CLINICAL RESEARCH PROTOCOL

TEST ARTICLE:	Cytalux™ (pafolacianine) injection: folate analog ligand conjugated with an indole cyanine green-like dye as a solution in vials containing 1.6 mL at 2 mg/mL
PROTOCOL TITLE:	Single Dose Investigator Initiated Pilot Study to Investigate CYTALUX (pafolacianine) for Intraoperative Imaging of Patients with Endometrial Cancer Planned for Surgery
IND NUMBER:	Exempt
PRINCIPAL INVESTIGATOR:	Janos L. Tanyi, MD, PhD
ORIGINAL PROTOCOL DATE:	10 June 2025
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1 PROTOCOL SUMMARY

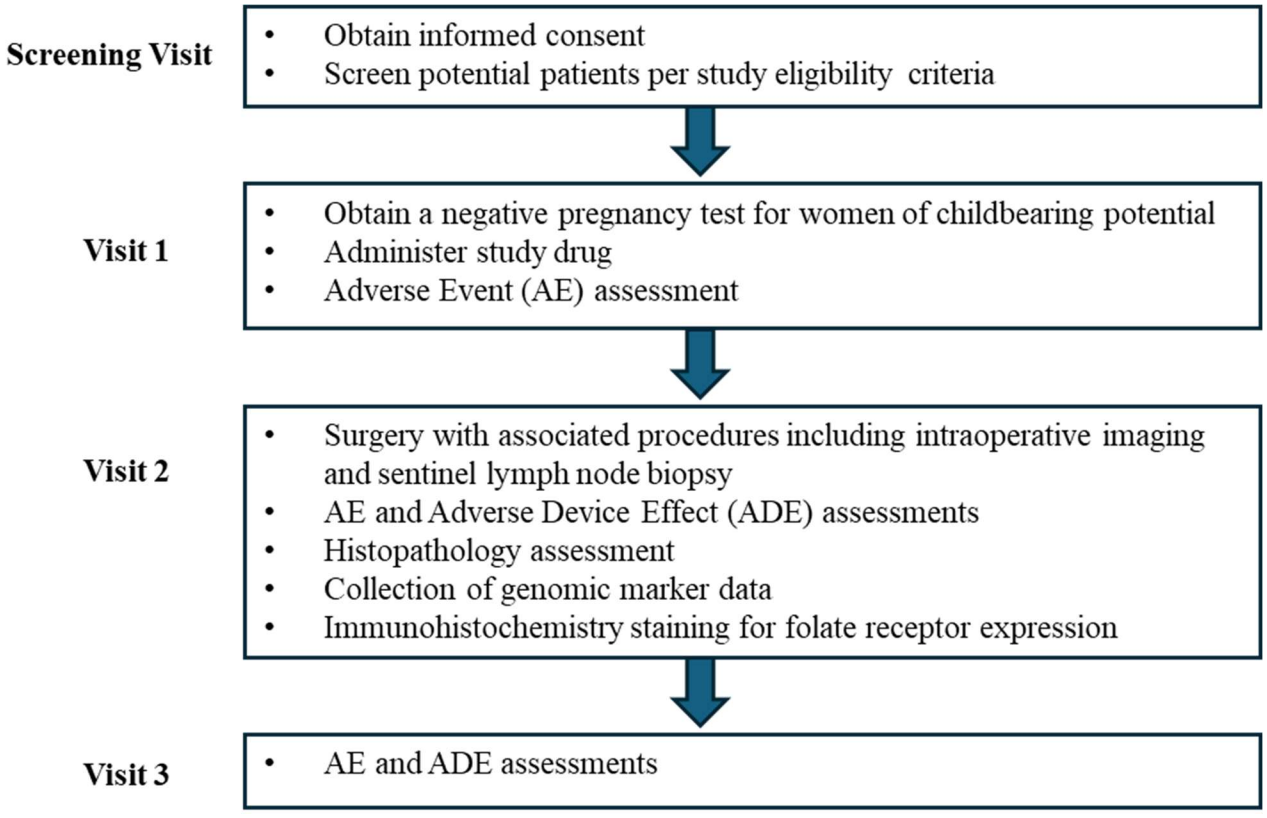
1.1 Study Synopsis

Title:	Single Dose Investigator Initiated Pilot Study to Investigate CYTALUX (pafolacianine) for Intraoperative Imaging of Patients with Endometrial Cancer Planned for Surgery
Study Description:	This is a single center, single dose, open-label investigator-initiated pilot study in adult subjects with a primary diagnosis of endometrial cancer who are being evaluated for surgery. Subjects will receive one dose of CYTALUX™ (pafolacianine) injection intravenously prior to the planned diagnostic laparoscopies. This hour-long infusion will be completed from 1 hour to up to 168 hours (7 days) prior to intraoperative near-infrared (NIR) imaging for the planned surgery. All subjects participating in the study are expected to receive CYTALUX™ (pafolacianine) injection and standard care laparoscopic evaluation of disease. Intraoperative imaging with Cytalux will be performed for assessment of disease detection in patients who are being evaluated to undergo surgery for endometrial cancer. Any tissues removed as part of standard of care will undergo assessment with NIR light imaging prior to and after resection. This will be then compared to gold standard histologic confirmation by pathology.
Objectives:	**Primary Objective** To assess the ability of CYTALUX™ (pafolacianine) injection used with near-infrared (NIR) fluorescent imaging for the detection of malignant tissue in subjects undergoing surgical resection for endometrial cancer **Secondary Objectives** 1. To assess the safety of CYTALUX in subjects undergoing surgery for endometrial cancer 2. To assess folate receptor (alpha and beta expression) in resected specimens **Exploratory Objectives** 1. To assess the feasibility of using genomic markers to predict utility of CYTALUX with NIR imaging 2. To assess the feasibility of CYTALUX to identify sentinel lymph nodes
Endpoints:	**Primary Endpoint** The primary efficacy endpoint is the sensitivity of CYTALUX with NIR imaging for detection of malignant lesions. Sensitivity is defined as the proportion of fluorescent light positive lesions that are histologically

	confirmed to be cancer relative to the total number of lesions confirmed to be cancer. Sensitivity = (True Positive)/(True Positive + False Negative) **Secondary Endpoints** 1. Incidence rates of all adverse events (AEs), adverse device effects (ADEs), and SAEs, from the time of CYTALUX administration through Visit 3 2. Sensitivity for cancerous lesions for: a. FRα positive lesions b. FRβ positive lesions **Exploratory Endpoints** 1. Genomic evaluation of tumor inclusive of, but not limited to: a. Estrogen receptor/progesterone receptor (ER/PR) status b. HER2 status c. Mismatch repair (MMR) status d. POLE status e. p53 status f. CARIS whole genome sequencing 2. The exploratory endpoint is the detection rate of CYTALUX with NIR imaging for identification of sentinel lymph nodes (SLNs). The detection rate is the proportion of the patients with SLNs detected by CYTALUX and NIR imaging in all enrolled patients.
Study Enrollment:	This study plans to enroll 10 subjects.
Study Population:	Adult subjects (>18 years old) undergoing surgery for endometrial cancer
Phase:	Investigator sponsored study (ISS)
Description of Sites/Facilities Enrolling Participants:	Department of Obstetrics and Gynecology Jordan Center for Gynecologic Cancer at Penn Perelman Center for Advanced Medicine 3400 Civic Center Boulevard 3rd Floor West Philadelphia, PA 19104

