CLINICAL STUDY PROTOCOL

Study Title: A Phase 2, Multi-center, Open-label Study to Evaluate the Safety and Efficacy of VGT-309, a Tumor-Targeted, Activatable Fluorescent Imaging Agent, in Subjects Undergoing Surgery for Cancer in the Lung

Sponsor: Vergent Bioscience, Inc
[redacted]

Protocol Number: VGT-309-2B-2023

IND Number: 143390

Medical Emergencies: [redacted]

Medical Monitor: [redacted]

Version: Version 3.0
15 March 2024

Replaces: Version 2.0
14 August 2023

VERGENT BIOSCIENCE, INC. – PROTOCOL APPROVAL
Version 3.0 – 15 March 2024

[redacted]

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[redacted]

[redacted]

PROTOCOL SIGNATURE PAGE

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Protocol Number:	VGT-309-2B-2023
Protocol Version/Date:	Version 3.0 15 March 2024
Sponsor Name:	Vergent Bioscience, Inc [redacted]

Declaration of Investigator

I confirm that I have read the above-mentioned protocol and its attachments. I agree to conduct the described trial in compliance with all stipulations of the protocol, regulations and ICH E6 Guideline for Good Clinical Practice (GCP).

Principal Investigator Written Name: _____

Principal Investigator Signature: _____

Date: _____

TABLE OF CONTENTS

Study Synopsis

Sponsor	Vergent Bioscience, Inc. [redacted]
Title	A Phase 2, Multi-center, Open-label Study to Evaluate the Safety and Efficacy of VGT-309, a Tumor-Targeted, Activatable Fluorescent Imaging Agent, in Subjects Undergoing Surgery for Cancer in the Lung
Protocol Number	VGT-309-2B-2023
Lead Clinical Investigator	[redacted]
Study Centers	Up to 7 Centers in the US and Australia
Investigational Medicinal Product (IMP) (also referred to as Study Drug)	VGT-309 for Injection, 10 mg/vial
Primary Efficacy Objective	Assess the efficacy of VGT-309 with near-infrared (NIR) imaging for lesion visualization when compared to standard surgical techniques in subjects undergoing surgery for proven or suspected cancer in the lung.
Secondary Efficacy Objective	Assess the utility of VGT-309 with NIR imaging to identify cancerous tissue as confirmed by histopathology.
Safety Objective	Determine the safety and tolerability of VGT-309 in subjects with proven or suspected cancer in the lung.
Introduction and Rationale	[redacted]

Primary Endpoint - Efficacy	Identify the proportion of subjects with <u>at least one</u> Clinically Significant Event (CSE) as defined by: A. Intraoperative localization of one or more preoperatively identified lung lesions using VGT-309 with NIR imaging when standard surgical techniques using white light and/or palpation failed to identify the lesion(s), and lesion(s) are confirmed by histologic examination to be other than normal lung tissue. B. Identification of one or more synchronous or occult lung lesions using VGT-309 with NIR imaging when standard surgical techniques using white light and/or palpation and preoperative imaging failed to identify the lesion(s), and lesion(s) are confirmed by histologic examination to be cancerous or precancerous. C. Identification of fluorescence within ≤10 mm from the inside edge of the closest staple line as measured by the investigator *ex vivo* in the operating room using NIR imaging, with pathologic margin confirmed by histologic examination to be ≤ 10 mm. NOTE: Margins from excisions of known or suspected metastases at the time of the surgery, OR diagnostic wedge resections where a completion lobectomy or segmentectomy was subsequently performed, will not be considered for Margin CSE inclusion. D. Identification of lymph nodes by VGT-309 with NIR imaging confirmed by histologic examination to be cancerous.
Safety Endpoints	Assessment of clinical laboratory tests, physical exam results, ECGs and vital sign measurements at various time points during the study, and documentation of treatment-emergent adverse events.
Secondary Endpoints - Efficacy	To evaluate the sensitivity, positive predictive value (PPV), and 1-PPV of VGT-309 with NIR imaging for lesion(s) *in vivo*: 1. Sensitivity is defined as the probability that the tissue fluoresces when it is cancer, as confirmed by histology (TP/(TP+FN)) * 2. Positive predictive value (PPV) is defined as the probability that a tissue sample contains cancer on histologic exam if it fluoresces ((TP/(TP+FP)) 3. 1-Positive predictive value (1-PPV) is defined as the probability that a tissue sample does not contain cancer when it fluoresces ((FP/(TP+FP))* * TP = true positive, FP = false positive, FN = false negative
[redacted]	[redacted]
Inclusion Criteria	In order to be enrolled in the study the subject must: 1. Be willing and able to sign the informed consent and comply with study procedures. 2. Be at least 18 years of age.

	3. Meet the following conditions: a. Female participants must be of non-childbearing potential, or, b. If of childbearing potential, be non-pregnant or non-lactating and agree to use highly effective contraception from screening through Day 30 after treatment. c. Male participants, if not surgically sterilized, and if engaging in sexual intercourse with a female partner of childbearing potential, must be willing to use highly effective contraception from screening through 30 days after treatment and agree not to donate semen during this waiting period. d. Highly effective contraception involves the use of a condom for the male, plus one of the following for the female: • Oral, injectable, implantable, intravaginal, or transdermal hormonal contraceptives, or • Intrauterine device or intrauterine hormone-releasing system • NOTE: Subjects who abstain from heterosexual intercourse as their usual and preferred lifestyle, will not be required to use contraception as described above. They are required to maintain abstinence from screening through Day 30 after treatment. • Note: Subjects in a same sex relationship, must use a barrier form of contraception (e.g., condom, diaphragm) to protect against the transfer of the study drug in any bodily fluids. 4. Have a lung nodule or mass that might be considered primary lung cancer or lung metastases whether or not it is biopsy-proven before surgery. 5. Be scheduled to undergo standard of care surgical resection for a lung nodule or mass with diagnostic and/or curative intent 6. Have acceptable kidney and liver functions at study entry as evidenced by: a. ALT/AST $\leq$ 1.5 times the upper limit of normal b. Calculated Creatinine Clearance (CrCl) $\geq$ 50 ml/min (manual calculation using Cockcroft-Gault equation) c. Total bilirubin $\leq$ 1.5 times the upper limit of normal 7. Have an ECOG score of 0-2. 8. Meet all standard of care surgical and general anesthesia requirements. 9. Have not participated in an *interventional* clinical trial within the last 30 days (participation in a disease registry or quality of life study is not exclusionary).
Exclusion Criteria	The subject may not be enrolled in the study if: 1. They are not a candidate for standard of care surgery based on opinion of the surgeon, anesthesiologist, or other consulting physician. 2. They have a known allergy or reaction to ICG, other radiographic contrast agent, or any component of VGT-309. 3. They have congenital long QT syndrome or QTcF > 470ms by history or at Screening ECG. 4. They have received chemotherapy or immunotherapy within 4 weeks prior to study enrollment. 5. They are prisoners, institutionalized individuals, or are unable to consent for themselves. 6. They have any other co-morbidity or habit that the Investigator believes will interfere with their ability to comply with and complete the study.

