

<b>Title</b>	A Multi-Center, Randomized, Placebo Controlled, Safety, Tolerability, and Efficacy Trial of a New Botanical Drug Product Containing East Indian Sandalwood Oil (EISO) at One Dose Level for the Treatment of Mild-to-Moderate Plaque Psoriasis in Adult Subjects
<b>Setting and Trial Center</b>	This trial will be conducted at approximately 5 study centers in the United States.
<b>Number of Subjects</b>	Up to 72 to ensure 60 complete the trial
<b>Objectives</b>	<p>The objectives of this trial are:</p> <ul style="list-style-type: none"><li>• To evaluate the safety of SAN021 when administered to adult subjects with mild-to-moderate plaque psoriasis</li><li>• To evaluate the tolerability of SAN021 when administered to adult subjects with mild-to-moderate plaque psoriasis</li><li>• To evaluate the preliminary efficacy of SAN021 when administered to adult subjects with mild-to-moderate plaque psoriasis</li></ul>
<b>Trial Design and Patient Population</b>	<p>This trial will be a multi-center, randomized, placebo controlled study to evaluate the safety, tolerability, and efficacy of SAN021 when administered for up to 42 days to adults between the ages of 18 to 65 years who have a clinical diagnosis of mild-to-moderate plaque psoriasis.</p> <p>Subjects will enter the Screening Period once the informed consent and consent process has been completed. Subjects with mild-to-moderate plaque psoriasis, as defined by a Psoriasis Area and Severity Index (PASI) score between 2 and 12,<sup>36</sup> appropriate for topical treatment that covers a minimum of 1.0% and a maximum of 10% BSA, in the permitted treatment areas, and who meet all of the inclusion and none of the exclusion criteria will be enrolled.</p> <p>Once patient eligibility is confirmed and the screening procedures completed, all enrolled subjects will start the Treatment Period of the study. All enrolled subjects will receive either 10% SAN021 or placebo serum (randomized in a 2:1 ratio) with the first dose applied at the Day 1 Study Visit. Subjects will be instructed on how to apply the study medication twice daily for 42 days. Subjects will return to the clinic for study-related assessments on Study Days 8, 15, 28 and a final visit on Day 42. On Study Day 49, patient will receive a Follow-up phone call and be queried for condition status since going off study.</p>
<b>Inclusion Criteria</b>	Subjects will be included in the trial if they meet all of the following

criteria:

1. Are  $\geq 18$  but  $\leq 65$  years of age
2. Have a clinical diagnosis of mild-to-moderate plaque psoriasis, as defined by a Psoriasis Area and Severity Index (PASI) score between 2 and 12,<sup>36</sup> appropriate for topical treatment that covers a minimum of 1.0% and a maximum of 10% BSA, in the permitted treatment areas.
3. Are willing to treat all psoriasis occurring in the permitted treatment areas with only SAN021
4. Are free of any systemic or dermatologic disorder, which, in the opinion of the investigator, will interfere with the study results or increase the risk of adverse events.
5. Are willing to avoid prolonged exposure of the treatment area to ultraviolet radiation (natural or artificial) for the duration of the study.
6. Are willing to refrain from using any lotions, moisturizer, cleansers, cosmetics or creams, other than those issued as part of the study, on the treatment areas during the treatment period.
7. If female of childbearing potential, must be willing to practice an acceptable form of birth control for the duration of the study.(i.e. oral contraceptive, barrier method and/or intra-uterine device)
8. Are able to give written informed consent in a manner approved by the Institutional Review Board or Ethics Review Committee and comply with the requirements of the study.
9. Are willing to avoid participation in any other clinical trial for the duration of this study.
10. Are willing to refrain from treating restricted areas, which will be excluded from PGA assessment and BSA calculation. These areas are as follows: head, neck, fingernails, toenails, soles of feet, and palms of hands, axillae, or intertriginous areas.

## Exclusion Criteria

Subjects will be excluded from the trial if they meet any of the following criteria:

1. Have spontaneously improving or rapidly deteriorating plaque psoriasis, or pustular psoriasis as determined by the Investigator.
2. Have been treated, with prescription medication for plaque psoriasis, within 60 days prior to the Baseline visit.
3. Are pregnant, breast-feeding, or planning to become pregnant during the study.
4. Have any evidence of systemic cancer, squamous cell carcinoma, basal cell carcinoma, in the past 5 years, or any other confounding skin condition.
5. Are undergoing treatments with topical antipsoriatic drug products other than corticosteroids within 14 days prior to the Baseline Visit, and for therapy containing corticosteroids or retinoids within 28 days prior to Baseline Visit.
6. Have open sores or open lesions in the treatment area(s).
7. Have any condition that, in the opinion of the investigator, would confound the safety and/or efficacy assessments of plaque psoriasis.
8. Have participated in any interventional clinical trial in the previous 30 days.
9. Have a known sensitivity to any of the constituents of the test product including sensitivities to sandalwood oil, fragrances, or any member of the Compositae family of vascular plants (e.g., sunflowers, daisies, dahlias, etc.).
10. Have used, are using, or are planning to use immunosuppressive or immunomodulatory medication (i.e., biologics), including oral or parenteral corticosteroids.
11. Have a history of alcohol or illegal drug/substance abuse, or suspected alcohol or illegal drug/substance abuse in the past two years.
12. Plan to seek alternative treatment of any kind for their psoriasis, in the eligible treatment areas or otherwise, during the trial period.