Description of Study Intervention:	CYTALUX™ (PAFOLACIANINE) INJECTION: folate analog ligand conjugated with an indole cyanine green-like dye as a solution in vials containing 1.6 mL at 2 mg/mL. Each subject will be administered a single intravenous dose of not less than 1 hour before and not more than 168 hours (7 days) before initiation of intraoperative NIR fluorescent imaging. The imaging systems used in this study will be assessed for meeting the criteria for use with CYTALUX™ (PAFOLACIANINE) INJECTION.
Study Duration:	The recruitment period is estimated at 12 months.
Participant Duration:	The maximum duration a subject is in the study is approximately 2 months.

1.2 Study Schematic



1.3 Schedule of Activities (SoA)

Study Procedure	Screening Visit	Visit 1	Visit 2	Visit 3
	-30 days prior to surgery	-7 days to day of surgery	Day of surgery	4 weeks ±1 week post-surgery
Informed consent	X			
Medical history	X			
Confirmed surgical candidate	X			
Pregnancy test for patients of childbearing potential		X		
Study drug administration		X		
Surgery with associated procedures including intraoperative imaging and sentinel lymph node biopsy			X	
Histopathology assessment of resected tissue*			X	
Collection of genomic marker data**			X	
AE assessments		X	X	X
ADE assessments			X	X

*Lesions will be resected during the surgery at Visit 2. Histopathology assessment and immunohistochemistry staining will be completed in accordance with local pathology procedures and timeline.
**Genomic marker data obtained prior to surgery will be utilized, if available. If tissue is collected during surgery for genomic testing, the testing will be completed in accordance with institutional procedures and timeline.

2 INTRODUCTION

2.1 Study Rationale

Intraoperative molecular imaging, specifically with pafolacianine (CYTALUX), has proven to be a valuable real-time adjunctive tool in identifying cancerous lesions for adults undergoing surgery for ovarian and lung malignancies. Marketing authorization for pafolacianine was granted by the FDA (trade name CYTALUX) on November 29, 2021.

Based on clinical evidence and experience from the phase 2 and phase 3 open-label trials for ovarian cancer and literature demonstrating the overexpression of FR, it is possible that CYTALUX could improve the surgeon's ability to comprehensively stage and resect all disease in endometrial cancer, which is important for delivering appropriate adjuvant therapy and improving outcomes for patients. Endometrial cancer is increasing in incidence, especially high-risk tumors. Innovative tools are needed to provide treatment for this patient population.

This study aims to explore the indication of CYTALUX™ (PAFOLACIANINE) for endometrial cancer. This study will evaluate the efficacy of CYTALUX™ (PAFOLACIANINE) binding to endometrial cancers to detect macroscopic cancers during cytoreductive surgery and assess the sensitivity as an intraoperative imaging adjunct.

Over 80% of advanced (stage III or IV) or recurrent endometrial carcinomas express folate receptor (FR), a folate binding protein, making this receptor an ideal target for marking most endometrial cancers (May 2025, Senol 2015). This also makes FR an ideal target for intraoperative imaging of this cancer, facilitating cytoreduction, and potentially improving outcomes in these patients (Kalli 2008). Chemotherapy does not appear to affect FR alpha (FRα) expression in endometrial cancer specimens as examined by immunohistochemistry (Despierre 2013), so prior treatment is unlikely to affect utility of FRα ligands as imaging agents.

Immunohistochemistry for FR of representative samples of resected tissue will be performed. This is essential to interpret the results of CYTALUX™ (PAFOLACIANINE) binding and intraoperative fluorescence imaging. Since cytoreductive surgeries typically have several specimens with large amounts of tumor, representative samples from pathology proven sites of cancer will be tested for folate expression and will be correlated with intraoperative fluorescence imaging.

Information on genomic markers for patients receiving CYTALUX will be collected and correlated with intraoperative fluorescence imaging to help predict the utility of CYTALUX with NIR imaging.

2.2 Background

Endometrial cancer is the fourth most common cancer for women in the United States (ACS 2025). Incidence has increased by more than 1% per year since the mid-2000s and mortality is increasing as well; from 2013 to 2022 the death rate rose by 1.5% per year. (ACS 2025).

Based on data from SEER 2015-2021, the overall five-year survival rate is 81.1% and for distant disease it is only 19.4% (SEER 2025). The standard management of endometrial cancer is surgery. Other treatments such as radiation, chemotherapy, and immunotherapy may be utilized as well. Tumor-specific intraoperative fluorescence imaging may improve staging and debulking efforts real time during surgery.

2.3 Overview of Study Drug

On Target has developed pafolacianine, a folate analog ligand conjugated with an indole cyanine green-like dye as a tumor-specific imaging agent. Pafolacianine binds specifically to the high affinity folate receptor (FR) and could be suitable for use as an imaging agent in patients with tumors that overexpress FR. Following intravenous injection of pafolacianine, the agent distributes throughout the body and is rapidly cleared from healthy tissue, while areas with a high concentration of folate receptors, such as several carcinomas, retain the agent. This fluorescence of the malignant tissue can be captured by an imaging system that can be used by the surgeon along with normal perioperative procedures such as palpation and visual observation to decide which tissues to remove during cytoreduction surgery, particularly after neoadjuvant chemotherapy. Clinical data demonstrate that near infrared (NIR) imaging devices that excite at 760 nm to 785 nm and detect emission at 790 nm to 815 nm are suitable for use with CYTALUX.

Pafolacianine will bind to the FRα receptors and enter the cell through endocytosis. Upon exciting the area under NIR in the appropriate range, the lesions will fluoresce, helping the surgeon identify the osteosarcoma cancer, enabling more complete resection, identification and removal of cancerous synchronous lesions, and adequate margins free of the disease. Pafolacianine has been evaluated in

ovarian cancer (Phase 1, Phase 2, and Phase 3), and also in Phase 2 and Phase 3 studies for intraoperative imaging during surgery for cancer in the lung. In these studies, additional cancer or positive cancer margins were identified in 25% to 40% of the subjects.

