STUDY SYNOPSIS

Title of Study: A MULTI-CENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED, PARALLEL-GROUP STUDY, COMPARING TEST TOPICAL PRODUCT TO BRAND TOPICAL PRODUCT AND BOTH ACTIVE TREATMENTS TO A PLACEBO CONTROL IN THE TREATMENT OF MODERATE FACIAL ROSACEA

Treatment Duration: The study treatment period will last for 84 days (12 weeks). A window ± 4 days will be considered acceptable for each scheduled visit following the first visit. Expected study duration is 6 to 9 months.

Test Product: Test topical product

Reference Product: Brand topical product

Placebo Control: Vehicle of the test topical product

Dose and Mode of Administration: A thin layer of study medication, approximately a pea-sized amount will be applied to cover the entire face once daily.

Objectives: To evaluate the therapeutic equivalence and safety of Test topical product and Brand topical product in the treatment of moderate facial rosacea.

To demonstrate the superiority of the efficacy of the test and reference products over that of the placebo control in the treatment of moderate facial rosacea.

To demonstrate the superiority of the efficacy of the test and reference products over that of the placebo control in the treatment of moderate facial rosacea.

Design: Subjects in this randomized, double-blind, placebo controlled, parallel-group, multiple-center study will be randomly assigned in a 1:1:1 ratio to treatment with the test product, reference product or placebo control, respectively.

Clinical Evaluations will be performed at:

Visit 1: Screening/Baseline Visit (Day 0);

Visit 2: First Interim Visit (Week 4 / Day 28 ± 4 Days);

Visit 3: Second Interim Visit (Week 8 / Day 56 ± 4 Days);

Visit 4: End of Treatment Visit (Week 12 / Day 84 ± 4 Days)

A window ± 4 days will be considered acceptable for each scheduled visit following the first visit. An Unscheduled Visit is allowed at any time, for any reason, if in the Principal Investigator's opinion it is warranted. If a Subject is discontinued from the study during an Unscheduled Visit, the Unscheduled Visit will be referred to as an Early Discontinuation Visit and all procedures scheduled for Visit 4 will be performed. If the Unscheduled Visit is not an Early Discontinuation Visit (i.e., the Subject will continue to take part in the study), then all procedures will be performed and treated as an interim visit, with the exception of the collection of Investigational Product and

Subject diaries from Subjects.

Subjects will be admitted into the study after informed consent has been obtained, a medical history and physical examination (with vital signs) have been performed and inclusion/exclusion criteria have been met. Subjects must have a clinical diagnosis of rosacea to qualify for inclusion in this study.

At the screening/baseline visit, a facial rosacea grade will be assigned to the subject using the Investigator Global Assessment (IGA) and a baseline lesion count will be performed. The subject will be evaluated for signs and/or symptoms of local irritation and telangiectasia.

At each subsequent visit the signs and/or symptoms of local irritation will be evaluated for the subject and the subject's facial rosacea will be assessed using the IGA, the subject's lesions will be counted and these results will be documented.

Safety will be assessed by the monitoring of all adverse events.

Study Population:

Inclusion Criteria

1. Healthy male or non-pregnant female aged ≥ 18 with a clinical diagnosis of facial rosacea.
2. Subjects must have provided IRB approved written informed consent.
3. Subjects must have at least 12 and not more than 50 inflammatory facial lesions (i.e., papules/pustules). For the purposes of study treatment and evaluation, these lesions should be limited to the facial treatment area including those present on the nose. Lesions involving the eyes, and scalp will be excluded from the count.
4. Subjects must have no more than 2 nodulocystic lesions on the face.
5. Subjects must have a definite clinical diagnosis of facial rosacea severity grade 3 as per the Investigator Global Assessment (IGA) (per Table 1 below).

Table 1: Investigator Global Assessment (IGA) Scale for Facial Rosacea

Score	Grade	Definition
0	Clear	No inflammatory lesions present; at most, mild erythema
1	Almost Clear	Very mild erythema present. Very few small papules/pustules
2	Mild	Mild erythema. Several small papules/pustules
3	Moderate	Moderate erythema. Several small or large papules/pustules, and up to 2 nodules
4	Severe	Severe erythema. Numerous small and/or large papules/pustules, up to several nodules

Subjects who worsen beyond Grade 3 will be described in the safety evaluation.