## Screening (Day -7)

Eligible subjects will be asked to read and sign an informed consent and photography consent form. No study procedures will be conducted until the informed consent and photography consent forms are signed.

At the Screening Visit, the following procedures will be performed:

- Conduct the informed/photography consent process.
- Record Demographics to include age, sex, and race.
- Review the inclusion/exclusion criteria.
- Record all concomitant medications including all prescription drugs, nonprescription drugs, and nutritional supplements taken in the 60-days prior to Screening.
- Perform a full physical examination including height (cm) and weight (kg).
- Record pertinent medical history including tobacco, illegal substance and alcohol history and current use.
- Administer the Physician's Global Assessment (PGA) and the Psoriasis Area Severity Index (PASI).
- Calculate the plaque BSA of the area(s) to be treated.

## Treatment Period

### Visit 1 Baseline (Day 1 [ $\pm$ 2 Days])

Eligible subjects will have the following procedures completed at Visit 1 (Baseline). It is possible for the patient to be screened and complete the Visit 1 (Baseline) procedures on the same day.

- Review inclusion and exclusion criteria to ensure the patient qualifies for the study.
- If this visit is NOT combined with the screening visit:
  - Perform an abbreviated physical examination including weight (kg),
  - Update concomitant medications including all prescription drugs, non-prescription drugs and nutritional supplements
  - Review and update the patient's pertinent medical history.

- Complete the PGA (only treatment area(s) are to be evaluated), PASI and tolerability assessment (only treatment area(s) are to be evaluated) including calculating the BSA of the affected area (only treatment area(s) are to be evaluated).
- If patient is a female of childbearing potential, collect a urine sample and perform a  $\beta$ -human chorionic gonadotropin pregnancy test.
- Instruct the patient on proper washing of the target treatment area(s) (using only study-approved cleanser) and application of SAN021 study medication on the treatment areas during the treatment period.
- Photograph the treatment area(s).
- Replace the cap with the dropper cap and weigh full bottle of SAN021 study medication and record weight prior to on site first dose.
- With the dropper cap on, weigh bottle of SAN021 study medication post on site dose and dispense to subject.
- Instruct the subject to return in one week for the next study visit with the study drug

Visit 2 (Day 7 [ $\pm 2$  Days]), Visit 3 (Day 14 [ $\pm 2$  Days]), Visit 4 (Day 28 [ $\pm 2$  Days])

All study visits have a  $\pm 2$ -day visit window.

- Query for adverse events.
- Update concomitant medications including all prescription drugs, nonprescription drugs, and nutritional supplements.
- Query for treatment regimen compliance.
- Weigh and record the weight of the study medication and re-dispense.
- Complete the PGA (only treatment area(s) are to be evaluated), PASI and tolerability assessment (only treatment area(s) are to be evaluated) including calculating the BSA of the affected area (only treatment area(s) are to be evaluated).
- Photograph the treatment area(s).
- Review the directions for use of the study medication with the patient, and re-educate if applicable.

- Instruct the patient to return for the next study visit with study drug.

#### **Final Visit (Visit 5)**

##### Final Visit (Day 42 [ $\pm 2$ Days])

- Query for adverse events.
- Update concomitant medications including all prescription drugs, nonprescription drugs, and nutritional supplements.
- Query for treatment regimen compliance.
- Collect and weigh the study medication and record the weight.
- Complete the PGA (only treatment area(s) are to be evaluated), PASI and tolerability assessment (only treatment area(s) are to be evaluated) including calculating the BSA of the affected area (only treatment area(s) are to be evaluated).
- Photograph the treatment area(s).
- Instruct the patient to return for another study visit only if study-related adverse events persist or, in the Investigator's opinion, an additional study visit is warranted to ensure the patient's safety.

#### **Follow-up Call**

##### Follow-up Call (Day 49 [ $\pm 2$ Days])

- Query for status of condition since going off study
  - i.e. has the condition been stable, worsened or improved since discontinuing study medication?

