB11

Similarity in quality, *in vitro* and *in vivo* toxicity behaviour between SB11 and Lucentis® was demonstrated through extensive quality and non-clinical similarity exercises. Phase I study was not conducted due to negligible systemic exposure of ranibizumab following intravitreal (ITV) administration. Phase III clinical study of SB11 (SB11-G31-AMD) was conducted to compare efficacy, safety/tolerability, PK, and immunogenicity between SB11 and Lucentis® [6]. The comparative clinical study for SB11 was not designed to establish patient benefit *per se*, which has already been established by the reference product in numerous clinical trials and published literature reports.

The primary objective of Study SB11-G31-AMD was to demonstrate the equivalence of efficacy of SB11 to Lucentis® in subjects with AMD. Retinal thickness (e.g., central subfield thickness [CST], central retinal lesion thickness [CRLT], centre point thickness [CPT]) was assessed by optical coherence tomography (OCT) and lesion characteristics such as CNV size and presence of leakage or hemorrhage were evaluated using fundus photography (FP) and/or fluorescein angiography (FA). Overall, the change from baseline in CST, CRLT, CPT, and total CNV size and the proportion of patients with active CNV leakage were all comparable between the SB11 and US Lucentis® treatment groups at Week 24 and Week 52.

In the clinical Phase III study (SB11-G31-AMD), safety profiles of SB11 and Lucentis® were comparable and in line with the known safety risks of Lucentis® reported in the clinical trials and published literature [1, 2]. The immunogenicity profiles in terms of anti-drug antibody (ADA) and neutralising antibody (NAb) incidences were evaluated as one of the secondary endpoints. The overall incidence of ADA to ranibizumab was comparable between the SB11 and Lucentis® treatment groups at all timepoints up to Week 52. In addition, the incidence of NAb at each timepoint was comparable among the patients who were determined as ADA positive at each timepoint. Therefore, it is concluded that the formation of ADA and NAb was similar between the SB11 and Lucentis® treatment groups in the clinical Phase III study (SB11-G31-AMD).

### 1.3. Study Rationale

Lucentis® has been approved as two different presentations of administration, including vial and pre-filled syringe (PFS). Lucentis® PFS was developed to improve the ease of administration of ranibizumab to physicians for ITV injection by reducing steps in injection preparation [7].

As a proposed similar biological medicinal product to Lucentis®, SB11 is presented as a single-use vial or a single-use PFS. In the Phase III study, SB11 vial was administered once every 4 weeks to subjects with neovascular AMD. Once equivalence between the vial and PFS is demonstrated through comprehensive data and justification regarding technical characteristics that could affect the drug and drug delivery, a usability study will be conducted to assess the successful use of SB11 PFS by Healthcare Professionals (HCPs).

This study will be conducted in compliance with the protocol, ICH guidelines, Good Clinical Practice (GCP), the Declaration of Helsinki (2013) and all applicable and current regulatory requirements.

### 1.4. Risk and Benefit Assessment

#### 1.4.1. Known Potential Risks

According to the EU Lucentis® Summary of Product Characteristics, the most frequently reported ocular adverse reactions following administration of Lucentis® in clinical trials are: eye pain, ocular hyperaemia, increased intraocular pressure (IOP), vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, increased lacrimation, blepharitis, dry eye, and eye pruritus. The most frequently reported non-ocular adverse reactions are headache, nasopharyngitis, and arthralgia.

According to the US Lucentis® Prescribing Information, the most common adverse reactions (reported more frequently in Lucentis®-treated subjects than control subjects) are conjunctival haemorrhage, eye pain, vitreous floaters, and increased IOP.

Similarity in quality, *in vitro* and *in vivo* behaviour between SB11 vial and Lucentis® vial was demonstrated through extensive quality and non-clinical similarity exercises. SB11-G31-AMD Phase III study showed that the efficacy, safety/tolerability, PK, and immunogenicity of SB11 vial was

comparable to those of Lucentis® vial. Therefore, the known and potential risks of administrating SB11 are expected to be similar to those seen with Lucentis®.

In order to ensure the safety of subjects who participate in the study, specific conditions such as intraocular inflammation, active disorder of ocular and skin including ocular surface infections, previous history of conjunctival haemorrhage of concern, and active infectious diseases are excluded from enrolment, and the subjects should be instructed to report their symptoms related to adverse events of special interest (AESIs) in Section 8.3 without delay and should be managed appropriately.

Participation in clinical study may require more frequent visits than usual medical practice, thus, additional risk under the COVID-19 should be considered, if needed. The Sponsor will consider whether to start, continue, temporarily halt, or close the study at some or all clinical study sites based on the risk assessment with relevant parties' input on an ongoing basis.

This study is a multicentre study that will be performed in clinical sites with accessible medical facilities which will allow immediate treatment of medical emergencies including systemic hypersensitivity. All study-related procedures will be conducted by medical staffs with appropriate level of training and expertise and an understanding of the investigational products (IPs), its target, and mechanism of action.

### 1.4.2. Known Potential Benefits

Lucentis® PFS was approved in Europe (2013) and US (2016) as a new presentation to the existing presentation in vials. The solutions for injection in the PFS and in the vials are identical in terms of formulation. Similarity in quality, *in vitro* and *in vivo* behaviour between SB11 vial and Lucentis® vial was demonstrated through extensive quality and non-clinical similarity exercises. SB11-G31-AMD Phase III study showed that the efficacy, safety/tolerability, PK, and immunogenicity of SB11 vial was comparable to those of Lucentis® vial.

The main advantage of Lucentis® PFS has shown to reduce syringe preparation times with less complex preparation procedures, which improves the convenience of use for HCPs, and potentially reduces risk of contamination [8]. The use of PFS during ITV injection of anti-VEGF agents including ranibizumab seems to be associated with a trend toward decreased risk of suspected endophthalmitis and a statistically significant decreased risk of culture-positive endophthalmitis [9, 10]

Even though single injection of ranibizumab will not gain therapeutic benefit dramatically in enrolled patients with AMD or macular oedema secondary to RVO, the results of the study will support clinical usability of SB11 PFS. Development of PFS presentation of SB11 is expected to be beneficial to the wider patient community treated with ranibizumab.

### 1.4.3. Assessment of Potential Risks and Benefits

Summaries of findings from both clinical and non-clinical studies conducted with SB11 in vial can be found in the Investigator's Brochure (IB). The available data demonstrate a high degree of physicochemical and biological similarity of SB11 with the reference medicinal product (Lucentis®). The intended commercial formulation (only in vial) has been used in the Phase III (SB11-G31-AMD) study. The clinical study of SB11 showed high similarities between SB11 vial and US Lucentis® vial in terms of efficacy, safety, PK, and immunogenicity.

The known and potential risks of administrating SB11 PFS are expected to be similar to those seen with Lucentis® PFS. Considering SB11 having a similar risk/benefit profile to that of Lucentis®, the risk/benefit balance of this study is expected to be favourable.

The clinical study protocol provides adequate instructions for the detection of adverse events (AEs)

arising following the administration of the SB11 PFS. The risks to subjects in this trial will be minimized by compliance with the eligibility criteria as well as close monitoring.

Women of child bearing potential (WOCBP) and sexually active males must be informed that taking the study treatment may involve unknown risks to the foetus if pregnancy were to occur during the study, and agree that in order to participate in the study they must adhere to the contraception requirements outlined in the inclusion criteria. If there is any question that the subject will not reliably comply, they should not be entered or continue in the study.

Risk assessment for the COVID-19 will be documented on an ongoing basis in relevant documents. The risk assessment and associated mitigation measures based on inputs from relevant stakeholders will be prioritised to consider the rights, safety, and wellbeing of the study subjects.

## 2. Study Objectives and Endpoints

### 2.1. Study Objectives

#### 2.1.1. Primary Objective

The primary objective is to assess the ability of HCPs to follow the instructions for use (IFU) to prepare and administer SB11 PFS ITV injection to subjects.

#### 2.1.2. Secondary Objective

The secondary objective is to evaluate the safety of SB11 PFS in subjects with neovascular AMD or macular oedema secondary to RVO.

### 2.2. Study Endpoints

#### 2.2.1. Primary Endpoint

- Percentage of successful task completions (Day 1)

#### 2.2.2. Secondary Endpoint

- Percentage of successful completion on critical tasks (Day 1)
- Percentage of successful completion on essential tasks (Day 1)

#### 2.2.3. Safety Endpoint

- Incidence of AEs and serious adverse events (SAEs) from Day 1 to Day 7

## 3. Study Design

### 3.1. Overview of Study Design

This is an open-label, single group, single-dose clinical study to evaluate the usability of the PFS of SB11 in patients with neovascular AMD or macular oedema secondary to RVO. HCPs will prepare and administer ITV injections of SB11 0.5 mg delivered via PFS to enrolled subjects (1 injection to each subject) on Day 1 (baseline), and safety will be assessed until Day 7.

Approximately 30 subjects will participate in the study.

Screening period will be up to 14 days. Screening and Day 1 visits can be performed on the same day.

An interim analysis is not planned for this study. No formal statistical analysis will be performed. All the endpoints will be summarized descriptively with appropriate statistics.

### 3.2. Rationale for Study Design

#### 3.2.1. Scientific Rationale for Study Design

This study is to evaluate the usability of SB11 in PFS presentation by HCPs in patients with neovascular AMD or macular oedema secondary to RVO.