Please note that counts of nodules will be reported separately and not included in the inflammatory lesion counts.

6. Subjects must have persistent erythema on the face with moderate (2) score (per table 2 below)

Table 2: Erythema Evaluation Scale for Facial Rosacea

Score	Grade	Definition
0	None	No redness present
1	Mild	Pink to light red
2	Moderate	Definite redness, easily recognized
3	Severe	Marked erythema
4	Very severe	Fiery red

7. Subjects must have a mild (1) to moderate (2) score for telangiectasia on the face. (per table 3 below)

Table 3: Telangiectasia Evaluation Scale for Facial Rosacea

Score	Grade	Definition
0	Clear	No telangiectasia
1	Mild	Only few fine vessels discernible, involves 10% or less of the facial area
2	Moderate	Multiple fine vessels and/or few large vessels discernible, involves > 10% - 30% of the facial area
3	Severe	Many fine vessels and/or large vessels discernable, involves > 30% of the facial area

8. Subjects must be willing to minimize external factors that might trigger rosacea flare-ups (e.g., spicy foods, thermally hot foods and drinks, hot environments, prolonged sun exposure, strong winds and alcoholic beverages)
9. Subjects must be willing to refrain from using all other topical medications for rosacea during the 12-week treatment period, other than the investigational product.
10. Female Subjects of childbearing potential (excluding women who are or premenarchal, surgically sterilized (by hysterectomy) or postmenopausal for at least 1 year), in addition to having a negative urine pregnancy test, must be willing to use an acceptable form of birth control during the study from the day of the first dose administration to 30 days after the last administration of study drug. For the purpose of this study the following are considered acceptable methods of birth control: oral or injectable contraceptives, contraceptive patches, Depo-Provera® (stabilized for at least 3 months), NuvaRing® (vaginal contraceptive), Implanon™ (contraceptive implant), double barrier methods (e.g. condom and spermicide), IUD, tubal ligation, Essure or abstinence with a 2nd acceptable method of birth control should the Subject become sexually active. Subjects on hormonal contraception must be stabilized on the same type for at least three months prior to enrollment in the study and must not change the method during the study. A sterile sexual partner is NOT considered an adequate form of birth control.
11. All male Subjects must agree to use accepted methods of birth control with their partners, from the day of the first dose administration to 30 days after the last administration of study drug. Abstinence is an acceptable method of birth control. Female partners should use an acceptable method of birth control as described in the above Item Number 10.

12. Subjects who use make-up must have used the same brands/types of make-up for a minimum period of 14 days prior to study entry and must agree to not change make-up brand/type or frequency of use throughout the study.
13. Subjects must be willing and able to understand and comply with the requirements of the protocol, including attendance at the required study visits.
14. Subjects must be in good health and free from any clinically significant disease, including but not limited to, conditions that may interfere with the evaluation of facial rosacea. Such conditions include, but are not limited to the following: auto immune disease; acne vulgaris; seborrheic dermatitis on the face; perioral dermatitis; corticosteroid-induced acne; carcinoid syndrome; mastocytosis; acneiform eruptions caused by make-up, medication, facial psoriasis and facial eczema.

Exclusion Criteria

1. Female Subjects who are pregnant, nursing or planning to become pregnant during study participation.
2. Subjects with a history of hypersensitivity or allergy to investigational product, propylene glycol and/or any of the study medication ingredients and its excipients.
3. Subjects with the presence of any skin condition that would interfere with the diagnosis or assessment of facial rosacea (e.g., on the face: acne vulgaris, seborrheic dermatitis; perioral dermatitis; corticosteroid-induced acne; carcinoid syndrome; mastocytosis; acneiform eruptions caused by make-up, medication, facial psoriasis and facial eczema).
4. Subjects with excessive facial hair (e.g. beards, sideburns, moustaches, etc.) that would interfere with diagnosis or assessment of facial rosacea.
5. Subjects who have performed wax depilation of the face within 14 days prior to baseline.
6. Subjects who have used within 6 months prior to baseline or use during the study of antiandrogens such as Spironolactone, oral retinoids (e.g. Accutane®), or therapeutic vitamin A supplements of greater than 10,000 units/day (multivitamins are allowed).
7. Subjects who have used estrogens or oral contraceptives for less than 3 months prior to baseline; use of such therapy must remain constant throughout the study.
8. Subjects who have used any of the following procedures on the face within 1 month prior to baseline or use during the study:
    a. cryodestruction or chemodestruction,
    b. dermabrasion,
    c. photodynamic therapy,
    d. acne surgery,
    e. intralesional steroids, or
    f. X-ray therapy.
9. Subjects who have used any of the following treatments within 1 month prior to baseline or during the study:
    a. topical retinoids to the face,
    b. systemic corticosteroids,