Study Methodology and Design	This is a Phase 2, multi-center, open-label study to evaluate the safety and efficacy of VGT-309, a tumor-targeted, activatable fluorescent imaging agent, to identify cancer using NIR imaging in subjects undergoing surgery for proven or suspected cancer in the lung. Approximately 100 subjects will be enrolled to ensure at least 86 subjects are evaluable with the option to expand enrollment by protocol amendment if deemed necessary by the DSC to meet primary and/or secondary objectives. Following agreement with and signing of the informed consent, subjects will undergo screening measurements for the study within 4 weeks prior to the anticipated dosing: 1. Medical, surgical and medication history. 2. Complete physical exam, including vital signs and height. 3. Weight (needed for dose calculation) 4. Chemistry, hematology, coagulation and urinalysis with microscopy clinical laboratory studies. 5. 12-lead ECG. 6. Serum pregnancy test for females of child-bearing potential. [redacted] [redacted] Following surgery, subjects will be monitored for safety during their hospitalization. Between 7 to 14 days and 25 to 35 days after surgery, the subjects will return to the clinic or have a telehealth visit for safety assessments. At the last visit, if there are no adverse events requiring further follow up, subjects will then be released from the study. If a subject chooses to withdraw from the study prior to the final visit, they will be asked to undergo a final safety assessment before their departure.
VGT-309 Description	[redacted].
VGT-309 Dosing	The dose for this study is 0.32 mg/kg of VGT-309 and [redacted] Based on ongoing investigations and after review by the DSC this dose may be modified. [redacted]
Data Safety Committee (DSC)	A Data Safety Committee will be appointed by Vergent Bioscience and will include at a minimum: [redacted]

	
Enrollment Period	It is expected that the time required to enroll 100 subjects in this study will be approximately 8 months.
Study Duration	Each subject may expect to be on study for up to 65 days: 
Primary Efficacy Assessments	*In vivo,* intra-operatively: • Use of white light and/or palpation followed by NIR imaging for localization of preoperatively identified lung lesion(s), potential synchronous or occult malignant lung lesion(s), and potential cancer-containing lymph nodes. *Ex vivo*, in the operating room: • NIR imaging to determine fluorescence proximity to closest resection margin. *Ex vivo* pathology • Histologic examination of resected tissues.
Secondary Efficacy Assessments	Comparison of NIR imaging, conducted both inside and outside the subject, to results of histologic examination.
Safety Assessments	• Treatment-emergent adverse events • Clinical laboratory assessments of blood and urine (See section 9.2.3 for details): o Hematology Panel o Coagulation – INR and aPTT o Chemistry Panel including liver function tests (LFTs) and amylase o Urinalysis with microscopy • Pre- and post-dose ECGs (in triplicate) • Vital signs (BP, HR, temp, resp) • Additional studies if identified during the trial as being necessary to adequately assess safety

	Pregnancies that occur between dosing and Day 30 will be followed until 6 weeks after delivery or termination of the pregnancy. (Refer to Schedule of Assessments for details)
Statistical Methods	**Sample Size:** For the primary efficacy endpoint of proportion of subjects with at least one CSE, assuming a 20% true rate of at least one CSE, two-sided 5% Type 1 error and 80% power, the sample size to rule out a CSE rate less than or equal to 10% requires 86 evaluable subjects in the primary analysis group. The trial will have met the primary endpoint if at least 15/86 (17.4%) subjects have at least one CSE. The 95% two-sided Clopper-Pearson exact confidence bound at 17.4% is (10.1%, 27.1%). **Efficacy** A descriptive analysis of the baseline subject and tumor characteristics will be performed. Quantitative data will be presented as a standard set of summary statistics (n/mean (standard deviation)/ median/minimum/maximum). Categorical data will be expressed as frequency (%). For the primary endpoint analysis, the proportion of subjects undergoing NIR imaging with at least 1 CSE will be identified and tested under the following null hypothesis: Ho: $P \leq 0.10$ The alternative hypothesis states that the proportion of subjects undergoing NIR imaging with at least 1 CSE will be greater than the chosen margin of 0.10: Ha:$P>0.10$ At 86 evaluable subjects, this trial is power at 80% to reject the null hypothesis of a 10% or fewer of subjects experiencing at least one CSE. Two-sided 95% exact confidence intervals for the proportion of subjects with at least one CSE will be constructed. For the secondary endpoint analysis sensitivity, PPV, and 1-PPV will be calculated and presented along with 95% confidence intervals using GEE model analysis to factor in within-subject correlation for subjects with multiple tumors. **Safety:** Adverse event (AE) data will be listed by subject. Treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and AEs leading to study drug discontinuation will be summarized by system organ class and preferred term using the current version of the Medical Dictionary for Regulatory Activities (MedDRA). Listings of individual subject laboratory results will be provided. Laboratory results, Clinically Significant and change from baseline for selected lab tests will be summarized by treatment at scheduled visits. Twelve-lead ECGs and vital signs measurements will be listed by subject and summarized by incidence of events/abnormalities or descriptive statistics as appropriate. Individual data for physical examination findings, prior and concomitant medications and medical history will be provided.

List of Abbreviations:

AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
APTT	Activated Partial Thromboplastin Time
AR	Adverse Reaction
AST	Aspartate Aminotransferase
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CFR	Code of Federal Regulations
CT	Computed Tomography
eCRF	Electronic Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DSC	Data Safety Committee
ECG	Electrocardiogram
EDC	Electronic Data Capture
FDA	Food and Drug Administration
GEE	Generalized Estimating Equation
GCP	Good Clinical Practice
GGT	Gamma-glutamyl-transferase
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
Hgb	Hemoglobin
HREC	Human Research Ethics Committee
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
INR	International Normalized Ratio
IRB	Institutional Review Board
ITT	Intent-to-treat
IV	Intravenous
kg	kilogram
L	Liter
LDH	Lactate Dehydrogenase
LFT	Liver Function Test
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
mL	Milliliter
NIR	Near-infrared (imaging)
NOAEL	No-Observed-Adverse-Effect-Level
PI	Principal Investigator
PICF	Patient Informed Consent Form
PK	Pharmacokinetic
RBC	Red Blood Cell
ROC	Receiver Operating Characteristic
SAE	Serious Adverse Event
SD	Sprague-Dawley (rats)
SUSAR	Suspected Unexpected Serious Adverse Reaction

1. INTRODUCTION

A comprehensive review of VGT-309 is contained in the Investigator's Brochure supplied by the Sponsor, Vergent Bioscience, Inc. The Investigator's Brochure should be reviewed prior to initiating the study.

1.1 Background and Rationale

[redacted]

Non-small cell lung cancer (NSCLC) is a particularly lethal cancer for which the best opportunity for cure comes from early detection and complete resection at surgery. Great advances in minimally invasive surgery (robotics; video-assisted thoracic surgery) have provided the opportunity to reduce the impact of major lung resection on the subject with lung cancer.

Minimally invasive surgery has come at the cost of increasing difficulty in localizing small cancers deep in the lung parenchyma due to the elimination of the ability to palpate the lung through a large thoracotomy incision. Currently this is overcome by one of three methods: a) remove a larger amount of tissue than required for biopsy of a suspicious lesion; b) wait until a suspicious lesion has grown sufficiently to allow easier detection at surgery; or c) perform a thoracotomy.

None of these options is optimal. The first, because a large amount of lung may be unnecessarily removed if the lesion is not cancer; the second, because the opportunity for early curative surgery may be missed if the cancer spreads in the months waiting for it to grow further; and the third negates the proven benefit of minimally invasive surgery.

The use of a tumor-targeted, activatable fluorescent imaging agent that can be taken up and bound by cancer tissues and visualized by tumor-specific fluorescence under NIR light during the surgical procedure could solve this problem if the drug readily identified the lesion for the surgeon. This could allow early and well-targeted surgical biopsy and subsequent appropriate cancer surgery for the correctly identified population.

[redacted]

1.2 Nonclinical *In Vitro* and *In Vivo* Experience

[redacted]

[redacted]

1.2.1 Genotoxicity

[redacted]

1.2.2 Safety Pharmacology

[redacted]

1.2.3 Local Tolerance

[redacted]

1.2.4 Single Dose Toxicity in Sprague-Dawley Rats and Beagle Dogs

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Refer to the Investigator's Brochure for further details.

2. STUDY OBJECTIVE AND ENDPOINTS

2.1 Objectives:

2.1.1 Primary Efficacy Objective:

Assess the efficacy of VGT-309 with near-infrared (NIR) imaging for lesion visualization when compared to standard surgical techniques in subjects undergoing surgery for proven or suspected cancer in the lung.

2.1.2 Secondary Efficacy Objective:

Assess the utility of VGT-309 with NIR imaging to identify cancerous tissue as confirmed by histopathology.

2.1.3 Safety Objective:

Determine the safety and tolerability of VGT-309 in subjects with proven or suspected cancer in the lung.