SB11 in a vial presentation (10 mg/ml) has been developed as a proposed biosimilar to Lucentis®, and is currently under the Agencies' review. Since the solutions for injection in the PFS and in the vials are identical in terms of formulation and the aim of this study is to assess successful use of PFS, single treatment arm (SB11 PFS only) is planned in this study.

Based on reported local AEs after ITV injection of anti-VEGF agents [11], most of the local AEs which are not affected by the underlying disease such as endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, IOP elevation, or subconjunctival haemorrhage occur within 6 days after ITV anti-VEGF injection. Therefore, 7 days of safety follow-up period are deemed appropriate.

#### 3.2.2. Rationale for Dose Selection

Considering approved indication and dose regimen for the study, neovascular AMD and macular oedema due to RVO were chosen to study usability. Those are approved indication and dose regimen by FDA and EMA as Lucentis® 0.5 mg (0.05 ml of 10 mg/ml solution) to be administered by ITV injection once a month via PFS [1, 2].

### 3.3. Duration of Study Participation

The duration of study participation will be approximately 7 days except screening period. One injection will be given on Day 1 (baseline) to support the assessment of the successful use of the PFS. After this ITV injection, the safety follow-up visit at Day 7 (+2) will be performed. Screening period will be up to 14 days. Screening and Day 1 visits can be performed on the same day.

### 3.4. Number of Subjects

Approximately 30 subjects are planned to be enrolled.

### 3.5. End of Study Definition

A subject is considered to have completed the study if he or she has completed all period of the study including the last scheduled visit shown in the Schedule of Activities (Table 2). The end of study (EOS) is defined as completion of the last scheduled visit (Day 7) shown in Table 2. The end of this clinical study is defined as completion of the last subject's Day 7 (EOS) visit or the last scheduled activity.

## 4. Study Population

### 4.1. Overview

The study population for this study is patients who required treatment for neovascular AMD or macular oedema secondary to RVO. Approximately 30 subjects are expected to be treated with ITV injection of SB11 PFS by HCPs.

### 4.2. Inclusion Criteria

Only one eye will be selected as the study eye. For subjects who meet eligibility criteria in both eyes, study eye is selected at the discretion of the Investigator.

Subjects must meet all of the following criteria to be eligible for the study:

1. Neovascular AMD or macular oedema secondary to RVO in the study eye

2. Study eye deemed to be indicated for ranibizumab ITV therapy at the discretion of the ophthalmologist (e.g., retina specialist)

3. Aged 18 years and older at the time of signing the informed consent form (ICF)

4. Written ICF must be obtained from the subject prior to any study-related procedure (if the subject cannot read ICF, an impartial witness should be present during the entire informed consent discussion)

5. Willingness and ability to undertake all scheduled visits and assessments

6. Non-childbearing potential female (e.g., permanently sterilized , postmenopausal [defined as 12 months with no menses without an alternative medical cause prior to Screening]), OR Childbearing potential female subjects or male subjects with their (respectively male or female) partners who agree to use at least 2 forms of appropriate contraception method (e.g., established use of oral, injected, intravaginal, transdermal or implanted hormonal contraceptive, placement of an intrauterine device or intrauterine hormone-releasing system, bilateral tubal occlusion, vasectomized partner or physical barrier [Note: Female condom and male condom should not be used together]) or 1 highly effective contraception method (e.g., sexual abstinence) from Screening until 3 months after the ITV injection of IP to achieve a failure rate of less than 1% per year. Vasectomy will be allowed for male subjects and female subjects of childbearing potential with a sole vasectomised male partner. Vasectomised subjects or partners should be medically confirmed for sterilisation. True abstinence alone will be allowed if this is in line with the preferred and usual lifestyle of the subject, or for subjects who do not have a partner. Periodic abstinence (e.g., calendar, ovulation, symptothermal post-ovulation methods) and withdrawal are not acceptable methods of contraception. Contraceptive methods do not apply for subjects whose partner is on the same gender.

### 4.3. Exclusion Criteria

Subjects meeting any of the following criteria are not eligible for the study:

1. Best Corrected Visual Acuity (BCVA) of the level of Finger Count or worse [i.e. 0 letter reading using Early Treatment Diabetic Retinopathy Study (ETDRS) chart] in one or both eyes at Screening or at Day 1

2. History of and/or current intraocular inflammation (any grading from trace and greater is excluded), including non-infectious uveitis, infectious uveitis, or scleritis, or history of sterile inflammatory reaction after the past ITV injections with any agent in either eye

3. Active or suspected infectious disease, or active disorder that preclude safe use of IP at the discretion of the Investigator, in either eye or adnexa of either eye at Screening or at Day 1

4. History of excessive bleeding and recurrent haemorrhages, including any prior excessive

intraocular bleeding or haemorrhages after ITV injection or intraocular procedures in either eye

5. History of massive subconjunctival haemorrhages of concern reported by the subject after an ITV injection in either eye

6. Uncontrolled IOP greater than (≥) 25 mmHg in the study eye at Screening or at Day 1

7. Treatment with any ITV injection within the 30 days prior to Day 1 in the study eye

8. History of treatment with ITV injection of brolucizumab (approved or investigational) in either eye

9. Any invasive ocular surgery including retinal detachment surgery, long-acting ocular therapeutic agent/implant including corticosteroid, or ocular drug release device implant (approved or investigational) in the study eye within 90 days prior to Day 1 or planned intraocular surgery within next 28 days after Day 1

10. Ocular laser surgery in the study eye at any time within the past 30 days prior to Day 1

11. Treatment with any ocular IP in either eye within 90 days prior to Day 1

12. Treatment with systemic anti-VEGF within 180 days prior to Day 1

13. Receipt of any systemic (non-ocular) IP within 180 days prior to Day 1

14. Use of therapies that are known to be toxic to ocular tissue within the 180 days prior to Day 1, including, but not limited to, deferoxamine, chloroquine/hydroxychloroquine, tamoxifen, phenothiazines, vigabatrin, or ethambutol.

15. Current systemic coagulation or bleeding disorders, or history of recurrent haemorrhages

16. Known ocular or non-ocular conditions that per the ophthalmologist (e.g., retina specialist) represent a contraindication to ranibizumab use in the patient or may represent an unwarranted patient risk.

17. Uncontrolled hypertension (defined as systolic blood pressure >160 mmHg and/or diastolic blood pressure >100 mmHg while sitting confirmed after repeated measurement) at Screening or at Day 1

18. Current systemic infectious disease or a therapy for active infectious disease

19. History of hypersensitivity to the active substance or to any of the excipients

20. Known history of intolerance or reaction, or ADA formation to prior biological therapies

21. Pregnant or lactating women at Screening or at Day 1

22. Have had a positive test result for COVID-19 within 8 weeks prior to ICF-signed date, or any suggestive sign and/or symptom of COVID-19 (e.g., fever, dry cough, dyspnoea, sore throat, or fatigue) at Screening or at Day 1. Subjects will adhere to local/national requirements (e.g., testing, isolation) for reduction of the public SARS-CoV-2.

### 4.4. Lifestyle Considerations

Subjects are advised to adhere to local requirements for reduction of the public COVID-19 exposure while ambulatory. All subjects should self-assess whether they have any symptoms consistent with COVID-19 through a questionnaire, and their body temperature will be measured at the site entry at each visit if COVID-19 symptom has not been reported on the phone and the on-site visit is planned. COVID-19 symptoms questionnaire will be used according to the site's local practice. The Investigator or designee will evaluate the subject for signs and symptoms of COVID-19 at Screening and Day 1, and document if the subject has been fully vaccinated any of anti-SARS-CoV-2 vaccine. If there are suspected signs or symptoms of COVID-19 or potential contact with COVID-19 patients, the subjects should not visit the site and should contact the site remotely (via phone, email, etc.) first. If applicable, subjects will be referred to the local health care system. Physical distancing and person-to-person contact restrictions will be applied and explained to subjects while staying at the site. Study participants will be asked to use surgical face masks and/or gloves if deemed appropriate by the Investigator and site staff and guided by local requirements. COVID-19-suspected or positive participants can be refused entry into the Investigational site.

### 4.5. Screen Failures and Rescreening

#### 4.5.1. Screen Failures

Screen failures are defined as subjects who consent to participate in the clinical trial but do not meet minimum one criterion required for participation in the trial during the screening procedures. If the subject does not receive IP administration within 14 days after signing ICF, the subject will be screen-failed unless conditions for rescreening described in Section 4.5.2 are fulfilled.

Once a subject is screen failed for one eye, he or she should not be re-screened for the same eye. Screening for the other eye is allowed within the screening period and the subject will use the same screening number.

#### 4.5.2. Rescreening

Rescreening is allowed only for administrative issue such as COVID-19-related travel or transport restrictions. Such subjects can be rescreened only once, based on Investigator recommendation and after discussion and agreement with medical monitor. The rescreened subject will have to undergo the full screening procedures (including ICF consent) again. Rescreening is not allowed for a medical issue. Subjects who did not meet eligibility criteria at Screening cannot be rescreened.

### 4.6. Replacement of Subjects

Subjects who are discontinued from study will not be replaced.

## 5. Treatment and Investigational Product

### 5.1. Treatment of the Subjects

#### 5.1.1. Dosing and Treatment Schedule

One ITV injection of SB11 PFS per subject will be administered once at Day 1 (baseline). Safety follow-up will be done at Day 7 (+2).