c. systemic antibiotics known to have an impact on the severity of facial rosacea (e.g., containing tetracycline and its derivatives, erythromycin and its derivatives, sulfamethoxazole, or trimethoprim),
d. systemic treatment for rosacea

10. Subjects who have used any of the following treatments within 2 weeks prior to baseline or during the study:
    a. topical corticosteroids,
    b. topical medications for rosacea (e.g., metronidazole, azelaic acid, ivermectin)
    c. topical over-the-counter preparations for rosacea,
    d. topical anti-inflammatory agents, or
    e. topical antibiotics.
11. Subjects with moderate or severe rhinophyma, dense telangiectases (score 3, severe), or plaque-like facial edema.
12. Subjects with a severe irritation (score 3 = severe (marked/intense)) for dryness, pruritus, or stinging/burning.
13. Subjects with ocular rosacea (e.g., conjunctivitis, blepharitis, or keratitis) of sufficient severity to require topical or systemic antibiotics.
14. Subjects who have received radiation therapy and/or anti-neoplastic agents within 90 days prior to baseline.
15. Subjects who have unstable medical disorders that are clinically significant or have life-threatening diseases.
16. Subjects who engage in activities that involve excessive or prolonged exposure to sunlight or weather extremes, such as wind or cold.
17. Subjects who consume excessive amounts of alcohol (greater than two drinks per day) or use drugs of abuse (including, but not limited to, cannabinoids, cocaine and barbiturates).
18. Subjects who have participated in an investigational drug study (i.e., Subjects have been treated with an investigational drug) within 30 days prior to baseline will be excluded from study participation. Subjects who are participating in non-treatment studies such as observational studies or registry studies can be considered for inclusion.
19. Subjects who have been previously enrolled in this study.
20. Subjects who have had laser therapy (for telangiectasia or other conditions), electrodessication and phototherapy (e.g., ClearLight®) to the facial area within 180 days prior to study entry.
21. Subjects who have had cosmetic procedures (e.g., facials) which may affect the efficacy and safety profile of the investigational product within 14 days prior to study entry.
22. Subjects who currently have or have recently had bacterial folliculitis on the face.
23. A subject who has used a sauna during the 2 weeks prior to study entry and during the study.
24. A subject who has a history of being unresponsive to topical investigational product therapy.

Number of Subjects:

Approximately 1000 Subjects will be enrolled into the study to the following study arms:

- **Test Product**: Test topical product
- **Reference Product**: Brand topical product
- **Placebo Control**: Vehicle of the test topical product

Each site will enroll approximately between 30 and 200 subjects. Approximately equal numbers of male and female subjects will be enrolled to each of the three study arms.

Criteria for Evaluation:

Primary Endpoints:

Percent change from baseline to week 12 in the inflammatory (papules and pustules) lesion counts

Secondary Endpoint:

The proportion of Subjects with a clinical response (IGA) of "success" at week 12. Success is defined as an IGA score 0 or 1.

Measures:

Lesion Counts will be performed using the following definitions:

- Papule: A papule is solid, raised spot on the skin that is ≤ 1cm in diameter.
- Pustule: small, inflamed, pus-filled, blister-like lesions on the skin surface.
- Nodules: Large, hard bumps under the skin's surface

The Investigator Global Assessment (IGA) will be performed and documented using the definitions in Table 1 (above).

The Erythema Evaluation will be performed and documented using the definitions in Table 2 (above).

The Telangiectasia Evaluation will be performed and documented using the definitions in Table 3 (above).

Application site reactions such as pain, dryness, burning/stinging, and itching will be recorded at each visit to allow a comparison between treatment groups.

Statistical Methods:

Demonstration of Bioequivalence
Bioequivalence will be established if the 90% confidence intervals on the test/reference ratio of the mean percent change from baseline to week 12 in the inflammatory (papules and pustules) lesion counts are contained within [0.80, 1.25] using the per protocol (PP) population.