In studies using a human cervical carcinoma cell line (KB) that overexpresses FRα, pafolacianine demonstrated a high affinity for FR (KD = 10.4 nM), which compared well with the binding affinity of folic acid (KD = 7.4 nM). In contrast, the D-isomer of pafolacianine (OTL0039) exhibited relatively lower affinity for the receptor (KD = 81.8 nM). Pafolacianine competed well with [3H]-folic acid for the receptor, indicating that pafolacianine is highly specific for FRα. In studies conducted in nude mice bearing KB xenografts, fluorescence was observed primarily in the tumors 2.5 hours after intravenous (IV) administration of 10 nmoL pafolacianine, with weaker fluorescence signal also seen in the kidneys. Similar sequestration of pafolacianine into the cancer cells is expected to occur when administered to subjects with ovarian cancer undergoing cytoreductive surgery, leaving only FRa+ cells visible under the appropriate excitation wavelength.

The safety profile of pafolacianine has been characterized in a comprehensive series of non-human pharmacokinetic and toxicology studies. The results of the pafolacianine Phase 1-enabling nonclinical safety program in rats and dogs demonstrated the safe use of pafolacianine as an intraoperative imaging agent. Additionally, a photoactivation study in rats showed no evidence of phototoxicity associated with pafolacianine. The results of the pafolacianine Phase 1-enabling nonclinical safety program in rats and dogs demonstrated the safe use of pafolacianine as an intraoperative imaging agent. Additionally, a photoactivation study in rats showed no evidence of phototoxicity associated with pafolacianine.

On Target Laboratories has completed the following clinical studies:

- Phase 1 ADME C14 An open-label, mass balance study to investigate the absorption, distribution, metabolism and excretion of [14C]-OTL0038 after a single intravenous dose to healthy volunteers (OTL-2019-14COTL0038-001)
- Phase 1a Clinical Study of CYTALUX™ (pafolacianine) injection in healthy volunteers, dosed in 23 subjects with a dose range of 0.025 – 0.20 mg/kg (CHDR1321A).
- Phase 1b Clinical Study of CYTALUX™ (pafolacianine) injection for the intra-operative imaging of folate receptor alpha positive ovarian cancer, dosed in 12 subjects with a dose range of 0.0125 – 0.0500 mg/kg (CHDR1321-B).
- Phase 2 Ovarian Clinical Study of CYTALUX™ (pafolacianine) injection for the intra-operative imaging of folate receptor alpha positive ovarian cancer, dosed in 44 subjects with a dose of 0.025 mg/kg (OTL-2016-CYTALUX™ -003).
- Phase 2 Lung Clinical Study of CYTALUX™ (pafolacianine) injection for the intra-operative imaging of folate receptor alpha positive lung cancer, dosed in 100 subjects with a dose of 0.025 mg/kg (OTL-2016-CYTALUX™ -005).
- Phase 3 Ovarian Clinical Study of CYTALUX™ (pafolacianine) injection for the intra-operative imaging of folate receptor positive ovarian cancer, dosed in 150 subjects with a dose of 0.025 mg/kg (OTL-2016-CYTALUX™ (pafolacianine) injection-006)

- A Phase 3, Single dose, Single-Arm, Open-Label Study to Investigate the Safety and Efficacy of CYTALUX™ (pafolacianine) injection for Intraoperative Imaging of Folate Receptor Positive Lung Nodules, dosed in 112 subjects at a dose of 0.025 mg/kg (ELUCIDATE study) (OTL-2019-CYTALUX™ -007).

2.4 Risk/Benefit Assessment

2.4.1 Known Potential Risks

The safety of CYTALUX was evaluated in four open label clinical studies, two studies (N = 44 and N = 150) in patients with ovarian cancer and two studies (N = 100 and N = 112) in patients with known or suspected cancer in the lung. A total of 406 patients received 0.025 mg/kg of CYTALUX via intravenous administration. Adverse reactions that occurred in ≥ 1% of patients were: nausea (13%), vomiting (5%), abdominal pain (2%), flushing (2%), other infusion-related reactions (2%), hypersensitivity (2%), elevation in blood pressure (1%), dyspepsia (1%), and chest discomfort (1%). Adverse reactions occurred during the administration of CYTALUX in 17% of patients. During the administration of PAFOLACIANINE, interruption of the infusion and/or treatment with an anti-histamine may be required in subjects who experience symptoms suggestive of hypersensitivity, followed by an observational period until the symptoms resolve. Anti-nausea (e.g. Zofran) and anti-histamine (e.g. benadryl) are frequently dosed prior to infusion of Pafolacianine in clinical practice to limit side effects. Symptoms to be aware of may include but are not limited to flushing, nausea, vomiting, abdominal pain and pruritis/urticaria. Other risks to subjects may include injection site adverse reactions (infusion and venous blood sampling), such as infection and hematoma. The use of a near-infrared fluorescence camera system during surgery may result in contamination of the sterile field or injury due to disengagement of the imaging device component coming in contact with the patient and/or surgical team. No clinically meaningful changes in vital signs, laboratory parameters, or electrocardiograms have been observed. Adverse events in the prior studies have been attributable to the underlying disease or to surgery (most commonly lymphedema, post-procedural hematoma, or urinary incontinence). Overall, the administered doses of PAFOLACIANINE have been well tolerated. The time spent visualizing the surgical field under NIR is quite short, with no meaningful prolongation of anesthesia. There are no known hazards associated with exposure of tissue to near-infrared light for short periods of time.

2.4.2 Known Potential Benefits

The potential benefits of CYTALUX for the imaging of endometrial cancer are:

- Identification of endometrial cancer burden
- Improved staging of the tumor
- Identification of tissues for further evaluation

2.4.3 Assessment of Potential Risks and Benefits

The anticipated benefits appear to outweigh the known and potential risks associated with exposure to PAFOLACIANINE.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS
Primary	
To assess the ability of CYTALUX™ (pafolacianine) injection used with near-infrared (NIR) fluorescent imaging for the detection of malignant tissue in subjects undergoing surgical resection for endometrial cancer	Sensitivity is defined as the proportion of fluorescent light positive lesions that are histologically confirmed to be cancer relative to the total number of lesions confirmed to be cancer. Sensitivity = (True Positive)/(True Positive + False Negative)
Secondary	
1. To assess the safety of CYTALUX in subjects undergoing surgery for endometrial cancer	1. Incidence rates of all adverse events (AEs), adverse device effects(ADEs), and SAEs, from the time of CYTALUX administration through Visit 3
2. To assess folate receptor (alpha and beta expression) in resected specimens	2. Sensitivity for cancerous lesions for: a. FRα positive lesions b. FRβ positive lesions
Exploratory	
1. To assess the feasibility of using genomic markers to predict utility of CYTALUX with NIR imaging	1. Genomic evaluation of tumor inclusive of, but not limited to: a. Estrogen receptor/progesterone receptor (ER/PR) status b. HER2 status c. Mismatch repair (MMR) status d. POLE status e. p53 status f. CARIS whole genome sequencing
2. To assess the feasibility of CYTALUX to identify sentinel lymph nodes	2. The exploratory endpoint is the detection rate of CYTALUX with NIR imaging for identification of sentinel lymph nodes (SLNs). The detection rate is the proportion of the patients with SLNs detected by CYTALUX and NIR imaging in all enrolled patients.