#### 5.1.2. Assignment of Subjects to Treatment Group

Treatment assignment and randomisation is not applicable for this open-label study.

### 5.1.3. Masking

This is an open-label study, therefore treatment will be open to subjects, Investigator staff, and study participants including qualified ophthalmologists and their assistants and representatives of the Sponsor.

### 5.1.4. Assignment of Subject Number

Each subject will be assigned with a unique subject number at Screening at the moment of signing the ICF.

## 5.2. Investigational Product

### 5.2.1. Identity of Investigational Product

The IPs will be supplied to Investigational sites as a PFS.

Details of the IPs are provided in Table 3.

**Table 3. Investigation Product Description**

| | SB11 |
|---|---|
| Formulation | Solution for intravitreal injection in pre-filled syringe |
| Active ingredient | Ranibizumab |
| Dose | 0.5 mg |
| Injection volume | 0.05 mL of SB11 10 mg/mL solution |
| Storage conditions | Stored in refrigerator (2-8°C), Do not freeze. |

### 5.2.2. Preparation and Administration of Investigational Product

One ITV injection of SB11 0.5 mg per subject will be administered via PFS at baseline (Day 1). IP preparation and injection will be performed by the qualified HCPs. HCPs will be allowed to have enough time to read IFU prior to IP administration.

The PFS is for single use only. The PFS is sterile. IP should not be used if the packaging is damaged or has been tampered. From opening of the sealed tray, all subsequent steps should be done under aseptic conditions. IPs should be inspected visually prior to administration. If particulates, cloudiness, or discoloration are visible, the IP must not be used. After removing syringe cap, attach a sterile 30 G x ½ inch injection needle firmly onto the PFS. After expelling air bubble and adjusting dose, injection procedure will be performed into injection site.

A detailed guideline for IP preparation and administration will be provided in the Pharmacy Manual or IFU.

### 5.2.3. Formulation, Packaging, and Labelling

SB11 is supplied for use as a solution for ITV injection in PFS (0.5 mg per PFS).

These IP PFSs will be packed and open-labelled for clinical use. The labels for carton and PFS will contain the protocol number, unique identifier, Sponsor company name, expiry or retest date, storage condition, and/or any other details according to the Good Manufacturing Practice and other relevant local laws and/or regulations.

The temperature will be monitored properly during the study period. The IP should be stored in a secure

area and clearly labelled and stored away from other IP or medication to prevent confusion (e.g., in a clearly marked box on a separate shelf of the refrigerator).

A detailed guideline for IP preparation, administration, storage, and destruction will be provided in the Pharmacy Manual.

#### 5.2.4. Product Storage and Stability

SB11 in PFS should be stored at 2°C to 8°C (36°F to 46°F) in the original carton until time of use to protect from light. The temperature will be monitored properly during the study period. If continuous monitoring is not available then manual temperature logs should be generated and recorded to ensure proper storage conditions. If a temperature deviation occurred, responsible person should contact the Sponsor to determine if the drug is still appropriate for use.

The IPs must not be frozen. The IPs must not be used beyond the expiration date. The IPs should be protected from light and stored in a dark place. Do not open the sealed tray until time of use.

#### 5.2.5. Treatment Compliance and Investigational Product Accountability

Compliance will be assessed by the subject's source documents and electronic case report form (eCRF). All dosing information including the exact date and time of IP administration must be recorded in the source document and eCRF.

The Investigator or designee should maintain the documents of IP accountability and record the IP kit number administered to subjects. IP accountability and dispensing records must be kept and contain the following information:

- The identification of the subjects to whom the drug was dispensed.
- The date(s) and quantity of the drug dispensed and exact package to the subject.
- The dispensing and inventory logs must be available for review.

A detailed guideline for IP return and destruction after accountability will be provided in the Pharmacy Manual.

### 5.3. Concomitant Medication or Treatment

#### 5.3.1. Permitted Concomitant Medications or Treatment

Any other medications and treatments except for prohibited medications or treatments that are considered necessary for the subject's welfare, and that are not expected to interfere with the evaluation of the IP may be given at the Investigator's discretion.

Considering the route of administration, known safety profiles of SB11 PFS, and the benefit to personal and public health from COVID-19 vaccination, COVID-19 vaccines are not prohibited during the study period. Only COVID-19 vaccines that have been approved and/or authorized by the appropriate regulatory authorities in the respective countries are allowed. Like any vaccine, COVID-19 vaccines can cause mild, short term side effects, such as a low-grade fever or pain or redness at the injection site. Most reactions to vaccines are mild and go away within a few days on their own. More serious or long-lasting side effects to vaccines are possible but extremely rare. Therefore, if possible, it is recommended to avoid COVID-19 vaccination within 14 days prior to IP administration and up to 6 days (+2 days) after IP administration (i.e., EOS visit), in order to minimize confusion and/or inaccurate attribution of AE causation.

### 5.3.2. Prohibited Medications or Treatment

Prohibited medication and therapy during the study period are presented in Table 4.

Details of any medications including both prescription, non-prescription drugs, or any therapy (except non-prescribed dietary supplements, vitamins or minerals) received locally, including the study eye and/or fellow eye, or systemically within 180 days prior to Screening will be collected until Day 7 (EOS visit) or early termination (ET) visit. Details to be recorded include: name (generic name preferred), dose number and unit, frequency of administration, route of administration, start and stop dates, and the AE it relates to (if applicable).

**Table 4. Prohibited Medication and Therapy**

| Medication or Therapy | Time to be prohibited | Eye to be prohibited |
|---|---|---|
| Treatment with any ITV injection | • Within 30 days prior to Day 1 | Study eye |
| Any ITV injection except SB11 PFS | • From Day 1 to EOS/ET visit | Study eye<br>Fellow eye |
| Treatment with ITV injection of brolucizumab (approved or investigational) | • Prior to Day 1 | Study eye<br>Fellow eye |
| Any invasive ocular surgery, long-acting ocular therapeutic agent/implant including corticosteroid, or ocular drug release device implant (approved or investigational) | • Within 90 days prior to Day 1<br>• From Day 1 to EOS/ET visit | Study eye |
| Any ocular laser surgery | • Within 30 days prior to Day 1<br>• From Day 1 to EOS/ET visit | Study eye |
| Ocular IP | • Within 90 days prior to Day 1 | Study eye<br>Fellow eye |
| Ocular IP except SB11 PFS | • From Day 1 to EOS/ET visit | Study eye<br>Fellow eye |
| Treatment with systemic anti-VEGF (e.g., bevacizumab) | • Within 180 days prior to Day 1<br>• From Day 1 to EOS/ET visit | N/A |
| Systemic (non-ocular) IP | • Within 180 days prior to Day 1<br>• From Day 1 to EOS/ET visit | N/A |
| Therapies known to be toxic to ocular tissue including, but not limited to, deferoxamine, chloroquine/hydroxychloroquine, tamoxifen, phenothiazines, vigabatrin, ethambutol | • Within 180 days prior to Day 1<br>• From Day to EOS/ET visit | N/A |

EOS = End of Study; ET = Early Termination; ITV = intravitreal; N/A = not applicable; PFS = Pre-filled syringe; VEGF = Vascular Endothelial Growth Factor

### 5.3.3. Rescue Medications

Not applicable

### 5.3.4. Fellow Eye Treatment

The fellow eye (non-study eye) will not be considered as an additional study eye. Prohibited medication and therapy for the fellow eye during the study period are presented in Section 5.3.2.

# 6. Study Assessment

## 6.1. Usability Assessment

### 6.1.1. Primary Outcome Assessment

The primary outcome measure is the HCPs' successful task completions as assessed by an independent observer who is trained for usability assessment. HCPs (ophthalmologist and/or assistants) will perform each task (Table 5), as per normal practice at the site. The observer will answer a questionnaire designed to record the successful task completions of HCPs (APPENDIX 1). The observer and HCPs should sign and date the completed questionnaire. After the completion of SB11 PFS administration, the following information will be collected in the source document and transcribed into eCRF.

- **Successful task completions:** The observer will record if each task is successfully completed by designated HCP(s). Tasks will be considered to be successfully completed if tasks meet success criteria or corrected results are achieved without a use failure, even if the IFU are not followed exactly. The information that describes success criteria will be provided to observer separately.

- **Use failure:** If any use failure of HCP(s) is observed by the observer, the observer will ask HCPs the reason why she/he commit use failure(s) on each task in the follow-up session.

- If use failures of HCPs which can result in unacceptable clinical impact or harm to the subject are observed, the observer will correct and/or instruct the HCPs. Unacceptable clinical impact or harm includes, but is not limited to, significant overdose and condition that can result in increased IOP or infection.