Demonstration of Superiority
The test product and RLD will be compared to placebo group to test statistical superiority at $p<0.05$ (two-sided test) with regard to mean percent change from baseline to week 12 in the inflammatory lesion counts using the modified intent-to-treat (mITT) study population and Last Observation Carried Forward (LOCF).

Analysis of Primary Endpoint
The evaluation of the primary endpoint will be based on the mean percent change from baseline to week 12 in the inflammatory (papules and pustules) lesion counts.

Analysis of Secondary Endpoint
The secondary endpoint will be evaluated as the proportion of Subjects with a clinical response of “success” at week 12. Success is defined as an IGA score 0 or 1. The dichotomized global severity scale will be treated as a secondary end point for supportive evidence.

Analysis of application site reactions
A descriptive analysis comparing the application site reactions for each treatment group will be conducted to ensure that the test product is not worse than the reference product with regard to the expected and unexpected application site reactions.

Summary of Subjects who terminate prematurely
Reasons for premature termination will be summarized by treatment group.

Concomitant medication
The start and stop date of concomitant medication use during the study will be provided in the data set in addition to the reason for the medication use.

Safety Analyses
Safety analyses will be conducted on the safety population. Incidence of all adverse events reported during the study will be summarized using the MedDRA dictionary by treatment group, body system, severity and relationship to study drug.
The report of AEs will include date of onset, description of the AE, severity, suspected relationship to study treatment, and date of resolution. Formal statistical evaluation(s) of the comparability of the two active treatment groups will be conducted with regard to the frequency and severity of any AE that occurs in at least 5% of the Subjects in either active treatment group.

SAFETY AND TOLERABILITY EVALUATIONS

General Safety Evaluations

A complete medical history will be obtained for the Subject's current and past medical conditions. Significant medical history should include, but not be limited to, evidence of hypertension, lipid disorders, obesity, heart attack, stroke, congestive heart failure, kidney disease, auto immune disease and gestational diabetes. Significant surgical history should include, but not be limited to, removal of blockage from an artery and gallbladder removal.

Concomitant medications, including the use of moisturizer and non-drug treatments/therapies, in addition to the reason for the medication use, will be assessed at baseline and at each subsequent study visit. The start and stop date of concomitant medication use during the study should be provided in the data set in addition to the reason for the medication use.

A brief physical examination will be performed at baseline. The physical examination will include, at a minimum, examination of the Subject's general appearance, skin, HEENT (head, eyes, ears, nose and throat), heart, lungs, musculoskeletal system, neurological system, lymph nodes, abdomen and extremities. The Subject's body weight will also be measured while the Subject is lightly clothed (e.g., no coat or shoes).

Physical Examination

The investigator, sub-investigator or appropriately delegated designee, (Physician's Assistant, Advanced Registered Nurse Practitioner, and Registered Nurse as per local regulations) will perform a brief physical examination, prior to the Subject starting study drug.

Vital signs, including blood pressure, pulse rate, respiratory rate and oral body temperature will be documented at Visit 1. Vital signs will be measured after the Subject has rested in a seated position for at least 5 minutes.

The Subject's body weight will also be measured while the Subject is lightly clothed (e.g., no coat or shoes). Height will be measured without shoes.

Pregnancy Test

All female Subjects of childbearing potential will undergo a urine pregnancy test during Visit 1 and at each subsequent study visit. All female Subjects are considered to be of childbearing potential unless they are premenarchal, have been surgically sterilized (by hysterectomy) or have been postmenopausal for at least 1 year. Women of childbearing potential, in addition to having a negative urine pregnancy test, must be willing to use an acceptable form of birth control during the study from the day of the first dose administration to 30 days after the last administration of study drug. For the purpose of this study the following are considered acceptable methods of birth control: oral or injectable contraceptives, contraceptive patches, Depo-Provera® (stabilized for at least 3 months), NuvaRing® (vaginal contraceptive), Implanon™ (contraceptive implant), double barrier methods (e.g. condom and spermicide), IUD, or abstinence with a 2nd acceptable method of birth control should the Subject become sexually active. A sterile sexual partner is NOT considered an adequate form of birth control. Subjects on hormonal contraception must be stabilized on the same type for at least three months prior to enrollment in the study and must not change the method during the study. Subjects who had used hormonal contraception and stopped must have stopped no less than three months prior to the study.