4 STUDY DESIGN

4.1 Overall Design

The study will include a screening period of up to 30 days prior to planned surgery to accommodate the typical timing of a pre-surgical consultation between patients and their surgeon and thus avoid the need for subjects to present for a screening visit immediately in advance of their planned surgery. Information from procedures completed as part of standard care during this period can be used for purposes of the trial.

4.1.1 Screening

Screening will overlap with the routine/standard pre-operative screening conducted by the hospital where the surgery is scheduled. Consented patients will be evaluated for eligibility prior to any non-screening study related procedures being performed.

4.1.2 Administration of PAFOLACIANINE

A single dose of PAFOLACIANINE will be administered to each subject 1 to 168 hours (7 days) prior to NIR imaging.

4.1.3 Surgical Procedure

All subjects participating in the study are expected to receive CYTALUX™ (pafolacianine) injection and standard care surgical evaluation of disease. Intraoperative imaging will be completed between one and one hundred sixty-eight hours after CYTALUX™ (pafolacianine) infusion is completed. Any tissues removed as part of standard of care will undergo assessment with NIR light imaging prior to and after resection. This will be then compared to gold standard histologic confirmation by pathology.
After the surgical site is visualized, location of the primary tumor and any clinically suspected additional tumors detected under normal light and/or palpation/endoscopic visualization will be recorded photographically or by video as per surgeon's standard clinical practice. Tumors detected under normal light will be indicated by an "o" on the image as well as on the schematic.

Once normal light assessment is completed, the surgical field will be visualized using an NIR imaging system under fluorescence. Any tumor and/or nodules detected using the NIR imaging system will be recorded on the intraoperative schematic using an "X". Those areas that were also identified under normal light, the "X" will be superimposed on the "O" as "⊗". For nodules identified only under fluorescence, they will be recorded only by an "X".

Light source	Notation
Visible light	O
Fluorescent	X
Both	⊗

4.1.4 Surgical Tissue Processing – Resected Lesions and Lymph Nodes

Each lesion obtained for evaluation will be sent to local pathology for processing according to their standard practice. An inventory of specimens sent to local pathology labeled as above will be maintained.

4.2 Scientific Rationale for Study Design

As stated in ICH guideline E4, "Knowledge of the relationships among dose, drug concentration drug concentration in blood, and clinical response (effectiveness and undesirable effects) is important for the safe and effective use of drugs in individual patients. This information can help identify an appropriate starting dose, the best way to adjust dosage to the needs of a particular patient, and a dose beyond which increases would be unlikely to provide added benefit or would produce unacceptable side effects."

4.3 Justification for Dose

The dose used for this study will be the dose approved by FDA as described in the prescribing information for CYTALUX™ (pafolacianine) injection.

4.4 End of Study Definition

A participant is considered to have completed the study if they have completed all phases of the study including the last visit or the last scheduled procedure shown in the Schedule of Activities (SoA), Section 1.3.

The end of the study is defined as completion of the last visit or procedure shown in the SoA.

5 STUDY POPULATION

Adult subjects (>18 years old) who are presumed high-risk patients or have advanced disease, and/or recurrent disease. Pregnant patients will be excluded.

5.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Provision of signed and dated informed consent form
2. Adult subjects 18 years of age and older
3. Primary diagnosis of endometrial cancer
4. Scheduled to undergo surgery for endometrial cancer
5. Ability to understand the requirements of the study and agree to abide by the study restrictions and to return for the required assessments

6. Willingness to stop the use of folate or folic acid supplements at least 48 hours prior to infusion of study drug

5.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Pregnancy or positive pregnancy test
2. Any medical condition that in the opinion of the investigator could potentially jeopardize the safety of the subject
3. History of anaphylactic reactions to products containing indocyanine green
4. History of allergy to any of the components of CYTALUX
5. Presence of any psychological, familial, sociological condition or geographical challenges potentially hampering compliance with the study protocol or follow-up schedule

5.3 Lifestyle Considerations

None.

5.4 Screen Failures

Screen failures are defined as participants who consent to participate in the clinical trial but are not subsequently entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

5.5 Strategies for Recruitment and Retention

Subjects will be recruited from the clinical practice of each Investigator. Follow-up visits are set to correspond with normal post-operative follow-ups by the surgeon. Retention is not expected to be a problem.

6 STUDY INTERVENTION

6.1 Study Intervention(s) Administration

6.1.1 Study Intervention Description

CYTALUX will be supplied in vials containing 1.6 mL of solution of 2 mg/mL OTL38 for a total of 3.2 mg of drug per vial. The contents of the vial are a frozen blue-green solution.

6.1.2 Dosing and Administration

The planned dose 0.025 mg/KG will be administered via IV over 60 minutes. Subjects will complete a single intravenous dose not less than 1 hour before and not more than 168 hours (7 days) before initiation of intraoperative fluorescent imaging. Pre-treatment with antihistamines and/or anti-nausea medication may be used. If the patient develops any symptoms or signs suggestive of a hypersensitivity reaction, including during infusion of the study drug, an antihistamine, and/or antiemetic may be administered based on the clinical judgement of the investigator. If such symptoms or signs suggestive of hypersensitivity develop during the infusion of the study drug, the infusion may be interrupted and then resumed based on the clinical judgement of the Investigator on the condition of the patient.

Folic acid may reduce the detection of cancerous tissue with CYTALUX. Patients should stop taking folate, folic acid, or folate-containing supplements 48 hours before administration of CYTALUX.

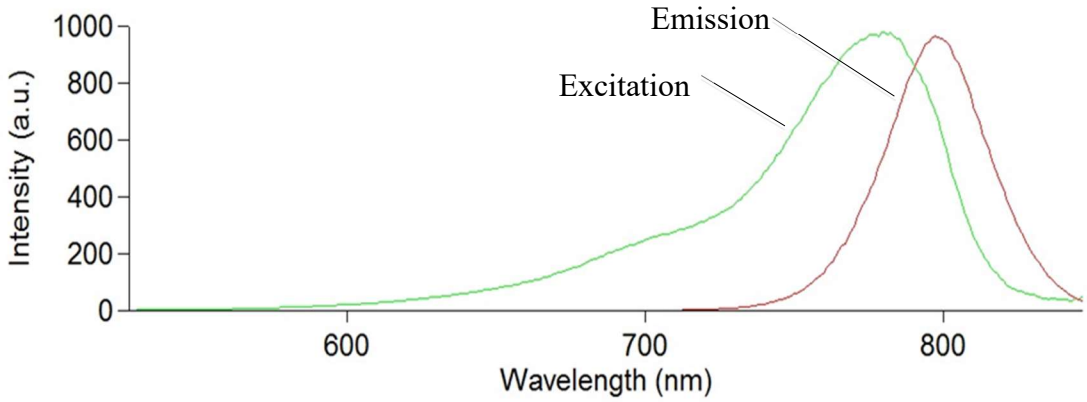
Note that CYTALUX should not be mixed with other medicinal products and should not be given simultaneously through the same IV line as another medicine.

