**Title of Study:** A Single-Center, Open-Label, Proof of Concept Trial to Evaluate the Efficacy, Safety and Tolerability of a New Botanical Drug Product Containing East Indian Sandalwood Oil (EISO) for the Prevention and Treatment of Oral Mucositis Induced by Radiation Therapy with or without Concurrent Chemotherapy

**Consent to be part of a Research Study**
**The University of Texas Health Science Center at San Antonio (UTHSCSA)**
**To be conducted at**
The University of Texas Health Science Center at San Antonio,
University Health System (UHS)

## Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are entitled.

## General Information – "Who is conducting this research?"

**Principal Investigator**
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Ying Li, M.D., Ph.D. of The University of Texas Health Science Center at San Antonio (UTHSCSA), Department of Radiation Oncology.

**Funding**
**Study Sponsor:** Santalis Pharmaceuticals
Santalis Pharmaceuticals, a for-profit company, is funding this study (the sponsor). The sponsor designed the study, drafted the study plan and is providing money to UTHSCSA so that the researchers can conduct the study.

## Purpose of this study – "Why is this study being done?"

Many patients experience oral mucositis as a result of the combination of radiation treatment and chemotherapy they receive for their head and neck cancer. Oral mucositis is the painful inflammation (swelling) of the mucous membranes (moist lining) in the mouth. Signs and symptoms of oral mucositis can include: red or swollen mouth and gums; sores in the mouth or on the gums or tongue; soreness or pain (burning sensation) in the mouth or throat; difficulty swallowing or talking; feeling of dryness, mild burning, or pain when eating food; and/or soft, whitish patches or pus in the mouth or on the tongue.

East Indian sandalwood is a tall evergreen tree native to southern India. Both the wood and oil of the East Indian sandalwood tree have been used to treat a variety of skin and general health conditions. In traditional Indian medicine, East Indian sandalwood oil (EISO) has been used as a treatment for inflammatory and eruptive skin diseases. Sandalwood has been used for over 4000 years and its oil has been used commercially as a food flavoring agent in the United States since the 1800s. Sandalwood oil is commercially available, but not regulated. Sandalwood oils offered for sale for medical use may be of low grade and may contain residual solvents or other oils. Santalis

Pharmaceuticals Eastern Indian Sandalwood Oil (EISO) (SAN005) is a medical grade EISO and manufactured in Australia. It has a Certificate of Analysis which confirms that it meets specifications regarding its content and documentation of the production process.

This is a proof of concept study; a type of study that provides the first measurable evidence that a product might work in humans. SAN005 has not been previously tested as a treatment for oral mucositis. It has not been approved by the U.S. Food & Drug Administration (FDA) for treating or preventing oral mucositis. The mouth rinse being studied is non-alcoholic, is sweetened and mint-flavored and contains EISO at a level of 0.25% (one quarter of one percent).

You are being asked to participate in this proof of concept research study of SAN005 in preventing and treating oral mucositis. Standard care does not prevent oral mucositis. The researchers hope to learn what effects, good and/or bad, SAN005 has on people who use it and on oral mucositis. The people in this study will be the first people to receive EISO to treat/prevent radiation induced oral mucositis. EISO has been used extensively in humans; however, some side effects may not yet be known.

## Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you have head and neck cancer and will be treated with radiation, which may or may not include chemotherapy.

How many people are expected to take part in this study?
This study will enroll approximately 20 study participants.

## Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 8 visits with the researchers or study staff. It will be necessary for you to return to the clinic every week for up to 8 weeks. The study visits will take place at the same time as visits that are part of routine care (during radiation you are routinely seen by the doctor every week).

While in the study you must agree to not eat or drink any products that are used to prevent or treat oral mucositis, other than what is approved or prescribed by the study doctor.

**Screening** – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. Many of the procedures are described below as "standard care" and would be done even if you do not take part in this research study. You will be told which ones are for "research only".

**Screening Procedures**

- The results of the physical examination and medical history done as part of your standard care will be used.
- If you are capable of becoming pregnant, a pregnancy blood test will also be done before you receive study treatment. (research only)
- You will complete two quality of life questionnaires asking how your life has been affected by cancer and its treatment and about pain you may be experiencing. The questionnaires take about 5 – 10 minutes to complete. (research only)
- You will be asked to confirm any medications that you are taking

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you and will discuss other possible options.

**Study Procedures** - as a participant, you will undergo the following procedures:

Before your first radiation treatment:

- You will be given the study mouth rinse bottle and diary and instructions on how to use the rinse. (research only)

Weekly during radiation treatments:

- The doctor will perform a physical examination of your mouth.
- You will complete two quality of life questionnaires asking how your life has been affected by cancer and its treatment and about pain you may be experiencing. (research only)
- The study mouth rinse bottle and diary will be collected and a new bottle and diary will be given to you. (research only)
- You will be asked about any side effects from treatment that you may be experiencing.
- You will be asked to confirm any medications that you are taking.

**Could your participation end early?** There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

The researchers will discuss your options for medical care when your participation in this study ends.

## Risks – "What are the risks of participation in the research?"

**Risks from the research**

There are risks to taking part in a research study. One risk is that you may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to each your participation in this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Although sandalwood and its oil have been used for centuries there are only a few studies documenting possible side effects. Its use as a flavoring agent in food is considered safe. There have been a few cases of irritation reactions (redness, itching) in humans.

Could I have an allergic reaction?

Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that happen during an allergic reaction may include: rash, having a hard time

breathing; wheezing when you breathe; dizziness; sudden drop in blood pressure; swelling around the mouth, throat, or eyes; fast pulse; sweating; fevers; and/or chills.

You should get medical help and contact the study doctor or study staff immediately if you have any of these symptoms or any other side effects during the study.

We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

**Are there Risks related to withdrawing from the study?**
If you decide to withdraw from this study early, please discuss your decision with the principal investigator. The researcher may ask you to complete study withdrawal procedures at a final study visit. This visit includes a physical examination of your mouth, completion of the two quality of life questionnaires, and return of the study mouth rinse bottle and diary. There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

**Reproductive Risks -**
**Concerns for sexually active women:** You should not become pregnant while taking part in this study because we do not know how the study drug could affect a fetus, if a woman becomes pregnant during the study. It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant while you are in this study, you must tell one of the study doctors right away so that management of the pregnancy and the possibility of stopping the study can be discussed.

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the study drug might affect a developing fetus. We will do a pregnancy test before you start treatment to make sure you are not pregnant.

**Risks to babies who are being breastfed:** Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs might have on their breast milk.

**Are there risks if you also participate in other research studies?**
Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

**What if a research-related injury occurs?**
If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

**Benefits – "How could you or others benefit from your taking part in this study?"**

The possible benefit of your participating in this study is prevention of oral mucositis. There is no guarantee or promise that you will receive any benefit from this study.

**Alternative procedures or course of treatment – "What other options are there to participation in this study?"**

There are other options available to you. Your other choices may include:

- getting treatment or care without being in a study
- taking part in another study

**Payments – Will there be any payments for participation?**

You will receive reimbursement for your time and travel for being in the study as follows:

Screening Visit - $10

Visit before your first radiation treatment - $10

You will also receive parking vouchers for those visits.

The researchers will provide you with a MasterCard® (ClinCard). This is a debit card and compensation will be automatically credited after completion of the study. Your name, address and date of birth will be shared with a third-party solely for the purposes of compensation processing. This information will only be used for the administration of the compensation (ClinCard) and will be kept strictly confidential.

**Costs – Will taking part in this study cost anything?**

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as chemotherapy treatment, radiation treatment, and blood tests. Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

The sponsor will provide the study drug (mouth rinse) free of charge during this study. At the end of your participation you must return all unused study drug to the researcher. If you are a woman of child bearing potential the sponsor will also pay for the required screening pregnancy test.

**Confidentiality – How will your records be kept confidential?**

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study.

**What is Protected Health Information (PHI)?**

Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see

and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include: your medical history and blood work, information that we get from your medical record, information contained in your underlying medical records related to your medical history and treatments prior to the study, information that is created or collected during your participation in the study including medical and treatment history, information you give us during your participation in the study such as during interviews or from questionnaires, results of blood tests; and demographic information like your age.

We will get this information by asking you, asking your doctor, and by looking at your chart at UTHSCSA and UHS.

**How will your PHI be shared?**
Because this is a research study, we will be unable keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- The sponsor of the study, Santalis Pharmaceuticals
- The members of the local research team
- The Institutional Review Board and the Compliance Office of The University of Texas Health Science Center at San Antonio, and other groups that oversee how research studies are carried out.
- The Research offices at The University of Texas Health Science Center at San Antonio and University Health System (UHS).

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to the people or groups listed above or it may be transmitted to them electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

**How will your PHI be protected?**
In an effort to protect your privacy, the study staff will use code numbers instead of your name to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of UTHSCSA or UHS for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

**Do you have to allow the use of your health information?**
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties but you will not be allowed to participate in the study. After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to Ying Li, M.D., Ph.D., UTHSCSA, Dept. of Radiation Oncology, 7703 Floyd Curl Dr., MC 7889, San Antonio, TX 78229-3900. If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

**Can you ask to see the PHI that is collected about you for this study?**
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

**How long will your PHI be used?**
By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends and all required study monitoring is over.

**Contact Information – Who can you contact if you have questions, concerns, comments or complaints?**

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:
Ying Li, M.D., Ph.D. can be reached at (210) 450-1719 during normal business hours (daytime) or after hours at (210) 215-4406 (cell phone) (evenings and weekends).

If primary is not available, contact:
Chul S. Ha, M.D. can be reached at (210) 450-1109 during normal business hours or after hours at (210) 563-2105.

The University of Texas Health Science Center committee that reviews research on human subjects (Institutional Review Board) will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the IRB by calling 210-567-8250, or by mail to IRB, UTHSCSA, Mail Code 7830, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.

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## Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE

- You have read the above information.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.

**Adult Signature Section**

- You have voluntarily decided to take part in this research study.
- You authorize the collection, use and sharing of your protected health information as described in this form.

| Printed Name of Subject | Signature of Subject | Date | Time (AM / PM) |
|---|---|---|---|
| Printed Name of Witness | Signature of Witness | Date | Time (AM / PM) |

☐ *Check if consent and authorization obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. Have witness initial below.*
Declaration of witness: I was present for the entire consent process. _____ ←(initials of witness)

| Printed Name of Person Obtaining Consent and Authorization | Signature of Person Obtaining Consent and Authorization | Date | Time (AM / PM) |
|---|---|---|---|

☐ Consent and authorization was obtained from this individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. The method used for communication with the subject was: _____.
The specific means by which the subject communicated agreement to participate was:

**Can you ask to see the PHI that is collected about you for this study?**
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.

**How long will your PHI be used?**
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Declaration of witness: I was present for the entire consent process. _____ ←(initials of witness)

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