**Table 5. Usability Task Description**

| Sequence | Task | Critical Task | Essential Task | Description |
|---|---|---|---|---|
| 1 | Open the carton | - | O | Open the carton |
| 2 | Remove contents | - | O | Removes sealed blister pack from carton |
| 3 | Peel the lid off the blister pack | - | O | Peels the lid off blister pack without damaging the product |
| 4 | Carefully remove the PFS from the blister using aseptic technique | - | O | Removes the PFS out of blister pack and does not damage the PFS |
| 5 | Remove the syringe cap | - | O | Removes syringe cap without damaging PFS |
| 6 | Attach a needle | O | - | Fully attaches a needle to the PFS Luer lock |
| 7 | Remove the needle cap | O | - | Pulls the needle cap straight off without damaging the PFS<br>*Note that it is acceptable to remove cap before or after setting dose |
| 8 | Set the dose | O | - | Removes air from PFS<br>Sets the required dose by pushing the plunger rod |

| | | | | |
|---|---|---|---|---|
| 9 | Insert the needle into the injection site | O | - | Inserts the needle into the injection site |
| 10 | Press the plunger down to inject the medication | O | - | Presses the plunger down completely |
| 11 | Remove the needle from the injection site | - | O | Pulls needle straight out from the injection site |
| 12 | Dispose product | O | - | Disposes of the PFS with attached needle according to local regulation |

PFS = Pre-filled syringe

### 6.1.2. Secondary Outcome Assessments

The secondary outcome measures are observer's assessment of successful completion on critical and essential tasks at baseline visit (Day 1). HCPs (ophthalmologist and/or assistants) will perform each task (Table 5), as per normal practice at the site.

After the completion of SB11 PFS administration, the following information will be collected in the source document and transcribed into eCRF.

- **Successful completion on Critical tasks**
  - Critical task [Tasks on which users could make errors, which would have direct implications on user's and/or subject's safety or lead to compromised medical care]: If any use failure of HCP(s) on critical tasks is observed by the observer, the observer will ask HCPs the reason why she/he commits use failure(s) on each task in the follow-up session.
- **Successful completion on Essential task**
  - Essential task [Tasks are not considered critical, but required in order to complete the use process for effective use of the product]: If any use failure of HCP(s) on essential tasks is observed by the observer, the observer will ask HCPs the reason why she/he commits use failure(s) on each task in the follow-up session.

### 6.1.3. Other Usability Assessments

HCP who performs designated tasks will self-assess the successful completion of each task of SB11 PFS use. The participating HCPs will answer a questionnaire designed to record their successful task completions (APPENDIX 2). The HCP should sign and date the completed questionnaire. After the completion of SB11 PFS administration, the information will be collected in the source document and transcribed into eCRF.

## 6.2. Safety Assessment

### 6.2.1. Adverse Events

All AEs will be recorded from the written informed consent is obtained from the subject until Day 7 (EOS visit) or ET visit. AEs should be elicited from subjects using non-leading questions such as 'How are you feeling?'. Further information on AE monitoring and reporting is presented in Section 8.

### 6.2.2. Pregnancy Test

For WOCBP, pregnancy test (serum or urine) must be performed at Screening.

Additional pregnancy test (serum or urine) can be performed in each Investigational site during the study period, if necessary (at the Investigator's discretion).

Deleted pregnancy test result at Screening with technical problems, such as handling error, sampling error, or tube breakage, should be followed by re-test.

### 6.2.3. Physical Examination

Physical examination will be performed at Screening. The physical examination may include an assessment of the subject's general appearance, skin, head, neck, throat, lymph nodes, cardiovascular, neurological, thyroid, musculoskeletal/extremities, respiratory systems, and the subject's abdomen. Other body systems may be examined at the discretion of the Investigator.

Abnormal findings will be documented on the source document, and any clinically significant abnormality should be recorded as an either medical history or AE as appropriate.

During COVID-19 pandemic situation, COVID-19 related signs and symptoms (e.g., fever, dry cough, dyspnoea, sore throat, fatigue, etc.) will be included as an assessment.

### 6.2.4. Vital Signs

Vital signs include blood pressure, heart rate, and body temperature. Vital signs will be assessed at Screening and prior to ITV injection of IP at Day 1 (baseline visit). Vital signs will also be assessed at Day 7 (EOS visit) or ET visit (Table 2).

The Investigator should assess all vital signs and any clinically significant abnormalities should be reported as medical history or AE as appropriate.

## 6.3. Ophthalmic Assessments

### 6.3.1. Full Ophthalmic Examinations

The full ophthalmic examination will consist of an external examination of the eye and adnexa (including but not limited to blepharoptosis, abnormal pupil shape, unequal pupils, abnormal reaction to light, and afferent pupillary defect), slit lamp biomicroscopy, IOP measurements and indirect ophthalmoscopy.

Abnormal findings will be documented on the source document, and any clinically significant abnormality should be recorded as a medical history or AE as appropriate.

Retesting is allowed during study period at the discretion of the Investigator, if deemed clinically necessary for the subject's safety.

**BCVA examination**

BCVA will be assessed in both the study eye and fellow eye (non-study eye) at Screening and prior to ITV injection of IP at Day 1. BCVA in the study eye will also be assessed during visit at Day 7 (EOS visit) or ET visit. Refraction and visual acuity (VA) testing must be performed before dilation of pupils and other ophthalmic procedures such as OCT assessment.

Subject must use the same chart consistently from Screening to Day 7 (EOS visit) or ET visit.

Manifest refraction should be performed to determine the best spectacle-corrected visual acuity. Subjects will be refracted while looking at the letters on Chart R (or numbers on Chart 2702). Thereafter, BCVA with the manifest refraction will be measured using Chart 1 (or Chart 2702A) for the right eye

and Chart 2 (or Chart 2702B) for the left eye. The type of chart used (Original Series ETDRS or 2702 Series Number) should be consistent for the duration of the study for each subject.

The subject must sit for the 4-meter VA test. The subject will be instructed to start reading each line in sequence from left to right and top to bottom starting from the top left-most letters of each chart. Testing of both eyes begins at 4-meters and continues at the 1-meter distance only if the subject reads less than (<) 20 letters/numbers on the chart at 4 meters. When performing testing at 1 meter, the +0.75 sphere should be added to the 4-meter correction already in the trial frame to compensate for the closer testing distance.

A decrease in VA of ≥ 15 letters in the study eye from the last assessment of VA should be reported as AEs/SAEs as appropriate.

If the event meets one or more of the following criteria in study eye, it should be reported as SAE.

- A decrease in VA of ≥ 30 letters from the last assessment of VA
- A decrease in VA to the level of Light Perception or worse

A detailed protocol for conducting BCVA examination will be provided in the VA Testing Manual.

**Slit lamp biomicroscopy**

The slit lamp examination [cornea, lens, iris, aqueous reaction (cells and flare), vitreous] will be performed in both the study eye and fellow eye at Screening and prior to ITV injection of IP at Day 1 (baseline). Slit lamp examination will also be performed at Day 7 (EOS visit) or ET visit.

The anterior segment as well as the vitreous inflammatory response will be examined using a slit lamp biomicroscopy. Vitreous inflammatory response will be examined after dilation of pupil with 2-3 drops of phenylephrine-tropicamid (or any other mydriatic drug) applied topically to the eye.

Grading scales for intraocular inflammation are provided in APPENDIX 3, APPENDIX 4 and APPENDIX 5.

**IOP measurement**

IOP will be measured on the study eye at Screening and prior to ITV injection of IP and 30-60 minutes after ITV injection of IP at Day 1 (baseline). IOP will also be measured on the study eye at any time during the visit at Day 7 (EOS visit) or ET visit.

The same method and device of IOP measurement must be used in each subject from Screening to Day 7 (EOS visit) or ET visit.

**Indirect ophthalmoscopy**

Indirect ophthalmoscopy using in a standard way (i.e., usually using a head-mounted light source and a 20-30 dioptre lens) will be performed on the study eye (including evaluation of posterior segment abnormalities of the vitreous, optic nerve, peripheral retina, and retinal vasculature, as well as retinal pigment epithelium detachment, ischemic events including cotton wool spots and microaneurysms) at Screening and prior to ITV injection of IP and 0-15 min after ITV injection of IP at Day 1 (baseline). Indirect ophthalmoscopy will also be performed on the study eye at any time during the visit at Day 7 (EOS visit) or ET visit.

#### 6.3.2. Optical Coherence Tomography

OCT will be performed on the study eye at screening and prior to ITV injection of IP at Day 1. OCT will also be performed on the study eye at Day 7 (EOS visit) or ET visit. The Investigational site should use the same OCT device during the study period.

Abnormal findings will be documented on the source document, and any clinically significant abnormality should be recorded as a medical history or AE, as appropriate.

## 7. Study Procedures

### 7.1. Study Flow and Visit Schedule

During this study, usability, safety, and ophthalmic assessments will be performed at the time points outlined in Table 2. All results should be recorded in the source documents along with the date and time the procedures were performed.

#### 7.1.1. Screening Visit (D-14 to D-1)

Screening should be performed within 14 days before Day 1. Screening and Day 1 visits can be performed on the same day.

- Written informed consent

Investigator must discuss the study with the subject and obtain written informed consent from the subject prior to any study-related procedures.

The following procedures should be performed:

- Evaluate subject eligibility with all inclusion and exclusion criteria
- Demographic data (year of birth, gender, race, and ethnicity)
- Review of medical, surgical, and ophthalmic history
- Physical examination
- Vital signs (temperature, blood pressure, and pulse rate)
- Pregnancy test for WOCBP (serum or urine)
- Ophthalmic examination:
  - BCVA examination using original series ETDRS charts or 2702 series Number charts (before dilation of the pupils and other ophthalmic procedure such as OCT)
  - Slit lamp biomicroscopy
  - IOP
  - Indirect ophthalmoscopy
- OCT
- AE monitoring
- Review of concomitant and previous medication or therapy

Once the subject is confirmed eligible for the study, the subject will be advised on study restrictions such as contraception, prohibited medications, and other study requirements if any.

