Electronic Supplemental Material

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Pharmacokinetics of Roflumilast Cream in Chronic Plaque Psoriasis

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Supplementary Table 1. Inclusion and Exclusion Criteria From Maximal Usage PK and Safety Study (Study 107; NCT04279119)

Inclusion Criteria

Subjects must fulfill all of the following inclusion criteria to be eligible for participation in the study:

1. Participants legally competent to sign and give informed consent or for adolescent assent with consent of a parent(s) or legal guardian, as required by local law
2. Males and females ages 12 years and older (inclusive) at the time of consent/assent
3. Clinical diagnosis of psoriasis vulgaris of at least 3 months duration as determined by the Investigator or through subject interview. Stable disease for the past 4 weeks.
4. Psoriasis vulgaris on the face, extremities, trunk, and/or intertriginous areas involving at least 10% of BSA in adolescents and at least 20% of BSA in adults (excluding the scalp)
5. An Investigator Global Assessment of disease severity (IGA) of at least Moderate ('3') at Baseline
6. Females of childbearing potential (FOCBP) must have a negative serum pregnancy test at Screening (Visit 1) and a negative urine pregnancy test at Baseline (Visit 2). In addition, sexually active FOCBP must agree to use at least one form of highly effective contraception throughout the study. Highly effective forms of contraception include: oral/ implant/ injectable/transdermal contraceptives, intrauterine device, and partner's vasectomy. If barrier methods are used (e.g., condom with spermicide, diaphragm with spermicide), then 2 forms of conception are required. The use of abstinence as a contraceptive measure is acceptable as long as this is a consistent part of a lifestyle choice and an acceptable backup method has been identified if the subject becomes sexually active.
7. Females of non-childbearing potential should be premenarchal, post-menopausal with spontaneous amenorrhea for at least 12 months or have undergone surgical sterilization (permanent sterilization methods include hysterectomy, bilateral oophorectomy, hysteroscopic sterilization, bilateral tubal ligation or bilateral salpingectomy).
8. Subjects in good health as judged by the Investigator, based on medical history, physical examination, vital signs, 12-lead electrocardiogram (ECG), serum chemistry labs, hematology values, and urinalysis.
9. Subjects are considered reliable and capable of adhering to the Protocol and visit schedule, according to the judgment of the Investigator

Exclusion Criteria

1. Subjects who cannot discontinue medication and treatments prior to the Baseline visit and during the study according to Excluded Medications and Treatments.
2. Planned excessive exposure of treated area(s) to either natural or artificial sunlight, tanning bed or other LED.
3. Subjects currently taking lithium or antimalarial drugs.
4. Planned initiation or changes to concomitant medication that could, in the opinion of the Investigator, affect psoriasis vulgaris (e.g. beta blockers, ACE inhibitors).
5. Current diagnosis of non-plaque form of psoriasis (e.g., guttate, erythrodermic/exfoliative, or pustular psoriasis). Current diagnosis of drug-induced psoriasis.
6. Subjects with any condition on the treatment area which, in the opinion of the Investigator, could confound psoriasis measurements.

7. Known allergies to excipients in ARQ-151 cream (petrolatum, isopropyl palmitate, methylparaben, propylparaben, diethylene glycol monoethyl ether, hexylene glycol, cetylstearyl alcohol, dicetyl phosphate and ceteth-10 phosphate).
8. Subjects who cannot discontinue the use of systemic strong P-450 cytochrome inhibitors (e.g., indinavir, nelfinavir, ritonavir, clarithromycin, itraconazole, ketoconazole, fluconazole, nefazodone, saquinavir, suboxone and telithromycin) for two weeks prior to the Baseline visit and during the study period.
9. Subjects who cannot discontinue the use of systemic strong P-450 cytochrome inducers (e.g., efavirenz, nevirapine, glucocorticoids, barbiturates (including phenobarbital), phenytoin, rifampin and carbamazepine) for two weeks prior to the Baseline visit and during the study period.
10. Females who are pregnant, wishing to become pregnant during the study, or are breast-feeding.
11. Subjects who have received oral roflumilast (Daliresp®, Daxas®) or other PDE-4 inhibitors (apremilast) within the past 4 weeks.
12. Known or suspected severe renal insufficiency or moderate to severe liver impairment (Child-Pugh B or C); known HIV infection; hypersensitivity to component(s) of the investigational products; history of severe depression, suicidal ideation, Baseline/Screening C-SSRS indicative of suicidal ideation, whether lifetime or recent/current
13. Adult subjects with PHQ-8 $\geq$10 or adolescent subjects with modified PHQ-A $\geq$10 at Screening or Baseline visits.
14. Subjects with a history of chronic alcohol or drug abuse within 6 months of initiation of investigational product.
15. Subjects with a history of a major surgery within 4 weeks prior to Baseline (Visit 2) or has a major surgery planned during the study.
16. Subjects who are unable to communicate, read or understand the local language, or who display another condition, which in the Investigator’s opinion, makes them unsuitable for clinical study participation. For adolescent subjects, parent(s)/legal guardian(s) who are unable to communicate, read, or understand the local language.
17. Subjects who are family members of the clinical study site, clinical study staff, or Sponsor.
18. Subjects with any serious medical condition or laboratory abnormality that would prevent study participation or place the subject at significant risk, as determined by the Investigator.
19. Current or a history of cancer within 5 years with the exception of fully treated skin basal cell carcinoma, cutaneous squamous cell carcinoma or carcinoma in situ of the cervix.
20. Subjects with active infection that required oral or intravenous administration of antibiotics, antifungal or antiviral agents within 7 days of Baseline/Day 1.