Concomitant medications

Concomitant medications, including the use of moisturizer and non-drug treatments/therapies, in addition to the reason for the medication use, will be assessed at baseline and at each subsequent

study visit. The start and stop date of concomitant medication use during the study should be provided in the data set in addition to the reason for the medication use.

A record of concomitant medications taken by the Subject is to be obtained using generic name, if known, with the corresponding indication. The medications to be recorded will include prescription and over-the-counter (OTC) medications and dietary supplements. All medications taken on a regular basis, including acetaminophen, should be recorded.

Signs/Symptoms of Local Irritation

At each study visit, beginning at Visit 1, Subjects will be evaluated for any signs and symptoms of local irritation, including pain, dryness, burning/stinging and itching. Baseline values will be used for comparative purposes against the scores documented at subsequent visits for each treatment group. Each Subject will be assigned a severity score by an Investigator based on the scale in Table 4.

Application site reactions such as pain, dryness, burning/stinging and itching will be recorded at each visit to allow a comparison between treatment groups.

Table 4: Expected Application Site Reactions

Pain:	Skin reaction pain score, e.g. 0=absent, 1=mild (slight, barely perceptible), 2=moderate (distinct presence), 3=severe (marked, intense)
Dryness:	Skin reaction dryness score, e.g. 0=absent, 1=mild (slight, barely perceptible), 2=moderate (distinct presence), 3=severe (marked, intense)
Burning/stinging:	Skin reaction burning/stinging score, e.g. 0=absent, 1=mild (slight, barely perceptible), 2=moderate (distinct presence), 3-severe (marked, intense)
Itching:	Skin reaction itching score, e.g. 0=absent, 1=mild (slight, barely perceptible), 2=moderate (distinct presence), 3=severe (marked, intense)

Subjects with a baseline irritation score of 3 (severe, marked/intense) will not be enrolled. After baseline, severe irritation (i.e., grade 3, described as severe or marked/intense) that requires treatment will be reported as an adverse event.

Local irritation reactions in the treatment area are common and the Investigator may instruct Subjects to stop the application of treatment ("rest period") to reduce Subject discomfort and to allow local skin reactions to subside based upon the Investigator's clinical assessment. Treatment should resume as soon as the reaction subsides sufficiently to allow reapplication. The Subject should not modify or resume the treatment regimen without consultation with the Investigator. The Investigator may make this decision based upon a documented phone consultation or at an unscheduled visit. All dose modifications must be reported on the appropriate Study Medication Log & Dosing Compliance eCRF.

The treatment period should not be extended beyond 12 weeks due to missed doses or rest periods. Subjects whose condition worsens or lesions do not respond to treatment should be re-evaluated by the Investigator and management reconsidered.

Adverse Events

An adverse event is defined as any untoward medical occurrence (sign, symptom or abnormal laboratory finding) regardless of severity in a Subject or clinical-trial Subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. All adverse events, whether observed by an Investigator or Study Coordinator or reported by the Subject, whether related to study drug or not related to study drug, shall be documented on the eCRF and Subject records, together with details, i.e. date of onset, the duration and intensity of each episode, the action taken, the relationship to the investigational product and the degree of severity, the seriousness and the outcome.

CLINICAL EVALUATIONS

An examination of the Subject's face will be performed at baseline and at each subsequent visit. During the dermatologic examination, evaluations to determine efficacy of treatment will be conducted, including lesion counts and grading of the Subject's facial rosacea using the criteria outlined in the IGA. The grading using the IGA should be done before lesion counts.

Preferably a single Investigator (i.e., Principal Investigator or Sub-Investigator) or qualified staff will perform evaluations of efficacy (i.e., lesion counts and IGA) for each Subject at each visit from the beginning to the end of the Subject's participation to maintain consistency; however, only up to two Investigators or qualified staff may perform evaluations of efficacy for a single Subject if necessary. **All efforts should be made to have the same evaluator at Visit 4 and Visit 1**. All Investigators or study staff who will perform evaluations of efficacy must be qualified by experience and/or training for the conduct of these evaluations (i.e., lesion counts and IGA).

Investigator Global Assessment

At each visit, including baseline, an Investigator will assess the overall status of the Subject's facial rosacea using the IGA. The IGA scores for each visit will be documented on the eCRF. The IGA assessment should be performed before lesion counts.