2.2 Endpoints:

2.2.1 Primary Efficacy Endpoint:

Identify the proportion of subjects with at least one Clinically Significant Event (CSE) as defined by:

A. Intraoperative localization of one or more preoperatively identified lung lesions using VGT-309 with NIR imaging when standard surgical techniques using white light and/or palpation failed to identify the lesion(s), and lesion(s) are confirmed by histologic examination to be other than normal lung tissue.
B. Identification of one or more synchronous or occult lung lesions using VGT-309 with NIR imaging when standard surgical techniques using white light and/or palpation and preoperative imaging failed to identify the lesion(s), and lesion(s) are confirmed by histologic examination to be cancerous or precancerous.
C. Identification of fluorescence within ≤ 10 mm from the inside edge of the closest staple line as measured by the investigator *ex vivo* in the operating room using NIR imaging, with pathologic margin confirmed by histologic examination to be ≤ 10 mm.
   NOTE: Margins from excisions of known or suspected metastases at the time of the surgery, OR diagnostic wedge resections where a completion lobectomy or segmentectomy was subsequently performed, will not be considered for Margin CSE inclusion.
D. Identification of lymph nodes by VGT-309 with NIR imaging confirmed by histologic examination to be cancerous.

2.2.2 Secondary Efficacy Endpoints:

To evaluate the sensitivity, positive predictive value (PPV), and 1-PPV of VGT-309 with NIR imaging for lesion(s) *in vivo*:

1. Sensitivity is defined as the probability that the tissue fluoresces when it is cancer, as confirmed by histology (TP/(TP+FN)) *
2. Positive predictive value (PPV) is defined as the probability that a tissue sample contains cancer on histologic exam if it fluoresces ((TP/(TP+FP)) *
3. One minus Positive predictive value (1-PPV) is defined as the probability that a tissue sample does not contain cancer when it fluoresces ((FP/(TP+FP))*

* TP = true positive, FP = false positive, FN = false negative

[redacted]

[redacted]

2.2.4 Safety Endpoints:

Assessment of clinical laboratory tests, physical exam results, ECGs and vital sign measurements at various time points during the study, and documentation of treatment-emergent adverse events.

3. STUDY DESIGN

This is a Phase 2, multi-center, open-label study to evaluate the safety and efficacy of VGT-309, a tumor-targeted, activatable fluorescent imaging agent, in subjects undergoing surgery for proven or suspected cancer in the lung. [redacted]

Following agreement with and signing of the informed consent, subjects will undergo screening measurements for the study within 4 weeks prior to the anticipated dosing:

1. Medical, surgical and medication history.
2. Complete physical exam, including vital signs and height
3. Weight (needed for dose calculation)
4. Chemistry, hematology, coagulation and urinalysis with microscopy clinical laboratory studies.
5. 12-lead ECG.
6. Serum pregnancy test for females of child-bearing potential.

After meeting all enrollment criteria, each subject will receive 0.32 mg/kg VGT-309 by IV administration 12-36 hours prior to surgery (refer to section VGT-309 Dosing, below). Subjects will be observed for 1 hour after dosing is completed and asked about possible treatment emergent adverse events.

Subjects will undergo surgical resection within 12-36 hours after completion of VGT-309 dosing. Measurements of efficacy will be taken during surgery and during the pathological examination of all surgical specimens. (Refer to Efficacy Endpoints and Efficacy Assessments sections).

Following surgery, subjects will be monitored for safety during their hospitalization. Between 7 to 14 and 25 to 35 days after surgery, the subjects will return to the clinic or have a telehealth visit for final safety assessments. At the last visit, if there are no adverse events requiring further follow up, subjects will then be released from the study.

If a subject chooses to withdraw from the study prior to the final visit, they will be asked to undergo a final safety assessment before their departure.

4. STUDY DRUG – VGT-309

VGT-309 will be administered over 15 to 20 minutes as an IV infusion. Following are details related to VGT-309 preparation, packaging and labeling and storage. Additional details will be supplied in the Pharmacy Manual.

4.1 VGT-309 Description

VGT-309 will be supplied in a lyophilized form in 5ml vials containing 10mg of VGT-309.

[redacted]

4.2 VGT-309 Proposed Dose

The dose for this study is 0.32mg/kg of VGT-309 [redacted]

4.3 VGT-309 Preparation

VGT-309 is stored frozen and must be thawed at room temperature for at least 30 minutes but not more than 2 hours before it is prepared for dosing.

[redacted]

4.4 VGT-309 Dose Administration

VGT-309 will be given between 12-36 hours prior to prior to induction of general anesthesia for the planned surgery as an IV infusion by syringe pump over 15 to 20 minutes.

4.5 VGT-309 Storage and Accountability

VGT-309 will be stored frozen (-20°C ± 10°C) in a secure, locked area under the responsibility of the clinical research unit pharmacy or its designee.

The Investigator or Investigational Pharmacy must maintain accurate records of the receipt of all study drug, including date received, lot number, amount received, condition of the package and the disposition. Dispensing records will be maintained including the date and amount of study drug dispensed and the identity of the subject receiving the study drug.

Empty and partially used vials can be destroyed per the study site Study Drug Destruction SOPs upon completion of VGT-309 dispensing.

Following final reconciliation, unused study drug should be returned to Vergent Bioscience, Inc., or its designee.

4.6 VGT-309 Packaging and Labeling

Labels will be in compliance with all applicable regulatory requirements for the labeling of active pharmaceutical ingredients for the US and Australia as noted below:

- For the US – according to 21 CFR § 312.6 labels will contain:

- "Limited by Federal Law to Investigational Use" statement
- IMP name, route of administration and amount of VGT-309 in the vial.
- Lot number.
- Storage conditions.
- Sponsor name (Vergent Bioscience, Inc).
- Manufacturer.

- For Australia - according to Annex 13 of GMP labels will contain:
  - "For Clinical Trial Use Only: Per Protocol" statement
  - IMP name, route of administration and amount of VGT-309 in the vial
  - Protocol number
  - Retest date and batch number
  - Storage conditions
  - Sponsor name (Vergent Bioscience Australia Pty LTD)

5. SUBJECT POPULATION

5.1 Enrollment

Approximately 100 subjects scheduled to undergo standard of care surgical resection for a lung nodule that is already proven or suspected to be cancer in the lung will be enrolled to ensure at least 86 evaluable subjects.

[redacted]

5.2 Inclusion Criteria

In order to be enrolled in the study, the subject must:

1. Be willing and able to sign the informed consent and comply with study procedures.
2. Be at least 18 years of age.
3. Meet the following conditions:
   a. Female participants must be of non-childbearing potential, or,
   b. If of childbearing potential be non-pregnant or non-lactating and agree to use highly effective contraception from screening through Day 30 after treatment.
   c. Male participants, if not surgically sterilized, and if engaging in sexual intercourse with a female partner of childbearing potential, must be willing to use highly effective contraception from screening through 30 days post-dose and agree not to donate semen during this waiting period.
   d. Highly effective contraception involves the use of a condom for the male, plus one of the following for the female:
      - Oral, injectable, implantable, intravaginal, or transdermal hormonal contraceptives, or
      - Intrauterine device or intrauterine hormone-releasing system.

NOTE: Subjects who abstain from heterosexual intercourse as their usual and preferred lifestyle, will not be required to use contraception as described above. They are required to maintain abstinence from screening through Day 30.

NOTE: Subjects in a same sex relationship, must use a barrier form of contraception (e.g., condom, diaphragm) to protect against the transfer of the study drug in any bodily fluids.

4. Have a lung nodule or mass that might be considered primary lung cancer or lung metastases, whether or not it is biopsy-proven prior to surgery.
5. Be scheduled to undergo standard of care surgical resection for a lung nodule or mass with diagnostic and/or curative intent.
6. Have acceptable kidney and liver functions at study entry as evidenced by:
   a. ALT/AST $\leq$ 1.5 times the upper limit of normal,
   b. Calculated Creatinine Clearance (CrCl) $\geq$ 50 ml/min (manual calculation using Cockcroft-Gault equation),
   c. Total bilirubin $\leq$ 1.5 times the upper limit of normal.
7. Have an ECOG score of 0-2.
8. Meet all standard surgical and general anesthesia requirements.
9. Have not participated in an interventional clinical trial within the last 30 days (participation in a disease registry or quality of life study is not exclusionary).