If it is deemed necessary to repeat the tests at the discretion of the Investigator, additional tests are permitted to repeat the tests within the Screening window but the latest result will be used to determine the subject's eligibility. Subjects whose eligibility is confirmed by these repeated tests within the Screening window can be enrolled in the clinical study.

If a subject is not eligible for this clinical study at the Screening visit, the subject is considered a screening failure. If the subject does not receive IP administration within 14 days after signing the ICF, the subject will be screen-failed unless conditions for rescreening described in Section 4.5.2 are fulfilled.

Once a subject is screen failed for one eye, he or she should not be re-screened for the same eye. Screening for the other eye is allowed within the screening period and the subject will use the same screening number.

The demographics of the subjects and the primary reason for screening failure must be recorded in the source document and eCRF.

**NOTE**

- A decrease in VA of ≥ 15 letters (compared with the last assessment of VA) in study eye should be reported as AEs/SAEs as appropriate.
- Intraocular inflammation should be recorded based on the location of inflammation (e.g., 'anterior uveitis', 'intermediate uveitis', 'posterior uveitis' or 'panuveitis' rather than 'uveitis'

### 7.1.2. Day 1/Baseline Visit

✓ **Before IP injection**

- Evaluate subject eligibility with all inclusion and exclusion criteria
- Vital signs (temperature, blood pressure, and pulse rate)
- Pregnancy test (serum or urine) at the Investigator's discretion
- Ophthalmic examination:
  - BCVA examination using original series ETDRS charts or 2702 series Number charts (before dilation of the pupils and other ophthalmic procedure such as OCT)
  - Slit lamp biomicroscopy
  - IOP
  - Indirect ophthalmoscopy
- OCT
- AE monitoring
- Review of concomitant and previous medication or therapy

✓ **ITV injection of IP**

- IP (SB11 PFS) will be given in the study eye.

✓ **After ITV injection of IP**

- Ophthalmic examination:
  - Indirect ophthalmoscopy (0-15 min post-dose)
  - IOP (30-60 min post-dose)
- AE monitoring

**Assessment of HCP's Usability of PFS**

✓ **ITV injection of IP**

- Task completion will be evaluated by the observer (APPENDIX 1) when HCP administers ITV injections of SB11 via PFS.

✓ **After ITV injection of IP**

- Self-assessment of task completion by HCP (APPENDIX 2)
- Use failure analysis (during follow-up session with an observer, if applicable: APPENDIX 1)

### 7.1.3. Day 7/End of Study Visit

EOS (Day 7) is defined as 6 days after the IP administration. EOS visit will be allowed within 2 days after Day 7. All subjects who complete the IP administration at Day 1 (baseline) will conduct EOS visit.

The following procedures should be performed:

- Vital sign (temperature, blood pressure, and pulse rate)
- Pregnancy test (serum or urine) at the Investigator's discretion
- Ophthalmic examination:
  - BCVA examination using original series ETDRS charts or 2702 series Number charts (before dilation of the pupils and other ophthalmic procedure such as OCT)
  - Slit lamp biomicroscopy
  - IOP
  - Indirect ophthalmoscopy
- OCT
- AE monitoring
- Review of all concomitant medications

### 7.1.4. Unscheduled Visit

Unscheduled visit is allowed during study period at the discretion of the Investigator, if deemed clinically necessary for the subject's safety. Any tests, procedures, or assessments performed at the unscheduled visits must be recorded in the source documents.

### 7.1.5. Early Termination Visit

When a subject withdraws/discontinues prior to study completion, all procedures scheduled at the EOS visit will be performed at the time of the subject's discontinuation or as soon as possible after

discontinuation. If the ET visit occurs before Day 7 (EOS), the Investigator should perform a follow-up phone call on Day 7 to check if there has been any new outcome or safety information regarding AEs since the subject's last visit. Any AEs which are present at the time of the ET will be followed in accordance with Section 8.1.3.

## 7.2. Discontinuation

### 7.2.1. Subject Discontinuation

This study is a single dose study, therefore IP discontinuation after the first dose is not applicable to the study. If the subject does not receive IP administration within 14 days after signing ICF, the subject will be screen-failed unless conditions for rescreening described in Section 4.5.2 are fulfilled. In the following situations, the subjects who administered IP will discontinue in the study.

- Consent withdrawal by subject
  - If subjects withdraw his/her consent, Investigator must inquire the reasons for consent withdrawal as to whether it is related to the study (e.g., AE or pregnancy); however, the subject could refuse to provide such reason
  - If the main reason for consent withdrawal is considered related to the study, the Investigator may select appropriate reason among the reasons listed below other than consent withdrawal
- Any ophthalmic abnormality in the study eye which require urgent ophthalmic procedure (e.g., ITV injection, vitrectomy, retinal detachment surgery) other than IP prior to EOS
- Death of any cause
- Lost to follow-up
- Unacceptable toxicity including AEs not manageable by symptomatic therapy or schedule modification (including severe or critical COVID-19 or COVID-19 with sequalae)
- Any other administrative reasons per the Investigator

When a subject withdraws/discontinues prior to study completion, all procedures scheduled at the EOS visit will be performed at the time of the subject's discontinuation or as soon as possible after discontinuation and the subjects should be followed up in accordance with Section 7.1.3

If a subject withdraws informed consent and does not agree for additional information to be collected and disclosed, no additional data should be collected. The Sponsor will retain the data collected before the withdrawal of informed consent.

Subjects who are discontinued will not be replaced.

### 7.2.2. Discontinuation of Study Sites

Investigational site participation may be discontinued if the Sponsor, the Investigator, or the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) of the Investigational site judge it necessary for any reason. Health authorities and IRB/IEC will be informed about the discontinuation of the study sites in accordance with applicable regulations.

### 7.2.3. Lost to Follow-up

A subject will be considered lost to follow-up if he or she fails to return for last scheduled visit (i.e., ET

or EOS visit) without pre-notification and is unable to be contacted by the study site staff.

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

- The site will attempt to contact the subject and reschedule the missed visit and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain if the subject wishes to and/or should continue in the study.
- Before a subject is deemed lost to follow-up, the Investigator or designee will make every effort to regain contact with the subject (where possible, 3 telephone calls and, if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts should be documented in the subject's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

### 7.3. Discontinuation of the Study

The Sponsor may terminate this study prematurely for reasonable cause provided that written notice is submitted to the Investigator, IRB/IEC, and relevant authorities in advance of the intended termination:

- Unsatisfactory enrolment with respect to quantity or quality
- Discontinuation of development of the study drug
- The decision by the Sponsor to terminate the study based on medical/ethical, business decision/strategic, or study conduct-related reasons

If the study is terminated or discontinued prematurely, the Sponsor will promptly notify to the Investigator. The Investigator may be informed of additional procedures to be followed to assure that adequate consideration is given to the protection of the subject's welfare and best interests.

Health authorities and IRB/IEC will be informed about the discontinuation of the study in accordance with applicable regulations.

## 8. Safety Monitoring and Reporting

### 8.1. Adverse Events

#### 8.1.1. Definition of Adverse Event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered the medicinal (investigational) product or other protocol-imposed intervention and which does not necessarily have to have a causal relationship with this treatment or intervention. An AE can therefore be an unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of any dose of a medicinal (investigational) product or other protocol-imposed intervention regardless of attribution.

All AEs during the period of observation (as specified in Section 8.1.3) including the events that occurred prior to administration of an IP should be reported as an AE in the AE section of eCRF.

Pre-existing conditions which worsen (i.e., increase in severity) that meet the definition of an AE during the study are to be reported as AEs.

Diagnostic and therapeutic non-invasive and invasive procedures, such as surgery, should not be reported as AEs. However, the medical condition for which the procedure was performed should be

reported if it meets the definition of an AE. For example, an acute appendicitis that begins during the AE reporting period should be reported as an AE and the resulting appendectomy should be recorded as treatment of the AE.

The AEs that emerge during treatment with an IP (i.e., treatment-emergent adverse event) will be analysed for the purposes of safety analyses.

### 8.1.2. Clinically Significant Abnormality

If there are any abnormalities discovered during vital signs, ophthalmic examination, and/or other safety assessments and the abnormality is assessed clinically significant by the Investigator, it should be reported as an AE. This does not apply to pre-existing conditions which have been documented at Screening or if the abnormality is consistent with a current diagnosis (underlying disease or other AEs). If it is not specified or defined elsewhere in the protocol, clinically significant abnormality may include the events that led to an intervention, including discontinuation from the study, significant additional concomitant medication, and others evaluated as clinically significant by the Investigator.

If the clinically significant abnormality from assessment is not a sign of a disease or syndrome, the abnormality itself should be reported as an AE in the eCRF. Observations of the same clinically significant abnormality from visit to visit should not be repeatedly reported as AEs in the eCRF, unless their severity, seriousness, or aetiology changes.

### 8.1.3. Period of Observation for Adverse Events

AEs will be reported from the time the ICF is signed until the EOS or ET visit.

Unresolved AEs during the study period should be followed up until the EOS or ET visit and recorded in the eCRF. The Investigator should observe the AEs for appropriate medical care of the subject until AE resolution or stabilisation up to EOS or ET visit.

SAEs that occurred after the subject had completed a clinical study and that are considered to be related to medicinal (investigational) product or procedure by the Investigator should be reported to the Sponsor if the Investigator becomes aware of the SAEs.

If the subject has an ongoing SAE or AESI at the EOS or ET visit, these cases will be followed until event resolution or stabilisation (see Section 8.2.2).