To be included in the study, subjects must have a definite clinical diagnosis of facial rosacea of severity grade 3 at baseline. The following scale will be used for the IGA:

Table 1: Investigator Global Assessment (IGA) Scale for Facial Rosacea

Score	Grade	Definition
0	Clear	No inflammatory lesions present; at most, mild erythema
1	Almost Clear	Very mild erythema present. Very few small papules/pustules
2	Mild	Mild erythema. Several small papules/pustules
3	Moderate	Moderate erythema. Several small or large papules/pustules, and up to 2 nodules
4	Severe	Severe erythema. Numerous small and/or large papules/pustules, up to several nodules

Subjects who worsen beyond Grade 3 will be described in the safety evaluation.

Please note that counts of nodules will be reported separately and not included in the inflammatory lesion counts.

Lesion Counts

At each visit, an Investigator or qualified staff will assess the Subject's facial rosacea by counting the number of pustules, papules, and nodulo-cystic lesions from the jaw line to the hairline. All lesions will be counted, including those present on the nose. A papule with a pustule on its apex will be counted as a pustule.

To be included in the study, Subjects must have at least 12 and no more than 50 inflammatory lesions (i.e., papules and pustules) at baseline on the face.

Table 5: Definition of inflammatory lesions

Lesion Type	Definition
Papule	Inflammatory lesion; a small (≤ 1cm in diameter), solid palpable lesion, usually with inflamed elevation of the skin that does not contain pus
Pustule	Inflammatory lesion; a small (≤ 5mm in diameter), inflamed skin swelling that is filled with pus
Nodules	Large, hard bumps under the skin's surface
Cysts	Similar to a nodule, but is pus-filled, and ≥ 5mm in diameter

Erythema Evaluation

At each visit, including baseline, an Investigator will assess the Subject's facial erythema to allow a comparison between treatment groups. To be included in the study, subjects must have persistent erythema on the face with moderate (2) score. The following scale will be used for the erythema evaluation:

Table 2: Erythema Evaluation Scale for Facial Rosacea

Score	Grade	Definition
0	None	No redness present
1	Mild	Pink to light red
2	Moderate	Definite redness, easily recognized
3	Severe	Marked erythema
4	Very severe	Fiery red

Telangectasia Evaluation

At a baseline visit, an Investigator will assess the Subject's facial telangiectasia. To be included in the study, subjects must have a mild (1) to moderate (2) score for telangiectasia on the face. The following scale will be used for the telangiectasia evaluation:

Table 3: Telangiectasia Evaluation Scale for Facial Rosacea

Score	Grade	Definition
0	Clear	No telangiectasia
1	Mild	Only few fine vessels discernible, involves 10% or less of the facial area
2	Moderate	Multiple fine vessels and/or few large vessels discernible, involves > 10% - 30% of the facial area
3	Severe	Many fine vessels and/or large vessels discernable, involves > 30% of the facial area

STUDY VISITS

Visit 1: Baseline (Day 0)

The following procedures will be performed at Visit 1:

1. **Written informed consent will be obtained**. Subjects must have provided IRB approved written informed consent. Subjects will be given the approved ICF describing the study and any risks associated with participation. The Subject will be allowed as much time as needed to read and understand the information presented in the consent form. Appropriate study personnel will be available to answer any questions the Subject might have regarding the study or study-related procedures. If the Subject chooses to participate in the study, he or she will be asked to sign and date the consent form and will be provided with a copy for his or her records. In addition, the Principal Investigator or the Principal Investigator's Designee will provide a HIPAA authorization form (if applicable) for the Subject to review and sign. Both the ICF and the HIPAA authorization form (if applicable) must be signed by the Subject before any protocol assessments can be undertaken.
2. A complete medical history will be obtained for the Subject's current and past medical conditions. Significant medical history should include, but not be limited to, evidence of hypertension, lipid disorders, obesity*, heart attack, stroke, congestive heart failure, kidney disease, and auto immune disease and gestational diabetes. Significant surgical history should include, but not be limited to, removal of blockage from an artery and gallbladder removal.