5.3 Exclusion Criteria

Subjects may not be enrolled in the study if:

1. They are not a candidate for standard of care surgery based on opinion of the surgeon, anesthesiologist, or other consulting physician.
2. They have a known allergy or reaction to ICG, other radiographic contrast agent, or any component of VGT-309.
3. They have congenital long QT syndrome or QTcF > 470ms by history or at Screening ECG.
4. They have received chemotherapy or immunotherapy within 4 weeks prior to study enrollment.
5. They are prisoners, institutionalized individuals, or are unable to consent for themselves.
6. They have any other co-morbidity or habit that the Investigator believes will interfere with their ability to comply with and complete the study.

5.4 Replacement of Subjects

Subjects who withdraw consent prior to receiving VGT-309 will be replaced. Subjects not meeting the evaluable criteria (see Section 5.1) *may* be replaced. Additional subjects may be added if determined necessary to adequately evaluate safety and efficacy.

6. STUDY PROCEDURES

Refer to Attachment A: Schedule of Assessments

6.1 Study Visits

Up to 3 in-clinic/hospital visits and 2 follow up visits in clinic and/or via telehealth are planned for this study. Additional visits may be added if follow up for an adverse event is needed or if screening cannot take place in a single visit. Investigators should schedule visits within the protocol-specified timelines unless they receive permission from Vergent, or unforeseeable events prevent the subject from complying.

For a complete schedule of study procedures, refer to the Schedule of Assessments presented in Attachment A. All study procedures must be recorded in source documentation (primary occurrence of a record) maintained by the clinical site.

6.1.1 Informed Consent

Prior to performing any study-related activities under this protocol, including screening tests and assessments, written informed consent with the IRB/HREC-approved ICF/PICF must be obtained from the subject in accordance with local practice and regulations.

All subjects must be provided either a written Informed Consent Form (ICF - US Sites) or a Participant Information and Consent Form (PICF - Australia) describing the study with sufficient information for them to make an informed decision regarding their participation. Subjects will be given the opportunity to ask questions about the study prior to participation.

A copy of the ICF/PICF, signed and dated by the subject, must be given to the subject and documented in the subject's source documentation. The original signed consent form will be retained with the study records.

NOTE: The ICF/PICF may be signed up to 30 days before Screening begins.

6.1.2 Screening (Days -30 to -1)

With 30 days of obtaining the informed consent, the following assessments will be done to establish a subject's eligibility for the study. Note: in cases where subjects have given consent for general pre-screening at the site, some of these assessments may be done by chart review.

When possible, the assessments should be done in the order listed here to avoid the demands of sample collection and ECG prior to the subject passing basic entry criteria requirements.

1. Review of eligibility requirements – inclusion and exclusion criteria.
2. Collection of demographic information and medical and surgical history, including review of prior and ongoing medications taken in the previous 30 days. Note: Specific attention should be paid to collecting information on any prior cancer and the treatment received for it, regardless of when that treatment was given.
3. Physical Exam.
4. Height and weight measurements (BMI will be calculated in the EDC).
5. Vital signs measurement (blood pressure, pulse rate, respiratory rate and oral/tympanic temperature).
6. Standard 12-lead ECG taken in triplicate (subject should be resting in a supine position for at least 5 minutes prior to the first ECG. There is no pausing between each of the 3 ECGs to be taken). (QTcF will be calculated as the ECG results are entered in the EDC.)
7. Blood sample collection for clinical chemistry, hematology and coagulation.
8. Urine sample collection for urinalysis, including microscopy.
9. In women of child-bearing potential, blood sample for serum pregnancy test.

Upon establishment of eligibility, subjects are scheduled for their VGT-309 infusion to take place 12-36 hours prior to induction of general anesthesia for their scheduled surgery.

NOTE: Screening exams may be done on Day 1 (Day of VGT-309 dosing) provided all results are available and the subject qualifies for the study prior to dosing.

6.1.3 Day 1: VGT-309 Dosing

Subjects will check in to the hospital or infusion center as scheduled. After confirming their eligibility by reviewing their medical and surgical history and concomitant medications for any changes since screening, those subjects still considered eligible will undergo the following:

1. Targeted Physical Exam (Focus on heart, lungs and any area of change since screening). Note: changes from Screening to be recorded in Medical History section of the CRF.
2. Measurement of weight for dose calculation unless taken within the prior 7 days or if site SOPs require that the subject's weight be taken before the dose is prepared on the day of dosing).
3. Vital signs measurement (blood pressure, pulse rate, respiratory rate and oral/tympanic temperature).
4. In women of child-bearing potential, urine or serum sample for pregnancy test.
5. Blood sample for chemistry, hematology, coagulation. (**ONLY** if not done within 4 weeks prior to dosing).
6. Urine sample collection for urinalysis with microscopy (**ONLY** if not done within 4 weeks prior to admission).
7. Standard 12-lead ECG in triplicate within 10 MINUTES PRIOR to start of dosing (subject should be resting in a supine position for at least 5 minutes prior to the first ECG. There is no pausing between each of the 3 ECGs).
8. VGT-309 dosing to take place at 12-36 hours prior to induction of general anesthesia. (Refer to Section 4: Study Drug – VGT-309, for instructions on dose preparation and dosing procedures).
9. Assessment for potential adverse events begins with the start of dosing. (See Section 9.2.1.2)
10. Upon completion of dosing, VGT-309 subjects:
    - will be observed for 1 hour and queried for possible adverse events,
    - will have ECGs taken in triplicate, between 1 to 10 minutes and 30 +/- 5
    - will have vital signs taken at 30 +/- 5 minutes and 60 minutes +/- 5 minutes.

NOTE: Subjects may be allowed to leave the hospital grounds/infusion center and return prior to surgery, provided they have been observed for at least 1 hour following their dose of VGT-309 and the Investigator does not observe any concerning safety issues

6.1.4 Day 1 or 2: Surgery and Pathology

Following dosing with VGT-309, subjects will undergo planned standard of care surgical resection for their lung nodule or mass followed by pathological assessment of the resected tumor(s) and/or nodule(s) (Refer to Section 8: Efficacy Evaluations, for details).

6.1.5 Day 3 +/- 1 day: In-hospital follow up

While still hospitalized, subjects will undergo the following:

9. Targeted Physical Exam (Focus on heart, lungs and any area of change since screening).
10. Review of concomitant medications.
11. Vital signs measurement (blood pressure, pulse rate, respiratory rate and oral/tympanic temperature).
12. Blood sample for chemistry, hematology, coagulation. (See section 9.2.3 for assessment of laboratory results for adverse events).
13. Urine sample collection for urinalysis with microscopy.
14. Observation for and solicitation of adverse events.

6.1.6 Days 7-14: Telehealth or In Clinic follow up

Each subject will have a telehealth visit or return to the clinic to assess their general well-being, query for possible adverse events and any changes in their use of concomitant medications.

If a subject has a qualifying AE based on Day 3 laboratory results (See Section 9.2.3.1) the subject must have an additional blood draw to assess the course of the abnormal laboratory value. If the qualifying value does not return to the baseline value, the subject must return for an additional blood draw at the End of Study Visit.

6.1.7 Day 25 - 35: End of Study Follow up -OR- Early withdrawal

This visit may be conducted in clinic or by telehealth visit. During this visit or if the subject withdraws from the study early, the following assessments will be done:

1. Review of concomitant medications for changes since last visit.
2. Observation for and solicitation of adverse events.
3. Blood draw ONLY to assess a laboratory value that did not return to baseline after the Day 7-14 draw (See Sections 6.1.6 and 9.2.3.1)

Following completion of these assessments, subjects will be released from the study. Additional follow-up may be necessary if an SAE is reported and has not yet resolved (See Section 10.2.2 for details).

7. STOPPING THE STUDY OR EARLY WITHDRAWAL OF SUBJECT

This study may be stopped (terminated) by the Sponsor at any time and for any reason. Subjects on study at the time the study is stopped will be asked to complete all assessments in the Early Termination visit (see Attachment A).