### 8.1.4. Reporting Adverse Events

AEs are to be reported in the eCRF and reviewed by the Investigator. When reporting an AE, a diagnosis (when possible and appropriate) rather than each individual sign and symptom should be reported.

Each AE is to be assessed to determine if it meets the criteria of an SAE (see Section 8.2.1 for SAE definition). If an AE is classified as an SAE, it must be reported to Sponsor, or its designated representative, promptly according to the timeline specified in Section 8.2.2. For an SAE, a diagnosis with a description of signs and symptoms as well as other supporting information that led to the diagnosis should be described in the SAE form provided by the Sponsor (see Section 8.2.2).

### 8.1.5. Severity Assessment

The Investigator is responsible for assessing and reporting the severity of AEs.

Following classifications should be used to classify AEs:

- Mild events are usually transient and do not interfere with the subject's daily activities,
- Moderate events introduce a low level of inconvenience or concern to the subject and may interfere with daily activities,
- Severe events interrupt the subject's usual daily activities.

#### 8.1.6. Causality Assessment

The Investigator is responsible for assigning a causal relationship to each AE. The causal relationship between the IP and the AE should be defined as not related (no) or related (yes).

Events should be classified as 'related' if there is a reasonable possibility that the IP caused the AE. This means that there are facts (evidence) or arguments to suggest a causal relationship.

Events should be classified as 'not related' if there is no reasonable possibility that the IP caused the AE.

#### 8.1.7. Expectedness Assessment

Expectedness of AEs will be assessed by referring to the safety information in IB of the relevant safety section. More detailed information on expectedness assessment will be explained in IB.

#### 8.1.8. Withdrawal due to Adverse Events

Subject withdrawal from the study due to an AE should be distinguished from withdrawal due to personal reasons and recorded on the appropriate eCRF section. Subjects withdrawn due to an AE should be followed up until the time point specified in Section 8.1.3. When a subject withdraws from the study due to an SAE, the SAE must be reported and followed in accordance with the requirements outlined in Section 8.2.2.

### 8.2. Serious Adverse Events

#### 8.2.1. Definition of Serious Adverse Event

An SAE is any untoward medical occurrence at any dose that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity,
- Results in congenital anomaly/birth defects,
- Is medically important.

Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation. However, if it is determined that the event may jeopardise the subject and may require intervention to prevent one of the other outcomes listed in the definition above, the important medical event should be reported as serious. Examples of such events

are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalisation or development of drug dependency or drug abuse.

The term 'severe' is often used to describe the intensity (severity) of a specific event (as in mild, moderate or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as 'serious', which is based on subject/event outcome or action criteria usually associated with events that pose a threat to a subject's life or functioning.

#### 8.2.1.1. Life-threatening

The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

#### 8.2.1.2. Hospitalisation

AEs reported from clinical studies associated with inpatient hospitalisation or prolongations of hospitalisation are considered serious. Staying at an observation unit in the emergency room for more than 24 hours qualifies for hospitalisation. Any events leading to subsequent emergency room visit for less than 24 hours should be in the discretion of Investigator to assess serious as medically important.

Hospitalisation or prolongation of hospitalisation in the absence of a precipitating clinical AE is not in itself an SAE. Examples include:

- Admission for treatment of a pre-existing condition not associated with the development of a new AE or with a worsening of the pre-existing condition (e.g., for work-up of persistent pre-treatment lab abnormality),
- Social admission for convenience (e.g., admission of a subject who does not have a carer),
- Administrative admission (e.g., for a yearly medical examination),
- Protocol-specified admission during a clinical study (e.g., for a procedure required by the clinical study protocol),
- Optional admission not associated with a precipitating clinical AE (e.g., for elective cosmetic surgery).

Pre-planned treatments or surgical procedures should be noted in the Screening documentation for the individual subject.

### 8.2.2. Reporting Serious Adverse Events

SAEs must be immediately reported at least within 24 hours of the Investigator becoming aware of the event to Sponsor or its designated representative using the SAE report form provided by Sponsor.

In particular, if the SAE is fatal or life-threatening, Sponsor must be notified immediately, irrespective of the extent of available AE information. This timeframe also applies to additional (follow-up) information that becomes available on previously forwarded SAE reports. Sponsor will then follow expedited reporting procedures according to local and international regulations as appropriate.

The Investigator is obligated to pursue and provide information to Sponsor on all SAEs in accordance

with the timeframes for reporting specified above. In addition, an Investigator may be requested by Sponsor to obtain specific additional follow-up information in an expedited fashion. In general, this will include a description of the SAE, which should be provided in sufficient detail so as to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses must be provided. In the case of a subject death, a summary of available autopsy findings must be submitted as soon as possible to Sponsor or its designated representative.

All SAEs will be followed until event resolution or stabilisation (for chronic events), if possible, even when a subject is withdrawn before study completion. For chronic events that do not fully resolve until years later, the outcome should be reported as 'resolved with sequelae' as soon as the event has stabilised or returned to baseline. Follow-up information for the SAE should be actively sought and submitted as the information becomes available.

If the Investigator detects an SAE in a subject after the EOS, and considers the event to be related to the IP or procedures, the Investigator should contact the Sponsor to determine how the SAE should be documented and reported.

### 8.3. Adverse Events of Special Interest

The following AEs in the study eye will be classified as AESIs in this study:

- Any case of pre-injection IOP of ≥ 25 mm Hg
- Any case of IOP ≥ 35 mmHg at any time
- Any case of intraocular infection such as endophthalmitis
- Any case of intraocular inflammation such as iritis, vitritis, and iridocyclitis
- Iatrogenic traumatic cataract

### 8.4. Pregnancy

Any pregnancy, including those of female partners of male subjects treated with the IP, should be reported to the Sponsor. If the female partner of a male subject becomes pregnant, a written consent must be obtained from the female partner before collecting any pregnancy-related information. All pregnancies associated with the subject, from the time the subject receives IP until either Day 7 (EOS visit) or ET visit should be reported to Sponsor. Pregnancy reports should be made within 24 hours of the Investigator becoming aware of the pregnancy using the pregnancy report form.

Although pregnancy is not an AE, all pregnancies must be followed up until 6-8 weeks after the outcome of the pregnancy becomes available, unless the subject is lost to follow-up. The pregnancy outcome should be notified to Sponsor by submitting a follow-up Pregnancy report form. If the outcome of the pregnancy meets SAE criteria then the Investigator should report this case according to the SAE reporting process (Section 8.2.2).

#### 8.4.1. Pregnancy Prevention

In order to minimise the foetal or embryonic risk to exposure, childbearing potential female subjects (i.e., fertile, following menarche and until becoming post-menopausal unless permanently sterile) or male subjects must agree to use at least 2 effective forms of hormonal/non-hormonal contraception method OR 1 highly effective non-hormonal form of contraception.

Effective forms of contraception are the following:

- Established use of hormonal contraception associated with inhibition of ovulation: oral, injected, intravaginal, transdermal or implanted hormonal contraception
- Placement of intrauterine device or intrauterine hormone-releasing system
- Bilateral tubal occlusion
- Vasectomy is allowed for male subjects and female subjects of childbearing potential with a sole vasectomised male partner. Vasectomised subjects or partners should be medically confirmed for sterilisation. Male sterilisation where the vasectomised male partner should be the sole partner.
- Physical barrier [Note: Female condom and male condom should not be used together]

And highly effective non-hormonal contraception includes the following:

- True abstinence when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal post-ovulation methods) and withdrawal are not acceptable methods of contraception.

## 9. Statistical Methods and Data Analysis

Further information on the statistical methods to be used in this study will be provided in the statistical analysis plan (SAP), which will be finalised prior to the database lock for reporting the main clinical study report (CSR).

### 9.1. Statistical Hypotheses

Not available.

### 9.2. Analysis Sets

The following sets will be used for the analyses performed in the study:

- Enrolled set (ENR) consists of all subjects who provide informed consent for this study.
- Full Analysis Set (FAS) consists of all subjects in ENR who are eligible and received IP during the study period and have usability assessment.
- Per-Protocol Set (PPS) consists of all subjects in FAS who have IP injection without any major protocol deviations (PDs) that have impact on the usability assessment. Major PDs that will lead to exclusion from this set will be pre-defined prior to analyses.
- Safety Set (SAF) consists of all subjects in ENR who receive at least one IP during the study period.

### 9.3. Subject Demographic and Baseline Characteristics

Subject demographics and baseline characteristics will be summarised for the FAS. Continuous variables (e.g., age) will be summarised with descriptive statistics (n, mean, SD, median, minimum, maximum) and categorical variables (e.g., gender, race, ethnicity) will be summarised with frequency and percentage.

### 9.4. General Approach of Statistical Analyses

For descriptive statistics in continuous variables, n, mean, SD, median, Min, and Max will be displayed. For categorical variables, frequency counts and percentage will be displayed.

Any surgical and medical history and prior/concomitant medications will be summarized for the FAS and SAF, respectively. Also, by-subject listings of surgical procedures, medical history, and prior/concomitant medications will be provided respectively.

For AEs, summary of AEs by several categories such as system organ class (SOC), preferred term (PT), severity, causality will be provided in tables. Also, by-subject listing of AE data will be provided for the SAF.

### 9.5. Analysis of the Primary Objective

Percentage of successful task completions (Day 1) will be summarized for the FAS.