   * Obesity = BMI ≥30 (as defined by Metropolitan Life Insurance Company Chart)
3. Demographics and vital signs (blood pressure, pulse, respiratory rate and oral body temperature) will be documented. Subjects must remain in a seated position for 5 minutes before vital signs are obtained.
4. A brief physical examination, including height (measured in inches) and weight (measured in pounds), will be performed. At a minimum, the physical examination will include the following: assessment of general appearance, skin, HEENT, heart, lungs, musculoskeletal system, lymph nodes, neurological systems, abdomen, extremities.
5. A complete list of current and past (within the previous 30 days) concomitant medications will be obtained for each Subject.
6. A urine pregnancy test will be conducted for all females of childbearing potential.
7. The overall status of the Subject's facial rosacea will be assessed using the IGA.
8. Lesion counts will be done by counting the number of facial pustules, papules and nodulo-cystic lesions from the jaw line to the hairline. All lesions will be counted, including those present on the nose.
9. The Subject's facial erythema will be assessed. To be included in the study, subjects must have persistent erythema on the face with moderate (2) score.
10. The Subject's facial telangiectasia will be assessed. To be included in the study, subjects must have a mild (1) to moderate (2) score for telangiectasia on the face.
11. Subjects will be evaluated for any signs and symptoms of facial irritation, including pain, dryness, burning/stinging, and itching. Each Subject will be assigned a severity score for each symptom based on the Local Irritation Scale.
12. When the Subject has completed all screening procedures, compliance with the inclusion and exclusion criteria will be reviewed. After the inclusion and exclusion criteria have been confirmed,

the Subject will be randomized to a treatment group. The Subject will be assigned a randomization number.

13. The following will be dispensed during Visit 1:
    - One unit of the investigational product
    - One Dove Beauty Bar
    - One bottle of Solbar Shield Sunscreen SPF 40
    - Two packs of Graham PST Professional Service Towels
    - A diary card to record product use from Visit 1 to Visit 2

    Depending upon the severity of facial irritation and to prevent the side effects, the Investigator may instruct the Subject to use a non-medicated moisturizer. CeraVe® Moisturizing Lotion may be dispensed during Visit 1 for use at the instruction of the Investigator.
14. Randomized Subjects will be instructed on the correct method for the application of the Investigational Product. The first application of the Investigational Product will be performed by the Subject at home. The study restrictions will also be reviewed with the Subject and an instruction sheet will be issued to the Subject.
15. Randomized Subjects will be provided with a diary and instructed how and when to complete the diary. They will be told that they are to document all treatments administered, including the date and all treatments missed. In addition, Subjects will be instructed to document all AEs. Subjects will also be instructed to call the study site if they experience any severe intolerability (i.e., local skin reactions) to Investigational Product.
16. Visit 2 (Day 28 ± 4 days from the date of Visit 1) will be scheduled and the Subject will be instructed to bring all Investigational Product (used, unused, and partially used) and the Subject diary with him or her to this visit.

Visit 2: Interim Visit (Week 4; Day 28 ± 4 Days)

The following procedures will be performed at Visit 2:

1. The overall status of the Subject's facial rosacea will be assessed using the IGA.
2. Lesion counts will be done by counting the number of facial pustules, papules and nodulo-cystic lesions from the jaw line to the hairline. All lesions will be counted, including those present on the nose.
3. The Subject's facial erythema will be assessed.
4. Subjects will be evaluated for any signs and symptoms of facial irritation, including pain, dryness, burning/stinging, and itching. Each Subject will be assigned a severity score for each symptom based on the Local Irritation Scale.
5. A urine pregnancy test will be conducted for all females of childbearing potential.
6. The occurrence of all AEs will be assessed and documented.
7. The use of concomitant medications since the previous study visit will be documented and assessed for each Subject. The use of moisturizer, including the type and how often it has been used, will be included.
8. The Subject's compliance with the study protocol, including use and application of Investigational Product, will be assessed. The Subject's diary will be collected and reviewed for completion. A new diary will be issued.

9. The Subject's used Investigational Product will be returned to the third-party drug dispenser.
10. The following will be dispensed during Visit 2:
    - One can of the investigational product
    - A new diary to record product use from Visit 2 to Visit 3
    - One pack of Graham PST Professional Service Towels

    Depending upon the severity of the side effects, the Investigator may instruct the Subject to use a non-medicated moisturizer. If the moisturizer was not dispensed Visit 1, one bottle of CeraVe® Moisturizing Lotion may be dispensed during Visit 2. It is not anticipated that Subjects will require additional supplies during this visit; additional supplies will be dispensed if required.
11. Study instructions will be reviewed with the Subject, including the procedure for application of the Investigational Product.
12. Visit 3 (Day 56 ± 4 days from the date of Visit 1) will be scheduled and the Subject will be instructed to bring all Investigational Product (used, unused and partially used) and the Subject diary with him or her to this visit.