6.1.3 Camera/Imaging System

The following are specifications for the imaging systems to be used in this study.

Spectral specifications: The light engine will provide an excitation channel that closely matches the optimal excitation wavelength of OTL38. As shown in Figure 1, OTL38 responds to light between the wavelengths of 760-776 nm with maximum excitation at 774-776 nm, and fluoresces, i.e., emits light at wavelengths in the near-infrared (NIR) spectrum (maximum emission 794-796 nm).

Figure 1. Excitation and Emission Spectra of OTL38



Exact spectral data for OTL38 is obtained using 1 µM of OTL38 in phosphate buffered saline with Cay Eclipse Fluorescence Spectrophotometer (Agilent) with auto filter setting in the Research and Development facility, On Target Laboratories, West Lafayette, IN.

Temperature: The temperature (T) of the camera head will not exceed 42°C. The limit T ≤ 42°C is taken from IEC60601-2-18 (Medical electrical equipment: Particular requirements for the basic safety and essential performance of endoscopic equipment).

Electrical and Electromagnetic Compatibility (EMC): The light engine will conform to international standards for EMC emission and susceptibility, as well as other specifications in IEC 60601-1-2.

Operating Conditions: The system shall function normally over the following range of environmental conditions:

Temperature: +10° C to +30° C, at sea level

Relative humidity: 10% to 85%, non-condensing

Enclosure: Rough surfaces, sharp corners and edges that could result in an unacceptable risk shall be avoided or covered.

Enclosure of the video processor / illuminator shall prevent fingers from reaching hazardous internal components.

Sterilization: Any component requiring sterilization shall tolerate the appropriate method of sterilization.

Draping: Drapes shall be provided to make the system suitable for application in the sterile field.

Light Power – Maximum Power at Exit of Illuminator: The maximum light power at the exit of the illuminator shall comply with skin and tissue exposure limits as defined by IEC 60825-1 and CIE S009.

Standard – Class 3R Laser Product: The system shall comply with the safety requirements for a Class 3R laser product according to IEC 60825-1:2007.

Standard – Radiation Safety: The system shall comply with the standard or broadband radiation CIE S009/E:2002.

Standard – General Safety: The system shall comply with general safety standards IEC 60601-1:2005 and IEC 60601-2-18, including all applicable amendments.

Training and Intended Use: The system can only be used by clinicians that have been qualified as trained by the system provider or the sponsor, and only for the intended use in this clinical study protocol that has been approved by an IRB.

6.2 Preparation/ Handling/ Storage/ Accountability

6.2.1 Acquisition and Accountability

CYTALUX will be provided by On Target Laboratories. The vials must be stored in a secure, temperature-controlled freezer with limited access. Unused, partially used and/or empty vials will be disposed of on-site according to standard site procedures.

A Pharmacist or other trained and qualified healthcare professional will prepare the IV solutions according to the manufacturer's label.

6.2.2 Formulation, Appearance, Packaging and Labeling

The study medication will be packaged in vials and labelled by On Target Laboratories' clinical supplies designee.

Study medication should be stored in a freezer at temperature -20°C, and with protection from light.

A Pharmacist or other trained and qualified healthcare professional will prepare the IV solutions according to the manufacturer's label. All prepared solutions should be protected from light and refrigerated (between 2-8°C) until use.

6.2.3 Product Storage and Stability

Study medication should be stored in a freezer at temperature, -25 to -15°C, and with protection from light. If not immediately used, store the diluted CYTALUX infusion solution in a refrigerator at 2°C to 8°C for not more than 24 hours. Once the bag is removed from refrigeration, the infusion must be completed within 3 hours.

6.2.4 Preparation

CYTALUX will be prepared according to the manufacturer's prescribing information.

Note that CYTALUX should not be mixed with other medicinal products and should not be given simultaneously through the same IV line as another medicine.

6.3 Measures to Minimize Bias – Randomization and Blinding

This trial will be an open-label study with no randomization or blinding. All subjects will receive the study drug.

6.4 Study Intervention Compliance

The IV infusion will be performed by qualified personnel and overseen by the investigator or a medically qualified delegate. The date and time of the infusion will be recorded, as well as the amount infused. Subjects may elect to have the infusion discontinued as for example if they withdraw consent for the study, or experience one or more adverse events that are suspected to be attributable to the test article or its infusion.

6.5 Concomitant Therapy

Necessary supportive measures for optimal medical care will be given throughout the study. Additional care may be administered as indicated at the discretion of the treating physician, and where appropriate after discussion with the medical monitor. Concomitant medications will include all medications that started, or were continuing, during or after administration of the study drug.

The following concomitant medications are prohibited within 48 hours prior to drug administration: folic acid, folate supplements, and multi-vitamins containing folate.

6.6 Rescue Medication

Rescue medication is not applicable to this study.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 Discontinuation of Study Intervention

Discontinuation from infusion of CYTALUX does not mean discontinuation from the study, and remaining study procedures should be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to, changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include the following:

- The weight of the infusion bag, or a measurement of remaining volume
- The time of discontinuation
- The reason for discontinuation

7.2 Participant Discontinuation / Withdrawal from the Study

Subjects are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- Cancelation or rescheduling surgery
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for discontinuation or withdrawal from the study will be recorded. Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

7.3 Lost to Follow-up

A subject will be considered lost to follow-up if they fail to return for scheduled safety follow-up visits and is unable to be contacted by the study site staff.

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

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

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 Study Activities by Visit

Each subject who enters study screening (i.e. signs an informed consent form) will be assigned a subject ID number for traceability. Any subject who signs an informed consent but fails to meet the eligibility criteria is considered to be a Screen Failure. Screen Failure subjects will have their demographic information and reason for screen failure captured.

8.1.1 Screening Visit

[Purpose: To determine initial eligibility and assign dose timing]

Screening can take place up to 30 days prior to the scheduled surgery. Prior to the initiation of study-specific screening assessments the Investigator or designee must provide the patient with a complete explanation of the purpose of the study and the planned evaluations (procedures and assessments). To be screened, the patient must sign and receive a copy of an Informed Consent Form and authorization of use and disclosure of protected health information (PHI) that was approved by the governing IRB. All consenting subjects will be screened for trial eligibility by completing the following procedures at this visit:

1. Assess all Inclusion/Exclusion Criteria
2. Obtain demographic data
3. Record endometrial cancer diagnosis information
4. Record relevant medical history

8.1.2 Visit 1: Infusion

[Purpose: To infuse CYTALUX™ (PAFOLACIANINE) INJECTION]

1. Patients with a known allergy to CYTALUX (pafolacianine) will be given pre-medication of 25 mg Benadryl and 4 mg Zofran as prophylaxis approximately 30 minutes prior to the start of infusion, unless a patient has a history of allergy to either drug.
2. A single dose of CYTALUX will be infused IV over 60 minutes
3. AEs will be recorded during infusion of CYTALUX.
   Should the patient experience suspected adverse events during infusion, the infusion will be stopped, and the Principal Investigator (PI) will be contacted for discussion and assessment. Per PI discretion, the patient will be treated for symptoms and infusion can be started again to assess for tolerance. If infusion is still not tolerated, amount infused will be recorded and imaging portion of study will proceed.
4. Intraoperative imaging should begin within 1 to 168 hours (7 days) after the completion of infusion.