### 9.6. Analysis of the Secondary Objective(s)

Percentage of successful completion on critical tasks (Day 1), percentage of successful completion on essential tasks (Day 1) will be summarized descriptively for the FAS.

All reported terms of AEs (ocular or non-ocular) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®). For all AE and SAE tables, subjects will be counted once for each PT and each SOC. All analyses of AEs will be performed using the SAF.

### 9.7. Sample Size Calculations

No formal statistical power calculations to determine sample size will be performed for this study.

## 10. Data Collection and Management

### 10.1. Data Confidentiality

Study information will be labelled with a code number, and will not include the subject's name, or other information that could identify them. A list linking the code and the subject's name will be kept in the site files as required by ICH-GCP.

The coded information will be sent to the Sponsor (or designee) who will analyse it and report the study results both to regulatory and ethical authorities. The Sponsor may also place data on public websites or publish journal articles based upon these results. Care will be taken to prevent subjects being identified through these publications. In addition, data may be shared with other companies or researchers to aid further research. Such data sharing practices will be covered by confidentiality agreements. No-one outside the Investigational site will have access to subject-identifiable information.

### 10.2. Monitoring

The Sponsor has engaged the services of a Contract Research Organisation (CRO) to perform all monitoring functions within this clinical study. The monitors will work in accordance with the CRO Standard Operation Procedures (SOPs) and have the same rights and responsibilities as monitors from the Sponsor organisation. Monitors will establish and maintain regular contact between the Investigator and the Sponsor.

Monitors will evaluate the competence of each Investigational site and inform the Sponsor about any problems relating to facilities, technical equipment or medical staff. During the study, monitors will

check that written informed consent has been obtained correctly from all subjects and that data are recorded correctly and completely. Monitors will also perform source data verification by comparing entries in the eCRF with corresponding source data and informing the Investigator of any errors or omissions. Monitors will verify adherence to the protocol at the Investigational site. All PDs will be reported to the Sponsor via the Monitoring Visit Reports. Monitors will arrange for the supply of IP and ensure appropriate storage conditions are maintained.

Monitoring visits will be conducted at regular intervals according to ICH-GCP. The monitor will provide written reports to the Sponsor on each occasion they contact with the Investigator regardless of whether it is by phone or in person.

Further details on the monitoring processes and the level of source data verification to be performed will be outlined in the monitoring plan.

### 10.3. Data Handling and Record Keeping

The Investigator must maintain essential study documents (protocol and protocol amendments, completed eCRFs, signed ICFs, relevant correspondence, and all other supporting documentation) until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years after the formal discontinuation of clinical development of the IP or at least 25 years after the end of the clinical trial. These documents should be retained for a longer period if required by the applicable regulatory requirements or the hospital, institution or private practice in which the study is being conducted. Subject identification codes (subject names and corresponding study numbers) will be retained for the same period of time. These documents may be transferred to another responsible party, deemed acceptable by the Sponsor, and who agrees to abide by the retention policies. Written notification of transfer must be submitted to the Sponsor. The Investigator must contact the Sponsor prior to disposing of any study records and obtain written permission to do so.

### 10.4. Database Management and Coding

Data generated within this clinical study will be handled according to the relevant SOPs of the data management of the Sponsor (or an appropriate company designated by the Sponsor to perform these activities). Subject data will be captured in an eCRF and reviewed by the monitor to check adherence to the protocol and to detect any data inconsistency or discrepancy.

The Investigator must ensure that the clinical data required by the clinical study protocol are carefully reported in the eCRF. He/she must also check that the data reported in the eCRF correspond to those in the medical records.

Data must be entered into eCRFs in English by the Investigator or designated site personnel in a timely manner. Source documents should be available during periodic visits by study monitors to enable review for completeness and acceptability. Any correction to the data entered into the eCRF must be carried out by the Investigator or a designated member of staff. These changes may be made either on the initiative of the site staff or in response to monitoring or data queries. Any changes to written data must be made using ICH-GCP corrections and any change to electronic data should be made in a system which can provide an audit trail. Monitors and clinical data managers will review the eCRF for accuracy and can generate queries to the investigational staff for resolution. Corrections will be recorded in an audit trail that records the old information, the new information, and identification of the person making the changes, date of correction made and reason for change. The Investigator must sign and date the eCRF pages as indicated.

Medical/surgical history and underlying diseases and AEs will be coded using the MedDRA.

Concomitant medications will be coded using the World Health Organisation-Drug Global. The versions of coding dictionaries used will be stated in the CSR.

### 10.5. Quality Control and Quality Assurance

During the conduct of the study, the Sponsor or its agent will conduct periodic monitoring visits to ensure that the protocol and ICH-GCP are being followed. The monitors may review source documents to confirm that the data recorded are accurate. The Investigator and institution will allow the domestic and foreign regulatory authorities, the authorized representative of the Sponsor including monitors and auditors' direct or remote access to source documents to perform this verification without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations. The Investigational site may be subject to review by the IRB/IEC, and/or to quality assurance audits performed by the Sponsor, and/or to inspection by appropriate regulatory authorities. It is important that the Investigators and their relevant personnel are available during the monitoring visit, possible audits and/or regulatory inspection(s) and that sufficient time is devoted to the process.

### 10.6. Protocol Deviation

PDs will be pre-defined prior to subject enrolment and documented separately named as Protocol Deviation Definition List which includes category (e.g., violation of inclusion/exclusion criteria, use of prohibited medication, non-compliance with treatment), deviation description, severity (major or minor), time point for each PD. Major PDs are defined as those deviations from the protocol likely to have an impact on the perceived safety and usability assessment of study treatments.

PDs will be reviewed and confirmed prior to database lock to decide which subjects and/or subject data will be excluded from certain analyses. Decisions regarding the exclusion of subjects and/or subject data from analyses will be documented and approved prior to database lock.

## 11. Ethics Considerations and Administrative procedures

### 11.1. Institutional Review Boards and Independent Ethics Committees

The Investigator and the Sponsor will follow all local laws and regulations relating to contact with and approvals from the IRB/IEC.

The CRO must provide the Sponsor with documentation of IRB/IEC approval of the protocol and informed consent before the study may begin at the Investigational site. The CRO will supply documentation to the Sponsor relating any approvals of revisions to the ICF or amendments to the protocol.

The Sponsor and/or the CRO will report promptly to the IRB/IEC any new information that may adversely affect the safety of subjects or the conduct of the study. Similarly, the Investigator will submit written summaries of the study status to the IRB/IEC on a regular basis and in accordance with the timelines required locally. Upon completion of the study, the Investigator will provide the ethics committee with a report on the outcome of the study if required by local regulations.

### 11.2. Ethical Conduct of the Study

This study will be conducted and informed consent will be obtained from each subject according to the ethical principles stated in the Declaration of Helsinki (2013), the applicable guidelines for ICH-GCP and the applicable drug and data protection laws and regulations of the countries where the study will be conducted.

### 11.3. Subject Information and Informed Consent

The ICF will be used to explain the risks and benefits of study participation to the subject in simple terms before the subject is entered into the study. The ICF contains a statement that the consent is freely given, that the subject is aware of the risks and benefits of entering the study, and that the subject is free to withdraw from the study at any time. Written consent must be given by the subject, after the receipt of detailed information on the study.

The Investigator is responsible for ensuring that informed consent is obtained from each subject or legal representative and for obtaining the appropriate signatures and dates on the ICF prior to the performance of any protocol procedures and prior to the administration of IP. The Investigator will provide each subject with a copy of the signed and dated ICF and this will be documented in the subject's source notes.

### 11.4. Investigator Information

#### 11.4.1. Investigator Obligations

This study will be conducted in accordance with the ICH-GCP (2016), the ethical principles that have their origin in the Declaration of Helsinki (2013) and local laws and regulations.

The Investigator is responsible for ensuring that the study is conducted according to the signed Investigator statement, the clinical study protocol and applicable regulations; for protecting the rights, safety, and welfare of subjects under the Investigator's care; and for the control of drugs under investigation. The Investigator must obtain the informed consent of each subject to whom IP is administered.

#### 11.4.2. Coordinating Investigator

The Sponsor will designate the Coordinating Investigator who will have the responsibility for the coordination of the Investigators in a multicentre clinical study.

#### 11.4.3. Training of Investigator Site Personnel

Before the first subject is enrolled into the study, a Sponsor representative will review and discuss the requirements of the clinical study protocol and related documents with the investigational staff and will also train them in any study-specific procedures.

The Investigator will ensure that appropriate training relevant to the study is given to all site staff and that any new information relevant to the performance of this study is forwarded to the staff involved.

The Investigator will maintain a record of all individuals involved in the study (medical, nursing, and other staff).

#### 11.4.4. Protocol Signatures

The Investigator must sign the Investigator Signature Page of this protocol prior to starting recruitment for the study. By signing the protocol, the Investigator confirms in writing that he/she has read, understands and will strictly adhere to the clinical study protocol and will conduct the study in accordance with ICH-GCP and applicable regulatory requirements. The study will not be able to start at any Investigational site where the Investigator has not signed the clinical study protocol.

#### 11.4.5. Financing and Insurance

Samsung Bioepis Co., Ltd. is the Sponsor of this study and will be providing the finances to cover the

operation of the study. Details of financial agreements are provided in the Clinical Study Agreements with the Investigational sites and in contracts with other companies involved in the running of the study.