NOTE: ***The study may also be stopped or delayed by the DSC as outlined in Section 9.1.2***.

7.1 Individual Subject Withdrawal

The participation of an individual subject in the study may be terminated in the following circumstances:

1. Withdrawal of informed consent by the subject.
2. Any occurrence that, in the Investigator's opinion, makes continued participation contrary to the subject's best interests.

If an Investigator removes a subject from the study, or if a subject declines further study participation, an Early Withdrawal Visit, consisting of the assessments required at the Day 25-35 visit, will be completed as soon as possible. It will be the responsibility of the Investigator to ensure that all withdrawn subjects receive appropriate follow-up and medical care if needed.

8. EFFICACY EVALUATIONS

Intra-operative and post-operative evaluations will be used to support the efficacy endpoints of the study.

8.1 Primary Efficacy Assessments:

Intra-operatively:

- Use of white light and/or palpation followed by NIR imaging for localization of preoperatively identified lung lesion(s), potential synchronous or occult malignant lung lesion(s), and potential cancer-containing lymph nodes.

Ex vivo, in the operating room

- NIR imaging to determine proximity of fluorescence to closest resection margin.

Ex vivo pathology

- Histologic examination of resected tissues

8.2 Secondary Efficacy Assessments:

Comparison of NIR imaging, conducted both inside and outside the subject, to results of histologic examination.

8.3 Intra-operative Evaluations

During the surgery, the Surgeon/Investigator will first utilize standard surgical techniques using white light and/or palpation followed by *in situ* NIR fluorescence imaging using an NIR imaging system capable of detecting ICG for localization of the primary tumor and any potential synchronous or occult lesions and lymph nodes.

The number and location of pulmonary nodules and synchronous lesions that are visualized by standard techniques and/or by VGT-309 NIR fluorescence imaging will be recorded. Lymph nodes visualized by VGT-309 NIR fluorescence imaging will be identified and recorded by nodal station and zone.

Following extraction of any tumor/nodules, synchronous lesions, and lymph nodes, *ex vivo* NIR fluorescence imaging will take place in the operative suite prior to closing the surgical field.

8.4 Post-operative Evaluations

Following completion of surgical procedures and imaging, the surgical specimen will be sent to the site's pathology laboratory for standard histological assessment of the surgical specimens.

NOTE: Pathology samples should be retained for at least one year and may be sent to a central location for additional analyses. (See Pathology Manual)

9. SAFETY EVALUATIONS

9.1 Data Safety Committee (DSC)

9.1.1 Constitution of the DSC

A Data Safety Committee will be appointed by Vergent Bioscience and will include at a minimum:

- An Independent Surgeon Reviewer
- An Independent Internist Reviewer
- The Project Statistician

[redacted]

9.1.2 DSC General Rules

9.1.2.1 Safety Review

The study may be paused if any of the following occur:

- Any subject experiences a Serious Adverse Event deemed to be related to the use of VGT-309.
- Any subject experiences an AE greater than Grade 2 attributed to VGT-309 in any single organ system

The DSC will evaluate these SAEs and AEs and determine whether:

- The study should continue, OR,
- The dose or time from infusion to surgery should be modified, OR,
- The protocol should be modified, OR,
- The study should be stopped.

9.1.2.2 Efficacy Review

[redacted]

9.2 Assessment of Safety

Safety will be assessed by the recording of adverse events, vital signs, changes in physical exam, 12-lead ECGs and the following clinical laboratory tests:

- **Hematology**

Hemoglobin (Hgb)	Hematocrit (Hct)
Platelet count	Red blood cell count
White blood cell count with differential	

- **Chemistry**

Urea	Creatinine
Total bilirubin	Alkaline Phosphatase
Aspartate transaminase (AST)	Alanine transaminase (ALT)
Gamma-glutamyl transferase (GGT)	Lactic dehydrogenase (LDH)
Glucose	Albumin
Total protein	Bicarbonate
Phosphate	Sodium
Potassium	Chloride
Calcium	Amylase

- **Coagulation:** INR, APTT
- **Urinalysis**

pH	Specific gravity
Protein	Glucose
Ketones	Bilirubin
Blood	Nitrites
Leukocytes	Urobilinogen
Microscopic urine analysis	

9.2.1 Adverse Events

NOTE: The content of this section is based on the FDA "Guidance for Industry and Investigators; Safety Reporting Requirements for IND and BA/BE Studies" issued in December 2012. A copy of this guidance will be provided in the to the site upon request and should be referred to if and when the following do not provide sufficient guidance for an investigator to make an assessment regarding the occurrence, severity, relationship and expectedness of an adverse event (AE).

Adverse event solicitation and recording will begin immediately upon start of dosing with the study product (VGT-309) and will include only on-treatment (treatment-emergent) events. Any changes to a subject's health that occur between the signing of the informed consent and start of dosing will be recorded as updates to the subject's medical history.

Subjects will be instructed to report AEs during the study and staff will query subjects regarding AEs throughout the study. The Investigator (and/or designee) must document all AEs reported from the time of dosing through completion of the End-of-study Visit (Days 25 -35). Any subject who is withdrawn from the study due to an AE shall be followed until the event has resolved or stabilized or 30 days after last dose and the Investigator will document available follow-up information on the subject's source documentation and CRF.

9.2.1.1 Definition of an Adverse Event

The FDA Safety Guidance, referencing 21CFR312.32(a), defines an Adverse Event as follows:

> *Adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.*
>
> *An adverse event (also referred to as an adverse experience) can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug and does not imply any judgment about causality. An adverse event can arise with any use of the drug (e.g., off-label use, use in combination with another drug) and with any route of administration, formulation, or dose, including an overdose.*

Adverse Events are **NOT**:

- Medical or surgical procedures (e.g., surgery, endoscopy, tooth extraction, transfusion). The *condition* that leads to the procedure is the AE.
- Situations where an untoward medical occurrence has not occurred (e.g., hospitalization for elective surgery, social and/or convenience admissions).

9.2.1.2 Evaluating and Reporting of Adverse Events

All AEs (i.e., a new event or an exacerbation of a pre-existing condition) that occur after the start of dosing with VGT-309 and through the end of the study - as evaluated in the End-of-Study Visit (Days 25 – 35) - or, if the subject is withdrawn due to an AE, must be recorded as an AE or SAE (if applicable), on the Adverse Event eCRF. The Investigator must follow all AEs until the AE resolves, or until the Investigator and/or the Medical Monitor determine the event is chronic or clinically stable. If an AE remains unresolved at the conclusion of the study, the Investigator and Medical Monitor will make a clinical assessment to determine whether continued follow-up of the AE is warranted. All subjects who have received any exposure to VGT-309 (even if dosing is not completed) must be evaluated for AEs.

The Investigator should attempt to establish a diagnosis of the event based on signs, symptoms and/or other clinical information. In such cases, the diagnosis should be documented as the AE and not the individual signs/symptoms.

All AEs or SAEs must be promptly documented on the Adverse Event eCRF and assessed by the Investigator. Details of the event must include the dates of onset and resolution, severity, relationship to study drug, seriousness, and whether the event caused the subject to withdraw from the study, outcome and timing with regard to administration of the study drug.

Grade: Each AE will be assigned a "Grade" based on the Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0 of the CTCAE will be used for this study. Refer to Section 9.1.2 for stopping rules based on the assigned Grade of AE.

Severity: Severity should be graded and recorded as follows:

- Mild: Awareness of event but easily tolerated.
- Moderate: Discomfort enough to cause interference with usual activity.
- Severe: Inability to carry out usual activity, incapacitating, requires medical intervention.

Relationship: The relationship of the Adverse Event to the study drug will be determined by the Principal Investigator, and assessed using the following definitions:

- **Related:** There is a distinct temporal relationship between the event onset and administration of the study drug. There is a known reaction to agent or chemical group or predicted by known pharmacology. The event cannot be explained by subject's clinical state or other factors.
- **Unrelated:** Evidence exists that the AE has an etiology other than the study drug (e.g., pre-existing condition, underlying disease, intercurrent illness, or concomitant medication).