8.1.3 Visit 2: Surgery

[Purpose: To collect data on the performance of intra-operative molecular imaging]

1. AEs and ADEs will be recorded during and following surgery.

2. After the surgical site is visualized under normal light and/or palpation, the number and location of suspect lesions detected under normal light will be recorded on the schematic using an "O".
3. Following the assessment by normal light, subjects will undergo fluorescence imaging of the surgical field. Suspect lesions detected under fluorescence imaging will be marked on the schematic using an "X".
4. All identified suspect lesions will be marked on the schematic ("O", "X", or "⊗" as described in Section 4.1.3) and excised, at the discretion of the Investigator.
5. Sentinel lymph node biopsy will be performed at the Investigator's discretion per the standard of care.
6. All excised lesions will be sent to the local laboratory for histopathology and immunohistochemistry staining. A unique identifier will be assigned to each excised lesion and the location of each will be recorded along with the unique identifier. If an organ/large section of tissue (e.g. uterus, omentum) with multiple lesions is excised *in toto,* one grossly positive lesion will be utilized for the purposes of calculating sensitivity and FR expression.
7. Histopathology, folate receptor expression, and genomic testing results will be recorded once data is received per institutional practices and timeline.

8.1.4 Follow-Up Visit (4 weeks, +/- 1 week)

[Purpose: To evaluate subjects for any new adverse experiences, and to ascertain the status of previously unresolved AEs]

This visit may take place in person or over the phone.
1. Inquire about new and unresolved AEs and ADEs

8.2 Efficacy Assessments

8.2.1 Surgical Reporting Schematics

Surgical Schematics will be used to record the lesions for each patient (see APPENDIX 1).

8.2.2 Pathology Samples

All excised lesions will be processed according to local pathology practices. The final pathology results will be recorded in the CRF.

8.3 Adverse Events and Serious Adverse Events

8.3.1 Definition of Adverse Events (AE) and Adverse Device Events (ADE)

An AE is any untoward medical occurrence temporally associated with the use of an investigational medicinal product, whether or not considered causally related to that product. An AE can be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease. The Investigator, or his/her designee, will document AEs. Only AEs and ADEs considered causally related to the investigational product will be documented during the trial period.

An ADE is an AE associated with exposure to a medical device, such as the camera system and NIR illumination in this study. Where the abbreviation AE is used in this protocol, it can be understood to incorporate ADEs where appropriate.

The Investigator should use his/her discretion in ordering additional tests as necessary to monitor the resolution of such events. Event outcome at resolution or at time of last follow up will be recorded as event resolved, resolved with sequelae, ongoing at discontinuation, or death. Events ongoing after the subject's last visit will be followed per the investigator's standard of care.

The Investigator should consider AEs both as they relate to the investigational product and as they relate to the procedures involved in the trial. The Investigator is responsible for determining the initial relationship and severity of adverse events.

8.3.2 Definition of Serious Adverse Events (SAE)

A serious adverse event (SAE) is defined by federal regulation as any AE occurring at any dose that results in any of the following outcomes: death, life-threatening AE, requires hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. All SAEs will be documented during trial.

Important medical events that may not result in death, be 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. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in subject hospitalization, or the development of drug dependency or drug abuse.

8.3.3 Unanticipated Adverse Device Effect (UADE)

Risk of Misinterpretation

Errors may occur with the use of OTL38 during intraoperative fluorescence imaging to detect ovarian cancer and lesions in the lung, including false negatives and false positives. Non-fluorescing tissue in the surgical field does not rule out the presence of ovarian cancer or lesions in the lung. Fluorescence may be seen in normal tissues including bowel, kidneys, lymph nodes, and lungs as well as in inflamed tissues.

8.3.4 Classification of an Adverse Event (AE)

8.3.4.1 Severity of Event

The severity of all AE will be assessed by the Investigator and should be classified as mild, moderate, or severe. Severity will be graded according to the following definitions:

Mild: The subject experiences awareness of symptoms but these are easily tolerated or managed without specific treatment. Clinical or diagnostic observations only, intervention is not indicated.

Moderate: The subject experiences discomfort enough to cause interference with usual activity, and/or the condition requires specific treatment. Minimal, local or non-invasive intervention is indicated.

Severe: The subject is incapacitated with inability to work or do usual activity, and/or the event requires significant treatment measures. Not immediately life-threatening but requires or prolongs hospitalization.

Life Threatening: Urgent intervention is indicated.

Fatal: The adverse event results in death or is death.

8.3.4.2 Relationship to Study Intervention

AEs must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfill this definition.
- **Not Related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study intervention) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments). Or, the AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician

8.3.4.3 Expectedness

The Investigator will be responsible for indicating whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the patient population under study, the known risks of major surgery, or the risk information previously described for the study intervention.

8.3.5 Adverse Event Reporting

Disease related events expected in this population may be reported by the investigator if they differ in nature or frequency from what is expected and appear to have a causal relationship to the test article. Adverse events must be reported in the subject's source documents. It is the Investigator's responsibility to forward to the site's IRB all SAE/SUSAR/unanticipated ADE reports.

8.3.6 Serious Adverse Event Reporting

- The Principal Investigator must be notified within 1 business day of study team's knowledge of any event meeting the criteria and definition of a serious adverse event, regardless of attribution, occurring during the study or within 30 days of the last administration of the study related intervention.

- The investigator must report all events meeting the criteria and definition of a serious adverse event that are unexpected and possibly related (definite, probable or possible) to study intervention as per the local IRB reporting requirements.
- Serious Adverse Events must be reported to the local IRB in accordance with the IRB's policies.
- The site must notify On Target Laboratories within 7 days of becoming aware of the event.

8.3.7 Reporting of Pregnancy

Patients will be screened for pregnancy and excluded from the study if they are found to be pregnant.

9 STATISTICAL CONSIDERATIONS

9.1 Statistical Hypotheses

- Primary Efficacy Endpoint:
  - The primary efficacy endpoint is the sensitivity of CYTALUX with NIR imaging for detection of malignant lesions. Sensitivity is defined as the proportion of fluorescent light positive lesions that are histologically confirmed to be cancer relative to the total number of lesions confirmed to be cancer.