The Sponsor has obtained suitable insurance for this study. A copy of the insurance details will be provided to each Investigator who will be responsible for providing the IRB/IEC with these details according to local requirements.

## 12. Publication Policy

The Sponsor supports the efforts of health authorities to increase the transparency of medical research conducted in human subjects. The Sponsor will register and maintain the information of clinical studies on a public registry program such as www.clinicaltrials.gov. The Sponsor is committed to the public disclosure of the results from clinical studies through posting on public clinical study data banks such as www.clinicaltrials.gov. The Sponsor will comply with the guidelines of regulatory authorities with regards to public registration and disclosure of clinical study data.

The clinical study data collected during the study are confidential and proprietary to the Sponsor. Sponsor shall have the right to delete any confidential or proprietary information contained in any proposed abstract or presentation.

Any publications from this study should be approved by the Sponsor prior to publication or presentation. The rights of the Investigator with regard to publication of this study are described in the Clinical Study Agreement.

## 13. References

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2. Prescribing Information of Lucentis®. FDA. (May 20, 2018). Retrieved Jul 05, 2021 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/125156s117lbl.pdf

3. Guidance on the management of clinical trials during the COVID-19 (Coronavirus) pandemic. EMA. (Mar 2020, Version 4.0 on Feb 04, 2021). Retrieved May 26, 2021 from https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf

4. Guidance on conduct of clinical trials of medical products during COVID-19 public health emergency. FDA. (Mar 2020, updated on Jan 27, 2021). Retrieved May 26, 2021 from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

5. Guideline on similar biological medicinal products containing biotechnology-derived protein as active substance: non-clinical and clinical issues. EMA. (Jul 01, 2015). Retrieved May 26, 2021 from https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-similar-biological-medicinal-products-containing-biotechnology-derived-proteins-active_en-2.pdf

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7. Sassalos TM, Paulus YM. Prefilled syringes for intravitreal drug delivery. Clin Ophthalmol. 2019, 13: 701-706.

8. Souied E, Nghiem-Buffet S, Leteneux C, et al. Ranibizumab prefilled syringes: benefits of reduced preparation times and less complex preparation procedures. Eur J Ophthalmol. 2015, 25(6):529-34.

9. Baudin F, Benzenine E, Mariet AS, et al. Association of acute endophthalmitis with intravitreal injections of corticosteroids or anti-vascular growth factor agents in a nationwide study in France. JAMA Ophthalmol. 2018, 136(12):1352-1358.

10. Storey PP, Tauqeer Z, Yonekawa Y, et al. The impact of prefilled syringes on endophthalmitis following intravitreal injection of ranibizumab. Am J Ophthalmol. 2019, 199:200-208.

11. Falavarjani KG, Nguyen QD. Adverse events and complications associated with intravitreal injection of anti-VEGF agents: a review of literature. Eye. 2013, 27(7):787-94.

# APPENDIX 1: TASK COMPLETION EVALUATION QUESTIONNAIRE (For Observer only)

**Protocol Number (version):**

**Subject ID:**

Please write down the performer, a designee (ophthalmologist or assistant) on each task.

Please check whether each task of Healthcare Professional (HCP) is successfully performed (Y/N, Yes or No). Note that tasks will be considered to be successfully completed if tasks meet success criteria or corrected results are achieved without a use failure, even if the instruction for use (IFU) are not followed exactly.

If task was not successfully completed, please describe the reason by asking HCP(s) in the follow-up session. Open-ended questions will be necessary when interviewing HCP(s) in the follow-up session.

| Order | Task | Task description | Performer | Success (Y/N) | Describe the reason of Use Failure by asking HCPs in the follow-up session |
|---|---|---|---|---|---|
| 1 | Open the carton | Open the carton | | | |
| 2 | Remove contents | Removes sealed blister pack from carton | | | |
| 3 | Peel the lid off the blister pack | Peels the lid off blister pack without damaging the Product | | | |
| 4 | Carefully remove the PFS from the blister using aseptic technique | Removes the PFS out of blister pack and does not damage the PFS | | | |
| 5 | Remove the syringe cap | Removes syringe cap without damaging PFS | | | |
| 6 | Attach a needle | Fully attaches a needle to the PFS Luer lock | | | |

| Order | Task | Task description | Performer | Success (Y/N) | Describe the reason of Use Failure by asking HCPs in the follow-up session |
|---|---|---|---|---|---|
| 7 | Remove the needle cap | Pulls the needle cap straight off without damaging the PFS<br>*Note that it is acceptable to remove cap before or after setting dose | | | |
| 8 | Set the dose | Removes air from PFS<br>Sets the required dose by pushing the plunger rod | | | |
| 9 | Insert the needle into the injection site | Inserts the needle into the injection site | | | |
| 10 | Press the plunger down to inject the medication | Presses the plunger down completely | | | |
| 11 | Remove the needle from the injection site | Pulls needle straight out from the injection site | | | |
| 12 | Dispose product | Disposes of the PFS with attached needle according to local regulation | | | |

PFS = Pre-filled syringe

| | |
|---|---|
| Observer Signature | Date |

| | |
|---|---|
| HCP Signature | Date |
| HCP Signature | Date |

# APPENDIX 2: TASK COMPLETION EVALUATION QUESTIONNAIRE (For HCP only)

**Protocol Number (version):** **Subject ID:**

Please mark which of the following tasks you performed (Y/N). For the task you performed, please check whether your task was successfully done (Y/N).

| Order | Task | Did you perform? (Y/N) | Do you think it was successful? (Y/N) | If not, please describe the reason. |
|---|---|---|---|---|
| 1 | Open the carton | | | |
| 2 | Remove contents | | | |
| 3 | Peel the lid off the blister pack | | | |
| 4 | Carefully remove the PFS from the blister using aseptic technique | | | |
| 5 | Remove the syringe cap | | | |
| 6 | Attach a needle | | | |
| 7 | Remove the needle cap | | | |
| 8 | Set the dose | | | |
| 9 | Insert the needle into the injection site | | | |
| 10 | Press the plunger down to inject the medication | | | |
| 11 | Remove the needle from the injection site | | | |
| 12 | Dispose product | | | |

HCP Signature _____ Date _____

# APPENDIX 3: Grading Scale for Anterior Chamber Flare

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

Reference: The Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of Uveitis Nomenclature for Reporting Clinical Data: Results of the First International Workshop. *American journal of ophthalmology*. 2005;140(3): 509-516.

# APPENDIX 4: Grading Scale for Anterior Chamber Cells

| **Grading scale for anterior chamber cells**<br>The intensity of the cellular reaction in the anterior chamber is graded according to the number of inflammatory cells seen in a 1 x 3 mm high-powered beam at full intensity at a 45°-60° angle. | |
|---|---|
| **Grade** | **Description** |
| 0 | No inflammatory cells. |
| Trace | < 5 cells. |
| 1+ | 5 – 9 cells. |
| 2+ | 10 – 19 cells. |
| 3+ | 20 – 29 cells. |
| 4+ | ≥ 30 cells, cells too numerous to count. |

Reference: Bloch-Michel E., Nussenblatt RB. International Uveitis Study Group recommendations for the evaluation of intraocular inflammatory disease. *Am J Ophthalmol*. 1987;103(2):234-5.

# APPENDIX 5: Grading Scale for Vitreal Inflammatory Response

| Grading scale for vitreal inflammatory response | | |
|---|---|---|
| **Cells in Retro-illuminated Field** | **Description** | **Grade** |
| 0-1 | Clear | 0+ |
| 2-20 | Few opacities | Trace |
| 21-50 | Scattered opacities | 1+ |
| 51-100 | Moderate opacities | 2+ |
| 101-250 | Many opacities | 3+ |
| > 251 | Dense opacities | 4+ |

Reference: Nussenblatt RB, Palestine AG, Chan CC, Roberge F. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. *Ophthalmology*. 1985;92:467-71.

# Protocol Signature Pages

## SIGNATURE PAGE

**Declaration of Sponsor Representative**

Protocol Title: An open-label, single group, single-dose clinical study to evaluate the usability of the pre-filled syringe (PFS) of SB11 in subjects with Neovascular Age-Related Macular Degeneration (AMD) or Macular Oedema Secondary to Retinal Vein Occlusion (RVO)

This clinical study protocol was subjected to critical review. The information it contains is consistent with current knowledge of the risks and benefits of the investigational medicinal product, as well as with the moral, ethical, and scientific principles governing clinical research as set out in the Declaration of Helsinki, 2013 and the guidelines on Good Clinical Practice applicable to this clinical study.

**Sponsor Representative**

Name: PPD

Institution: Samsung Bioepis Co., Ltd.

Signature: PPD

# SIGNATURE PAGE

**Declaration of the Principal Investigator**

Protocol Title: An open-label, single group, single-dose clinical study to evaluate the usability of the pre-filled syringe (PFS) of SB11 in subjects with Neovascular Age-Related Macular Degeneration (AMD) or Macular Oedema Secondary to Retinal Vein Occlusion (RVO)

This clinical study protocol was subjected to critical review. The information it contains is consistent with current knowledge of the risks and benefits of the investigational medicinal product, as well as with the moral, ethical, and scientific principles governing clinical research as set out in the Declaration of Helsinki, 2013 and the guidelines on Good Clinical Practice applicable to this clinical study.

**Principal Investigator**

Name: _____

Institution: _____

Signature: _____ Date: _____
(MMM DD, YYYY)