These criteria, in addition to good clinical judgment, should be used as a guide for determining the causal assessment.

9.2.2 Serious Adverse Events (SAEs)

All SAEs as defined below that occur after the start of dosing of VGT-309 and through the End-of-Study Visit (Days 25 – 35) must be reported to Vergent as soon as the site becomes aware of them. Any SAEs occurring more than 30 days after last study drug administration and considered drug-related must also be reported.

An SAE is an AE from this study that results in any of the following outcomes:

- Death.
- Life-threatening situation (subject is at immediate risk of death).
- Inpatient hospitalization or prolongation of existing hospitalization.
- Persistent or significant disability/incapacity.
- Congenital anomaly/birth defect in the offspring of a subject who received study drug. (Refer to Section 9.2.4 for reporting of pregnancy)

NOTE: Important medical events that may not result in death, be immediately life-threatening, or require hospitalization, may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the subject *and* may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

A life-threatening AE is defined as any adverse experience that places the subject in the view of the Investigator, at immediate risk of death from the event as it occurred. This does not include an event that might have led to death *if* it had occurred with greater severity.

"Inpatient hospitalization" means the subject has been formally admitted to a hospital for medical reasons, for any length of time. Presentation and care within an emergency department does not necessarily constitute an SAE. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization, it is an SAE.

All deaths, regardless of cause, must be reported for subjects on study (within 30 days of last study drug dose). The SAE term should reflect the event that leads to the death with "death" recorded as the outcome

9.2.2.1 SAE Reporting Requirements to Vergent

The procedure for reporting SAEs, regardless of causal relationship, is as follows:

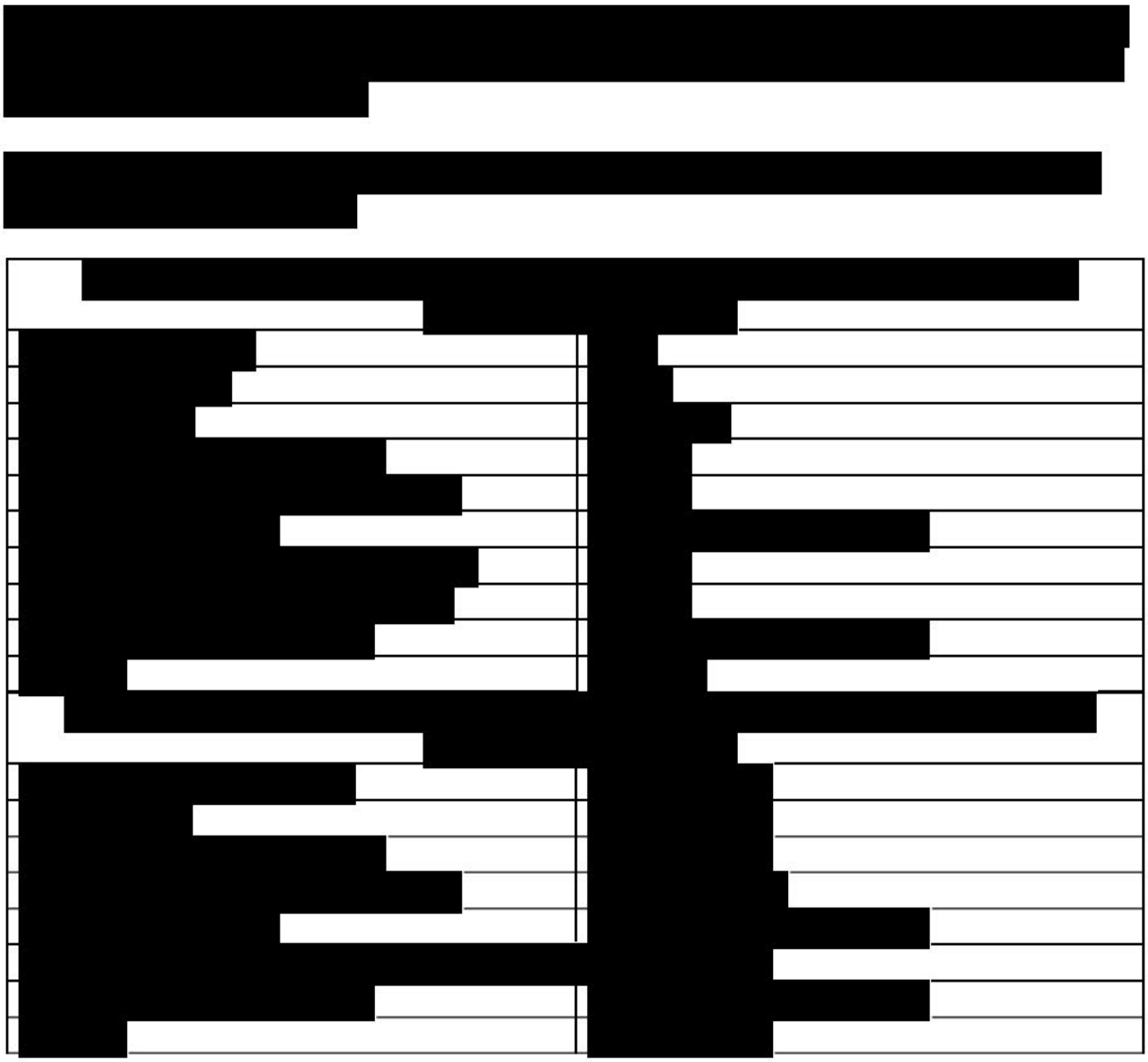
- Within 24 hours of the Investigator's knowledge of an SAE, the site must notify Vergent by phone call to their site monitor, medical monitor or other Vergent representative. They should also immediately complete the AE eCRF and select "Serious".
- The initial reporting of an SAE should contain as much information as is available to the Investigator. Submission of the SAE via the EDC should not be delayed in order to collect additional information to complete the form.
- When available, de-identified hospital records, autopsy reports, and other documents should be sent to the Vergent Safety Mailbox: safety@vergentbio.com.
- The Investigator is responsible for reporting their site SAEs to their IRB/HREC according to site specific procedures. The CRA will follow-up at monitoring visits to ensure each SAE for the site has been submitted to their IRB/HREC per their site-specific requirements and the information will be routinely tracked by the CRA in their monitoring visit report.
- If a related SAE or SUSAR is reported at any site, Vergent will distribute the report to every site involved in the study for distribution to their IRB/HREC.
- The Investigator must take all therapeutic measures necessary for resolution of the SAE. Any medications necessary for treatment of the SAE must be recorded onto the concomitant medication section of the subject's eCRF.

9.2.3 Clinical Laboratory Abnormalities

Laboratory abnormalities are usually not recorded as AEs unless considered to be clinically significant by the site clinician. In this study "clinically significant" is defined as an abnormality that induces clinical signs or symptoms, if the abnormality is of a degree that requires active management (e.g., discontinuation of the study drug, dose modification) or when the event is requiring treatment or other therapeutic intervention (e.g., potassium supplements, blood transfusion, etc.).

The Investigator will evaluate the relationship of any significantly abnormal result to protocol treatment or clinical condition, if possible. All clinically significant abnormal laboratory results will be followed until they return to normal or become stabilized.

9.2.3.1 Evaluation of Key Clinical Laboratory Values Post-Basline:



9.2.4 Pregnancy Reporting

Pregnancy is not considered an AE. Nevertheless, any pregnancy that occurs between dosing and as evaluated in the End-of-Study Visit (Days 25 – 35), should be verified and recorded. Sites should complete the Pregnancy Form provided by Vergent, and submit it to the Vergent Safety Mailbox (safety@vergentbio.com) within 24 hours of knowledge. Subjects or their female partner will sign a separate consent form allowing the Study Site and Sponsor to follow up with them through 6 weeks post-delivery or termination of the pregnancy.

10. STATISTICS

The study analyses will be conducted in a GCP environment (ICH E6). All analyses will be pre-specified in a Statistical Analysis (SAP) and finalized prior to database lock. If the methods in the SAP do not agree with this protocol, the methods described in the SAP will govern the analysis.

Additional post-hoc statistical tests may be performed and will be further described in the SAP.

