Complete List of Inclusion/Exclusion Criteria

Inclusion criteria

1. *Informed consent obtained**

*Written informed consent, before any study-related procedure, personally signed and dated by the patient if the patient is ≥ 18 years old, or signed and dated by the parent(s) or the legal guardian if patient is ≥ 12 to < 18 years old. An additional informed assent form must be signed by patient if ≥ 12 to <18 years old to confirm his willingness to participate in the study. If the patient becomes 18 years of age during the study, the patient must provide written informed consent at that time to continue study participation.

2. *Sex and age:* Male and female patients aged ≥ 12 to ≤ 30 years old inclusive;

3. *Diagnosis:* Patients with facial acne vulgaris with an investigator's global assessment (IGA) score of 3–4 at screening and baseline visits;

4. *Inflammatory lesions:* Patients with ≥ 20 and ≤ 100 inflammatory lesions (papules and pustules) on the face (excluding the nose) and ≤ 1 nodules;

5. *Non-inflammatory lesions:* Patients with ≥ 20 and ≤ 100 non-inflammatory lesions (open and closed comedones) on the face (excluding the nose);

6. *Full comprehension:* Patient and parent(s)/guardian for < 18 years old patient's ability to comprehend the full nature and purpose of the study, including possible risks and side effects; ability to cooperate with the investigator and to comply with the requirements of the entire study;

7. *Contraception and fertility:* Women of childbearing potential must be using an effective contraception method during the entire duration of the study. Stable treatment period is required for the following reliable methods of contraception:
• Hormonal oral, implantable, transdermal, or injectable contraceptives must be stable for at least 6 months before the screening visit
• A non-hormonal intrauterine device (IUD) must be started at least 2 months before the screening visit

Exclusion criteria

1. *Acne*: Patients with spontaneously improving or rapidly deteriorating acne within at least 3 months before study baseline. Patients who have a known history of acne unresponsive to topical and/ or oral treatments. In particular subjects with history of persistent acne (a continuation of the disease from adolescence into adulthood) and subjects with history of relapsing acne. Patients with generalized or localized acne forms other than acne vulgaris, e.g., acne conglobata, acne fulminans, acne rosacea, secondary acne (chloracne, drug-induced acne, etc), nodule-cystic acne, acne tarda or acne requiring systemic treatment.

2. Beard and facial hair, tattoos: Patients who have a beard or who intend to grow a beard and/or to perform a facial tattoo during the study. Patient has facial hair or facial tattoos that could interfere with the study assessments in the opinion of the investigator.

3. *Skin diseases:* Patients with other active skin diseases (e.g., urticaria, atopic dermatitis, sunburn, seborrheic dermatitis, perioral dermatitis, rosacea, skin malignancies) or active skin infections in the facial region (bacterial, fungal, or viral) or any other facial disease or condition that might interfere with the evaluation of acne or place the patient at unacceptable risk.

4. *Allergy:* Known or suspected hypersensitivity to any active or inactive ingredient in the study products. Patients with a history of an allergic reaction or significant sensitivity to the formulations' ingredients

5. *Topical therapies:* Patients using, will use during the study, or discontinued less than 4 weeks before study baseline, prescribed or over-the counter topical therapies for the treatment of acne including but not limited to: corticosteroids, antibiotics, azelaic acid, benzoyl peroxide, salicylates, α-hydroxy/glycolic acid, any other topical cosmetic therapy for acne and retinoids on the face.

6. *Facial procedures:* Patients using, will use during the study, or discontinued less than 4 weeks before study baseline, facial application of products containing glycolic or other acids, masks, washes or soaps containing benzoyl peroxide or salicylic acid, non-mild cleansers or moisturizers containing retinol, salicylic or alpha- or beta-hydroxy acids, facial procedures such as chemical peel, laser treatment, photodynamic therapy, acne surgery, cryodestruction or chemodestruction, x-ray therapy, intralesional steroids, dermabrasion, or depilation (except eyebrow shaping).

7. *Phototherapy:* Patients using, will use during the study, or discontinued less than 12 weeks before study baseline, phototherapy for the treatment of acne including but not limited to: UV-A, UV-B, heliotherapy. Patients who have the need or plan to be exposed to artificial tanning devices or excessive sunlight during the study.

8. *Systemic therapies:* Patients using, will use during the study, or discontinued less than 12 weeks before study baseline, systemic therapies for the treatment of acne including but not limited to: antibiotics, isotretinoin. Other systemic therapy which, in the opinion of the investigator, could affect the patient's acne (i.e., anabolics, lithium, EGFR inhibitors, iodides, systemic corticosteroids or other immunosuppressants).

9. *Known systemic diseases that can lead to acneiform eruptions:*
a. Increased androgen production. 1) Adrenal origin: e.g., Cushing's disease, 21-hydroxylase deficiency; 2) Ovarian origin: e.g., polycystic ovarian syndrome, ovarian hyperthecosis
b. Cryptococcosis disseminated
c. Dimorphic fungal infections
d. Behçet's disease

10. *Investigative studies:* Participation in the evaluation of any investigational product or device within 30 days before study baseline

11. *Diseases:* Patient with underlying uncontrolled or unstable conditions (including, but not limited to metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal) which in the opinion of the investigator could significantly

compromise the patient and/or place the patient's safety at an unacceptable risk. Any condition which in the investigator's opinion would make it unsafe for the patient to participate in the study

12. *Alcohol and other substance abuse:* History of alcohol or other substance abuse within one year before screening

13. *Communication:* Patient and parent/guardian (if applicable) unable to communicate or cooperate with the investigator due to e.g., language problems, impaired cerebral function, bad mental conditions

14. *Reliability:* Patient who may be unreliable for the study including patients who are unable to return for the scheduled visits

15. *Pregnancy* (females only):* Pregnant or breastfeeding women or planning to become pregnant during the study.
*For all female patients of childbearing potential, pregnancy test result must be negative at screening.