#### **Duration of Treatment and Trial Participation**

The maximum duration of trial participation for each patient is approximately 49 days:

- 7-day Screening Period (Day -7)
- Single-day Baseline Visit 1 (Day 1)
- 42-days of treatment (Visits 2 (Day 7), Visit 3 (Day 14), Visit 4 (Day 28) and Final Visit (Day 42))
- Follow-up Call (Day 49)

If the patient's treatment is interrupted by illness or other

circumstances, every attempt will be made to have the patient return to the clinic for a final visit.

**Trial Population**

Up to 72 subjects, 18 – 65 years of age inclusive, with a clinical diagnosis of mild-to-moderate plaque psoriasis, as defined by a Psoriasis Area and Severity Index (PASI) score between 2 and 12,<sup>36</sup> that, in the opinion of the investigator, is appropriate for topical treatment, that covers a minimum of 1.0% and a maximum of 10% BSA, in the permitted treatment areas.

**Trial Drug, Dose and  
Mode of  
Administration**

Study medication will be provided by Santalis Pharmaceuticals.

The following treatment product will be provided:

- SAN021 10% - to be used morning and night,

OR

- Placebo- to be used morning and night.

Subjects will also be provided with:

- Cetaphil Gentle Skin Cleanser - to be used for the duration of the trial.

The first treatment of SAN021 will be applied at the Baseline Visit, then patient will be instructed on the procedure for self-administration at home.

**Criteria For Evaluation**

Subjects that receive one application of study medication will be included in the safety and tolerability analysis.

Subjects that complete at least 80% of treatments, as determined by product usage, will be included in the efficacy analysis.

Missing efficacy data will be imputed using the last observation carried forward. No imputations will be made for missing safety data.

**Safety Evaluations**

The primary purpose of this study is to determine the safety profile of SAN021.

Safety will be assessed by evaluating adverse events (AEs) with respect to severity, duration, and relationship to study drug.

**Tolerability  
Evaluations**

Tolerability will be based on the number of subjects reporting discomfort during or immediately following application of SAN021, This will also be recorded as an AE. The study restricted treatment

areas are to be not to be used in this evaluation. (see #10 under Inclusion Criteria)

## **Preliminary Efficacy Evaluation**

### **Preliminary Efficacy Endpoints:**

The preliminary efficacy will be evaluated as follows:

- Percentage of subjects achieving at least a 1-grade improvement in PGA score
- Percentage of subjects achieving a 2-grade improvement in the PGA score
- Percentage of subjects who have a  $\geq 25\%$  reduction in the Psoriasis Area and Severity Index (PASI) score at any point during the trial.
- Percentage of subjects who have a  $\geq 50\%$  reduction in the Psoriasis Area Severity Index (PASI) score at any point during the trial.
- Number of subjects achieving a Physician's Global Assessment of "clear" or "almost clear" at any time point during the 42 days of therapy. The study restricted treatment areas are not to be included in this evaluation. (see #10 under Inclusion Criteria)

A. Physician's Global Assessment (PGA): The PGA will be based on a 5-point scale ranging from 0 (clear) to 4 (severe), and will be assessed, preferably by the same evaluator at each visit for the overall affected areas with plaque psoriasis which were treated with the study drug. The study exclusion areas and those areas not treated are not to be used in this assessment. The following scores will be used to describe the severity of overall plaque psoriasis of the treatable areas:

Grade	Score	Description
Clear	0	No signs of psoriasis (post-inflammatory hyperpigmentation may be present)
Almost Clear	1	Intermediate between mild and clear
Mild	2	Slight scaling plaque elevation, scaling, and/or erythema
Moderate	3	Moderate plaque elevation, scaling, and/or erythema
Severe	4	Very marked plaque elevation, scaling, and/or erythema



## Data Analysis

### **Safety**

The number and percentage of subjects reporting at least one occurrence of an AE for each unique System Organ Class and Preferred Term will also be tabulated by severity and by the relationship to trial drug. All AEs will be presented in a data listing.

### **Tolerability**

Tolerability will be based on the number of subjects reporting discomfort during or immediately following application of SAN021, this will also be recorded as an AE.

### **Preliminary Efficacy**

The efficacy will be assessed as follows:

- Percentage of subjects achieving at least a 1-grade improvement in PGA score
- Percentage of subjects achieving a 2-grade improvement in the PGA score
- Percentage of subjects who have a  $\geq 25\%$  reduction in the Psoriasis Area and Severity Index (PASI) score at any point during the trial.
- Percentage of subjects who have a  $\geq 50\%$  reduction in the Psoriasis Area Severity Index (PASI) score at any point during the trial.
- Number of subjects achieving a Physician's Global Assessment of "clear" or "almost clear" at any time point during the 42 days of therapy. The study restricted treatment areas are not to be included in this evaluation. (see #10 under Inclusion Criteria)

## Planned Dates of Study

April 2017 to December 2017

### **Trial Contacts**

<b>Name</b>	<b>Affiliation / Address</b>	<b>Responsibility</b>
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