Visit 3: Interim Visit (Week 8; Day 56 ± 4 Days)

The following procedures will be performed at Visit 3:

1. The overall status of the Subject's facial rosacea will be assessed using the IGA.
2. Lesion counts will be done by counting the number of facial pustules, papules and nodulo-cystic lesions from the jaw line to the hairline. All lesions will be counted, including those present on the nose.
3. The Subject's facial erythema will be assessed.
4. Subjects will be evaluated for any signs and symptoms of facial irritation, including pain, dryness, burning/stinging, and itching. Each Subject will be assigned a severity score for each symptom based on the Local Irritation Scale.
5. A urine pregnancy test will be conducted for all females of childbearing potential.
6. The occurrence of all AEs will be assessed and documented.
7. The use of concomitant medications since the previous study visit will be documented and assessed for each Subject. The use of moisturizer, including the type and how often it has been used, will be included.
8. The Subject's compliance with the study protocol, including use and application of Investigational Product, will be assessed. The Subject's diary will be collected and reviewed for completion. A new diary will be issued.
9. The Subject's used Investigational Product will be returned to the third-party drug dispenser.
10. The following will be dispensed during Visit 3:
    - One can of the investigational product
    - A new diary to record product use from Visit 3 to Visit 4
    - One pack of Graham PST Professional Service Towels

    Depending upon the severity of the side effects, the Investigator may instruct the Subject to use a non-medicated moisturizer. If the moisturizer was not dispensed Visits 1 and 2, one bottle of CeraVe® Moisturizing Lotion may be dispensed during Visit 3. It is not anticipated that Subjects

will require additional supplies during this visit; additional supplies will be dispensed if required.

11. Study instructions will be reviewed with the Subject, including the procedure for application of the Investigational Product.
12. Visit 4 (Day 84 ± 4 days from the date of Visit 1) will be scheduled and the Subject will be instructed to bring all Investigational Product (used, unused and partially used) and the Subject diary with him or her to this visit.

Visit 4: End of Treatment Visit (Week 12; Day 84 ± 4 Days)

The following procedures will be performed at Visit 4:

1. The overall status of the Subject's facial rosacea will be assessed using the IGA.
2. Lesion counts will be done by counting the number of facial pustules, papules and nodulo-cystic lesions from the jaw line to the hairline. All lesions will be counted, including those present on the nose.
3. The Subject's facial erythema will be assessed.
4. Subjects will be evaluated for any signs and symptoms of facial irritation, including pain, dryness, burning/stinging, and itching. Each Subject will be assigned a severity score for each symptom based on the Local Irritation Scale.
5. A urine pregnancy test will be conducted for all females of childbearing potential.
6. The occurrence of all AEs will be assessed and documented.
7. The use of concomitant medications since the previous study visit will be documented and assessed for each Subject. The use of moisturizer, including the type and how often it has been used, will be included.
8. The Subject's compliance with the study protocol, including use and application of Investigational Product, will be assessed. The Subject's diary will be collected and reviewed for completion..
9. The Subject's used Investigational Product will be returned to the third-party drug dispenser.

Unscheduled Visits and Early Discontinuation Visit

An Unscheduled Visit is allowed at any time, for any reason, if in the Principal Investigator's opinion it is warranted. If the Unscheduled Visit is due to an AE, the Principal Investigator will determine whether additional visits are needed.

If a Subject is discontinued from the study during an Unscheduled Visit, the Unscheduled Visit will be referred to as an Early Discontinuation Visit and all procedures scheduled for Visit 4 will be performed. If the Unscheduled Visit is not an Early Discontinuation Visit (i.e., the Subject will continue to take part in the study), then all procedures scheduled for that interim visit will be performed, with the exception of the collection of Investigational Product and Subject diaries from Subjects.

If the Subject's condition has worsened to the degree that it is unsafe for the Subject to continue in the study, the Subject may be discontinued from the study as treatment failure and a standard of care treatment may be advised at the Principal Investigator's discretion.