Quantitative data will be presented as a standard set of summary statistics (n, mean, standard deviation, median, minimum and maximum values). Categorical data will be expressed as frequency (%).

10.1 Sample Size Determination

10.2 Populations for Analysis

The study includes three prospectively defined study populations.

1. The Safety Population includes any subject who received any amount of VGT-309.
2. The Intent to Treat (ITT) Population will include all patients who received any amount of VGT-309 and had surgery with NIR imaging after the surgeon first attempts to locate the tumor/nodule by white lightpalpation.
3. The Evaluable Population (EP) will include the subset of ITT patients who were eligible, who had no major protocol deviations, who received at least 90% the prescribed amount of VGT-309, and the surgeon first attempted to locate the tumor/nodule by adequate white light and/or palpation followed by adequate NIR imaging.

10.3 Hypothesis Tests

10.3.1 Treatment Comparisons

There is only one treatment in this unblinded single-arm study. The hypothesis to be tested is not a treatment comparison. The hypothesis to be tested is that the lower bound of a 95% confidence interval for the observed proportion of subjects with at least one CSE exceeds 10%.

10.3.2 Primary Hypothesis

The primary study hypothesis is that VGT-309 with NIR imaging is superior to white light and/or palpation for the intraoperative localization of preoperatively identified lung lesions.

The null hypothesis for the primary endpoint is that <= 10% of subjects will have at least one CSE, while the alternative hypothesis is that proportion of subjects with at least one CSE will exceeds 10% as demonstrated by at least 15/86 (17.4%) evaluable subjects with at least one CSE.

For the primary endpoint analysis, the proportion of subjects with at least 1 CSE will be tested under the null hypothesis that this proportion is <=10%.

$$H_o: p \leq 10\%$$

The alternative hypothesis states that the proportion of evaluable subjects with at least 1 CSE will be greater than 10%:

$$H_a: p > 10\%$$

The primary analysis will use the EP population. This analysis may be repeated using the ITT population. One-sided 2.5% exact binomial test will be used to test the null hypothesis. Clopper-Pearson exact two-sided 95% confidence intervals will be reported.

For the secondary endpoint analysis sensitivity, PPV, and 1-PPV will be calculated and presented along with 95% confidence intervals using GEE model analysis to factor in within-subject correlation for subjects with multiple tumors.

10.4 Safety Analysis

Unless otherwise specified, safety analyses will be conducted in the safety population. Safety will be evaluated by assessment of clinical laboratory tests, physical exams, ECGs and vital sign measurements at various time points during the study, and by the documentation of AEs.

10.4.1 Adverse Events

No statistical testing will be performed for safety data.

Adverse events will be summarized by the Medical Dictionary for Regulatory Activities (MedDRA)system organ class and preferred term. The MedDRA version current at the start of the study will be used throughout the study. A treatment-emergent adverse event (TEAE) is defined as any adverse event that begins on or after the date of administration of VGT-309.

An overall summary of TEAEs will be provided. The following summaries (number and percentage of subjects) of TEAEs (by System Organ Class and Preferred Term) will be provided:

- TEAEs.
- Treatment-related TEAEs.
- TEAEs leading to study drug discontinuation (infusion interruption or discontinuation)
- Serious TEAEs.
- Treatment-related Serious TEAEs.

10.4.2 Clinical Laboratory Data

Summaries of clinical laboratory results and change from baseline will be performed using descriptive statistics by scheduled visit. No statistical testing will be performed.

10.4.3 Other Safety Evaluations

Individual data for physical examination findings, clinical labs, ECGs and vital signs will be listed by subject and summarized by incidence of events/abnormalities or descriptive statistics as appropriate. Clinically Significant (CS) findings for PE, clinical labs, ECG and vital signs will be reviewed, and when appropriate, these CS findings will be reported as AEs.

11. RECORDING AND COLLECTION OF DATA

11.1 Case Report Form

The Investigator or designee will record all data collected by an Electronic Data Capture system (EDC) containing the electronic Case Report Form (eCRF) provided for that purpose. The site will be suitably trained on the use of the EDC and eCRF and appropriate site personnel will be provided electronic signatures.

All site entries will be made in a secured web site and the Principal Investigator will review the record for completeness. Upon completion of the review, the PI will sign electronically in the signature page of the eCRF.

The Investigator or designee will make necessary eCRF corrections. The Investigator must authorize the corrections to the entered data on eCRF.

Specific instructions on use of the EDC system and guidelines for data entry and correction will be provided to the sites in the Case Report Form Completion Guidelines available as part of the EDC system.

11.2 Study Files and Subject Source Documents

Subject confidentiality is strictly held in trust by the participating investigators, research staff, Vergent and their designees. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to subjects. Authorized representatives of Vergent may inspect all documents and records required to be maintained by the Investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the subjects in this study. Any data, specimens, forms, reports, and other records that leave the site will be identified only by a subject identification number to maintain confidentiality.

The Investigator must maintain adequate and accurate records to enable the conduct of the study to be fully documented and the study data to be subsequently verified. These documents include Investigators' Study Files and original subject clinical source documents generated at the study site. The term "original" means the first recording of the data.

The Investigator will ensure the site master files are maintained, including the study protocol and its amendments, IRB/HREC and regulatory approvals with associated correspondence, informed consents, study drug records, staff curriculum vitae, all correspondence, and other appropriate documents.

Subject clinical source documents may include, but are not limited to, subject hospital/clinic records, physicians' and nurses' notes, appointment books, laboratory reports, ECGs, radiographs, and consultant letters. The Investigator must assure that all original source documents are available to support monitoring activities.

11.3 Monitoring

During the study monitoring will occur on a regular basis as agreed to by the site. Monitoring visits may be conducted on site or remotely, via a secured internet connection. For this study, at least 2 monitoring visits must be conducted on site, unless otherwise agreed to by Vergent, in writing. Monitoring visits will be conducted according to the applicable ICH and GCP guidelines to ensure protocol adherence, quality of data, drug accountability, compliance with regulatory requirements and continued adequacy of the investigational site and its facilities. The Investigator will cooperate in the monitoring process by ensuring the availability of the eCRFs, source documents and other necessary documents at the time of the monitoring visits and by prompt attention to any matters brought to his/her attention by the monitor.

11.4 Audit

ICH guidelines for GCP require independent inspection of clinical program activities. Such inspections may be performed at any time - before, during and/or after the study. The Investigator and study staff are responsible for maintaining the site master file containing all study-related regulatory documentation as outlined by Vergent that will be suitable for

inspection at any time by Vergent, its designees, and/or regulatory agencies. The Investigator understands and agrees to give access to the necessary documentation and files.

11.5 Retention of Data

Institution shall maintain all Study Data for a period of ten (10) years following the Completion Date. Without limiting the foregoing, Institution and Principal Investigator will at a minimum retain Study Data to the extent and for the periods required under Applicable Law, including 21 C.F.R. § 312.62(c). Institution will take reasonable and customary precautions, including the application of cybersecurity measures, password protection, and periodic back-up of computer files and storage of all records and files in a secure area reasonably protected from fire, theft, destruction, and unauthorized access to prevent the loss or alteration of any Study Data..