    Sensitivity = (True Positive)/(True Positive + False Negative)

- Secondary Efficacy Endpoints:

  1. Incidence rates of all adverse events (AEs), adverse device effects(ADEs), and SAEs, from the time of CYTALUX administration through Visit 3
  2. Sensitivity for cancerous lesions for:
     a. FRα positive lesions
     b. FRβ positive lesions

- Exploratory Endpoints:

  1. Genomic evaluation of tumor inclusive of, but not limited to:
     a. Estrogen receptor/progesterone receptor (ER/PR) status
     b. HER2 status
     c. Mismatch repair (MMR) status
     d. POLE status
     e. p53 status
     f. CARIS whole genome sequencing
  2. The exploratory endpoint is the detection rate of CYTALUX with NIR imaging for identification of SLNs. The detection rate is the proportion of the patients with SLNs detected by CYTALUX and NIR imaging in all enrolled patients.

9.2 Statistical Analyses

9.2.1 General Approach

Demographic and baseline patient characteristics will be summarized and described as numbers and percentages or means, median, standard deviations, quartiles and range, as appropriate. Pearson's Chi square tests will applied for categorized data, and students t-test and Mann Whitney U tests for continuous variables. Univariate analyses will be used to assess potential factors primary and secondary efficacy

endpoints as laid out below. Data analysis will be performed using the software package STATA. Free text options will be analyzed qualitatively.

9.2.2 Analysis of the Primary Efficacy Endpoint

The primary analysis of the primary endpoint will include subjects exposed to CYTALUX™ (pafolacianine) injection and undergo fluorescent imaging (CYTALUX™ (pafolacianine) injection+Imaging) who:

- Received study drug and were evaluated under NIR fluorescent light imaging during surgery

The primary analysis of the efficacy endpoint will be a one-sample test for a proportion via an exact binomial test conducted at the two-tailed alpha level of 0.05. The test will compare the observed proportion against a threshold of 0.10. The efficacy of CYTALUX™ (pafolacianine) injection in combination with fluorescent imaging will be confirmed if the null hypothesis is rejected and the observed proportion is greater than 0.10. The two-sided 95% confidence interval (CI) will also be calculated.

9.2.3 Safety Analyses

Safety will be described via subject incidence of treatment emergent adverse events (TEAEs) including serious TEAEs as well as adverse device effects (ADEs) considered as causally related.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 Regulatory, Ethical, And Study Oversight Considerations

10.1.1 Informed Consent Process

10.1.1.1 Consent/Assent and Other Informational Documents Provided to Participants

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting any study procedure. IRB-approved consent forms will contain at a minimum the following information:

a. That the trial involves research.
b. The purpose of the trial.
c. The trial treatment(s) and the probability for random assignment to each treatment.
d. The trial procedures to be followed, including all invasive procedures.
e. The subject's responsibilities.
f. Those aspects of the trial that are experimental.
g. The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
h. The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
i. The alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks.
j. The compensation and/or treatment available to the subject in the event of trial-related injury.
k. The anticipated prorated payment, if any, to the subject for participating in the trial.
l. The anticipated expenses, if any, to the subject for participating in the trial.

m. That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
n. That the monitor(s), the auditor(s), the IRB, and the regulatory authority(ies) will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
o. That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject's identity will remain confidential.
p. That the subject or the subject's legally acceptable representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
q. The person(s) to contact for further information regarding the trial and the rights of trial subjects, and whom to contact in the event of trial-related injury.
r. The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
s. The expected duration of the subject's participation in the trial.
t. The approximate number of subjects involved in the trial.

10.1.1.2 Consent Procedures and Documentation

Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants will have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Only authorized trial staff should obtain consent and the most currently approved IRB consent form must be used.

10.1.2 Confidentiality and Privacy

Subject confidentiality and privacy are strictly held in trust by the Sponsor Investigator, their staff, and OnTarget Laboratories, Inc. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to subjects. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning

the study or the data will be released to any unauthorized third party without prior written approval of the Principal Investigator and OnTarget Laboratories, Inc..

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the IRB, or the FDA 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 participants in this study. The clinical study site will permit access to such records.

The study subject's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, or sponsor requirements.

Study subject research data, which is for purposes of statistical analysis and scientific reporting, will be stored in the secure and password protected IU REDCap data management system. Any data or images transmitted to OnTarget Laboratories, Inc., manufacturer and provider of CYTALUX™ (PAFOLACIANINE) INJECTION, will be deidentified; individual subjects and their research data will be identified by a unique study identification number.

10.1.3 Future Use of Stored Specimens and Data

This protocol does not include storage of any biological samples for future testing. All study data will remain de-identified and kept securely by the sponsor or by a qualified contracted vendor, for at least the period of time required by FDA.

10.1.4 Safety Oversight

Safety oversight will be under the direction of a licensed physician with training, experience and qualifications. This study is a low-risk study utilizing an FDA-approved agent for intra-operative imaging.

10.1.5 Data Handling and Record Keeping

10.1.5.1 Data Collection and Management Responsibilities

During the trial, the Investigator will maintain adequate records for the trial, including medical records, records detailing the progress of the trial for each subject, CRFs, signed informed consent forms, investigational product disposition records, correspondence with the IRB/IEC, AE/SAE reports, and information regarding subject discontinuation and completion of the trial.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

10.1.6 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol or ICH GCP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of serious or repeated deviations, corrective and preventative actions are to be developed by the site and implemented promptly.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations.

10.1.7 Publication and Data Sharing Policy

At a minimum, the trial and its results will be posted on ClinicalTrials.Gov. The investigator/sponsor may prepare manuscripts for publication.

10.2 Additional Considerations

Not Applicable.

10.3 Protocol Amendments

Any permanent change to the protocol must be handled as a protocol amendment. The written amendment must be submitted to the IRB and the investigator must await approval before implementing the changes.

If in the judgment of the IRB, the investigator, and/or, the amendment to the protocol substantially changes the study design and/or increases the potential risk to the subject and/or has an impact on the subject's involvement as a study participant, the currently approved written informed consent form will require similar modification. In such cases, informed consent will be renewed for subjects enrolled in the study before continued participation.

Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
N/A	Original Issue	

11 REFERENCES

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3. Despierre E, Lambrechts S, Leunen K, Berteloot P, Neven P, Amant F, O'Shannessy DJ, Somers EB, Vergote I. Folate receptor alpha (FRA) expression remains unchanged in epithelial ovarian and endometrial cancer after chemotherapy. Gynecol Oncol. 2013 Jul;130(1):192-9. doi: 10.1016/j.ygyno.2013.03.024. Epub 2013 Apr 2. PMID: 23558051.

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5. Leamon CP, Low PS. Membrane folate-binding proteins are responsible for folate-protein conjugate endocytosis into cultured cells. Biochem J. 1993 May 1;291 (Pt 3)(Pt 3):855-60. doi: 10.1042/bj2910855. PMID: 8387781; PMCID: PMC1132447.