12. PUBLICATION POLICY AND SHARING OF DATA

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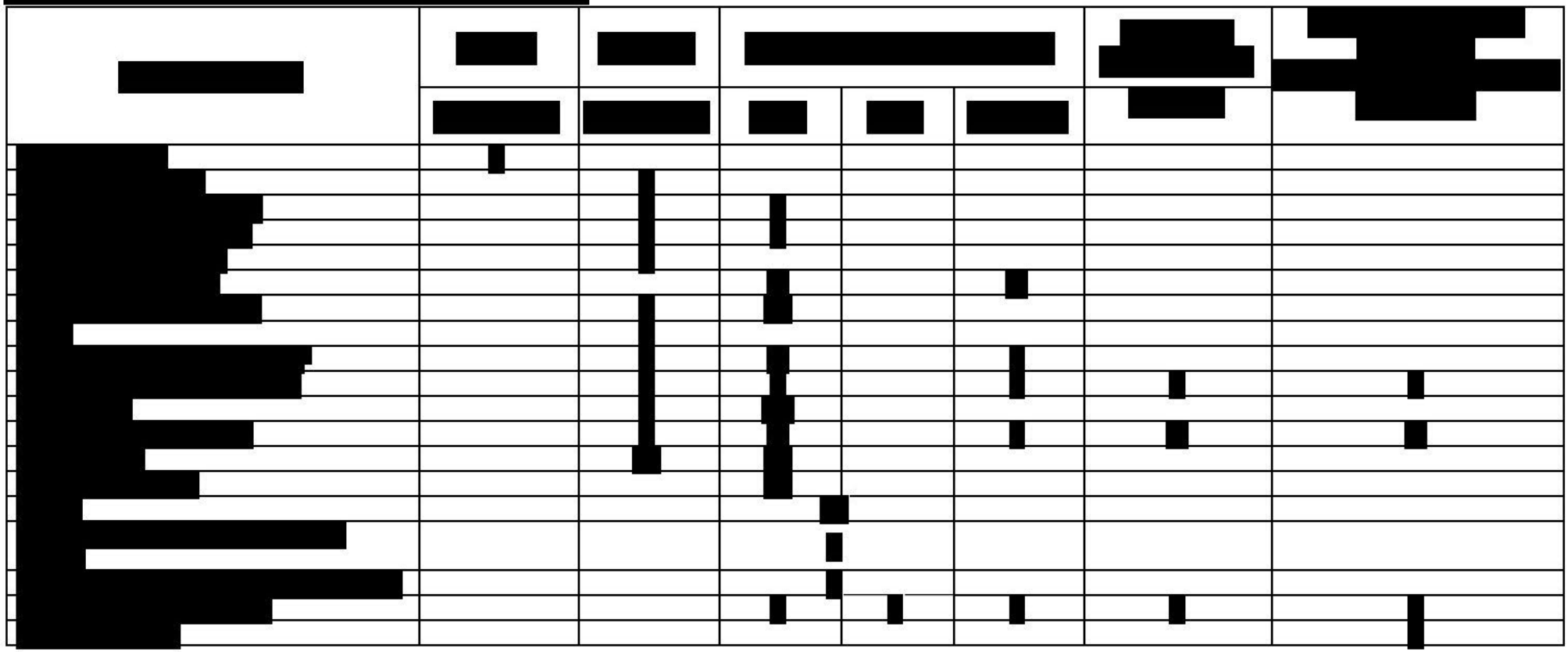
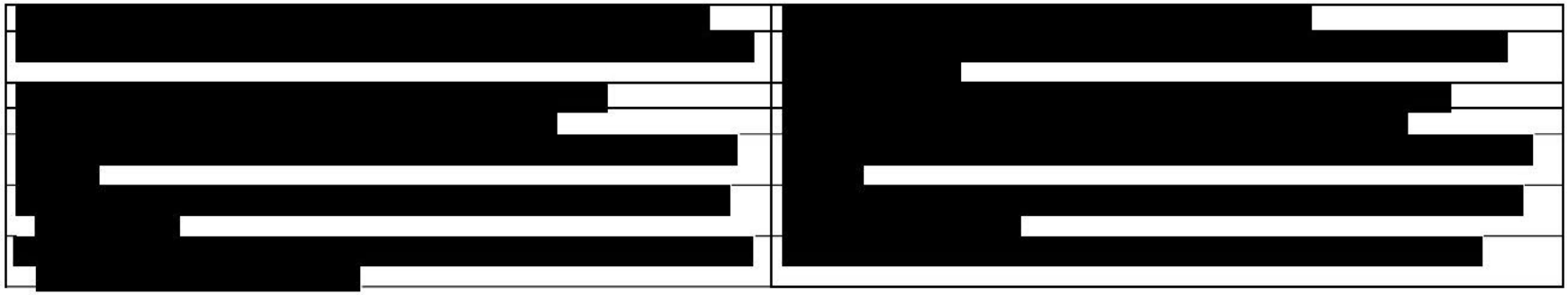
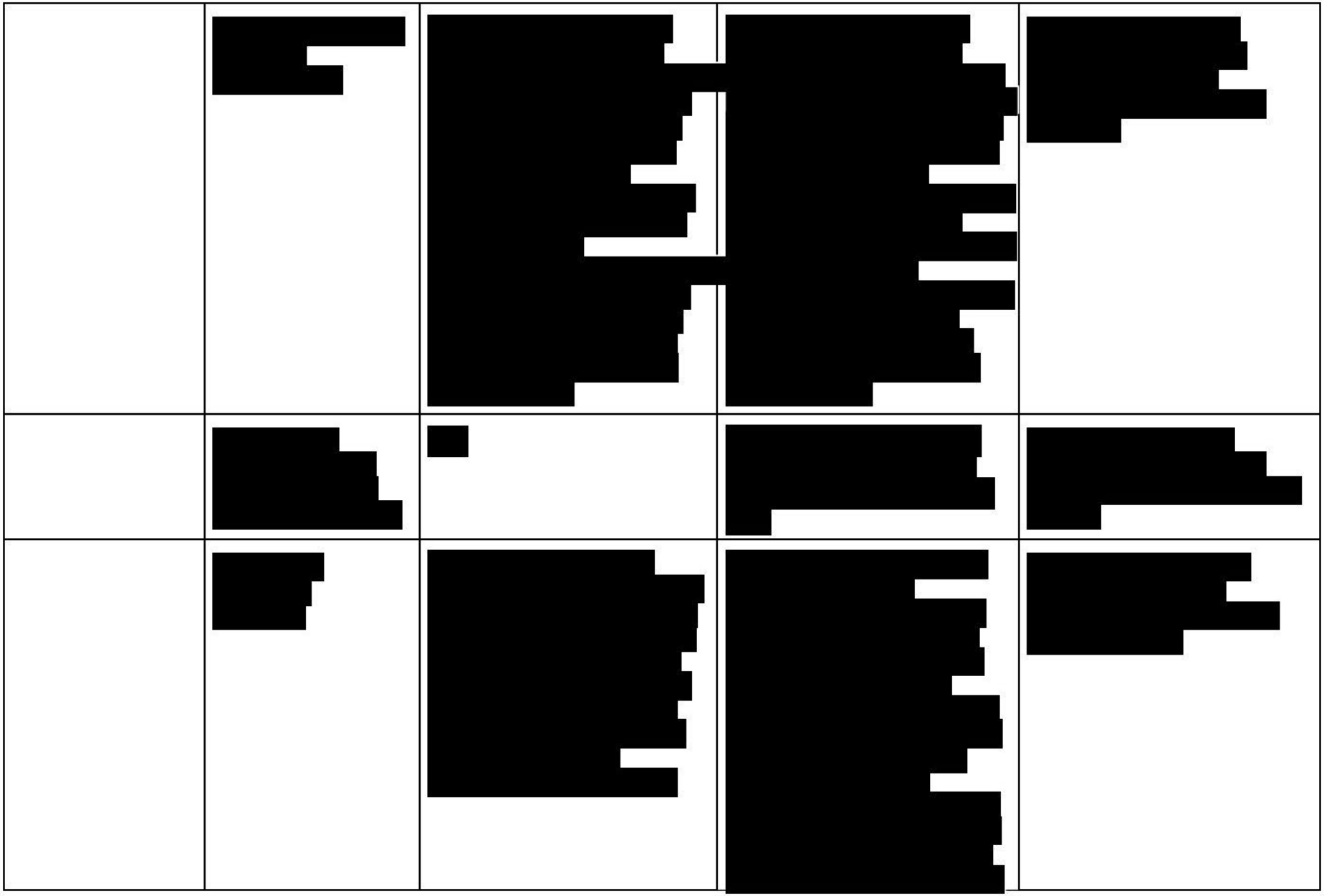




ATTACHMENT B: SUMMARY OF CHANGES

Protocol Version	Location in Protocol	Original Text	Modified Text	Reason for Change
V1.0, 15JUNE2023 to V2.0, 14August2023,	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]

	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	
V2.0, 14AUGUST2023 to V3.0, 15MARCH2024	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]



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