6. American Cancer Society. (2025). Cancer Facts & Figures 2025. Retrieved from https://www.cancer.org/cancer/types/endometrial-cancer.html

7. SEER. Surveillance Epidemiology and End Results US National Cancer Institute; 2025 [cited 2025 05 May]. Available from: https://seer.cancer.gov/statfacts/html/corp.html.

12 INVESTIGATOR SIGNATURE

Study Title:	The role of CYTALUX for endometrial cancer
Original Version Date:	DD-MMM-YYYY

By my signature, I confirm that my staff and I have carefully read and understand this protocol, and agree to comply with the conduct and terms of the trial specified herein. In particular, I/we have agreed to:

1. Abide by all obligations stated in the Clinical Trial Agreement (Contract)
2. Maintain confidentially and assure security of all confidential documents such as the protocol, product information documents, final trial reports, manuscript drafts, unpublished data, correspondence, etc.
3. Obtain Institutional Review Board approval of trial, any amendments to the trial, recruitment advertisements, informed consent document, and periodic re-approval as required.
4. Keep the Institutional Review Board and OnTarget, informed of serious adverse events and periodically report status of the trial to them as required.
5. Obtain written informed consent from each participant or his/her legal representative.
6. Make immediate reports of serious adverse events (SAE) to OnTarget or designee.
7. Abide by manuscript preparation/authorship guidelines established at the outset of the trial.

Investigator's Signature: _____

Investigator's Name (please print): _____

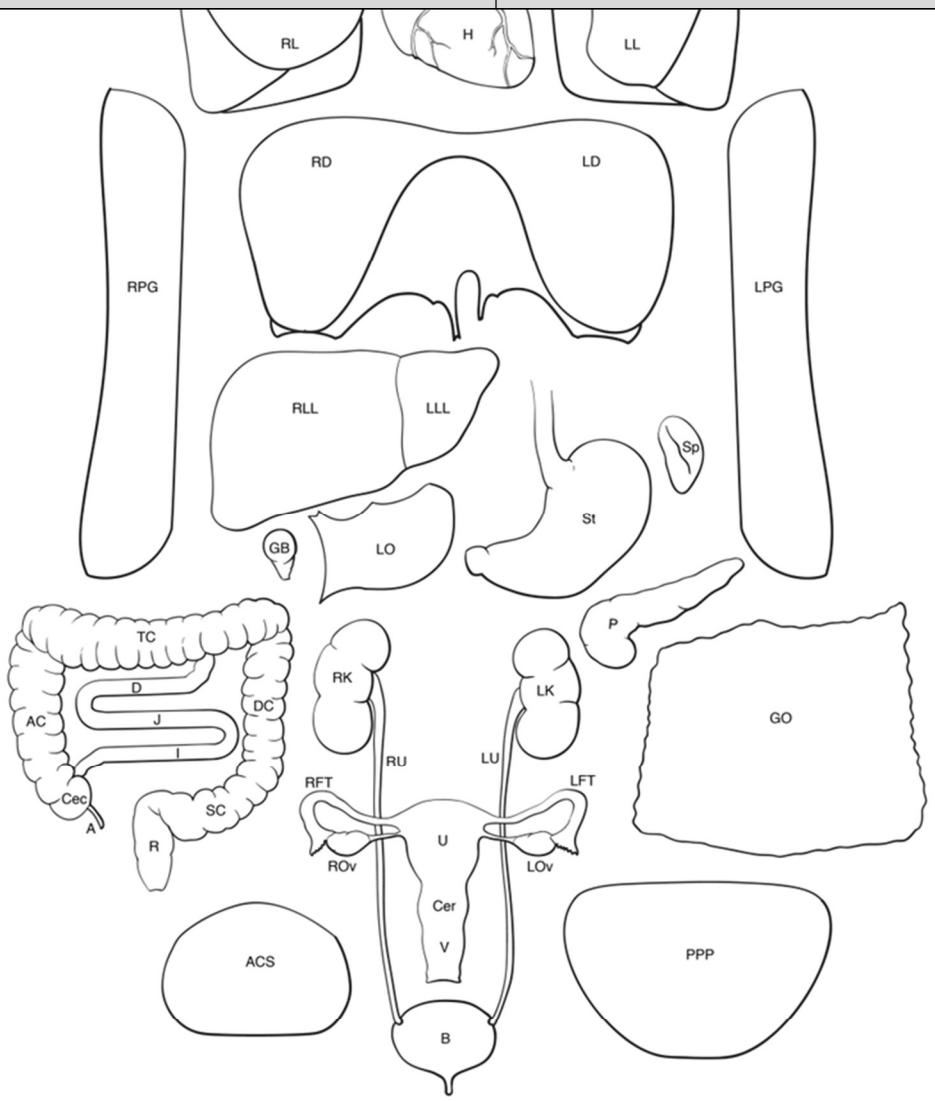
Date: _____

Appendix 1 Surgical Schematic Reporting Form

Surgical Schematic Report Form

Study: The role of CYTALUX for endometrial cancer

Patient Study ID No:	**Recorded by:**	**Date:**



A- Appendix
AC- Ascending Colon
ACS- Anterior Cul de Sac
B- Bladder
Cec- Cecum
Cer- Cervix
D- Duodenum
DC- Descending Colon
GB- Gallbladder
GO- Greater Omentum
H- Heart
I- Illeum
J- Jejunum
LD- Left Diaphragm
LFT- Left Fallopian Tube
LK- Left Kidney
LL- Left Lung
LLL- Left Lobe of the Liver
LO- Lesser Omentum
LOv- Left Ovary
LPG- Left Paracolic Gutter
LU- Left Ureter
P- Pancreas
PPP- Posterior Pelvic Peritoneum
R- Rectum
RD- Right Diaphragm
RFT- Right Fallopian Tube
RK- Right Kidney
RL- Right Lung
RLL- Right Lobe of the Liver
ROv- Right Ovary
RPG- Right Paracolic Gutter
RU- Right Ureter
SC- Sigmoid Colon
Sp- Spleen
St- Stomach
TC- Transverse Colon
U- Uterus
V- Vagina

Para-aortic lymph nodes:

- ❑ Right supra-renal
- ❑ Left supra-renal
- ❑ Right infra-renal (upper)
- ❑ Left infra-renal (upper)
- ❑ Right infra-renal (lower)
- ❑ Left infra-renal (lower)

Pelvic lymph nodes:

- ❑ Right common iliac
- ❑ Left common iliac
- ❑ Right external iliac
- ❑ Left external iliac
- ❑ Right internal iliac
- ❑ Left internal iliac

LESION DETECTION	INDICATE LESION TYPE
Normal Operating Environment Only	O
Fluorescence Only	X
Fluorescence and Normal Operating Environment	⊗

_____ _____

Signature of person recording information Date