Abbreviation	Definition of term
Hct	Hematocrit
HCV	Hepatitis C virus
HDL	High density lipoprotein
HEENT	Head, ears, eyes, nose, throat
HEK	Human embryonic kidney
hERG	Human ether-a-go-go-related gene
Hgb	Hemoglobin
HIV	Human immunodeficiency virus
hs-CRP	High sensitivity C-reactive protein
IB	Investigator's brochure
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IFNγ	Interferon γ
IL	Interleukin
IL-1β	Interleukin-1β
IL-2	Interleukin-2
IL-6	Interleukin-6
IL-17	Interleukin-17
IL-23	Interleukin-23
IMP	Investigational medicinal product
IND	Investigational new drug application
IRB	Institutional Review Board
ITK	Interleukin-2-inducible T cell kinase
ITT	Intent-to-treat population
IV	Intravenous
IWRS	Interactive Web Response System
LC-MS/MS	Liquid chromatography/tandem mass spectrometry
LCL	Lower confidence level
LDH	Lactate dehydrogenase
LOCF	Last observation carried forward
LRV	Lower reference value
MedDRA	Medical Dictionary for Regulatory Activities
MOA	Mechanism of action
mRNA	Messenger ribonucleic acid
MTD	Maximum tolerated dose
MTX	Methotrexate
N/A	Not applicable
[redacted]	
NOAEL	No observed adverse effect level
NSAID	Non-steroidal anti-inflammatory drug

KEY ELIGIBILITY CRITERIA	• Male or female, 18 to 70 years of age (inclusive) at Visit 1 (Screening Visit) and diagnosed with moderate to severe plaque psoriasis at least 6 months prior to Visit 1; • No medical history of treatment failure to any systemic agents for plaque psoriasis; • Plaque-type psoriasis covering ≥10% of body surface area (BSA) at Visit 1 and Visit 2 (Baseline); • Psoriasis Area and Severity Index (PASI) score ≥12 at Visit 1 and Visit 2; • Static Physician's Global Assessment (sPGA) score ≥3 at Visit 1 and Visit 2; • Body Mass Index (BMI) ≤40 kg/m^2 at Visit 1; • Negative QuantiFERON®-TB Gold test or PPD test, negative chest radiographic findings for tubercle bacillus (TB) and no other evidence of active or latent TB; • No history of a clinically-significant infection (e.g., that required oral antimicrobial therapy) within 8 weeks prior to Visit 2; • No history of infections requiring hospitalization or parenteral antibiotic, antiviral, antifungal or antiparasitic therapy within 6 months prior to Visit 2 and no history of recurrent infections or conditions predisposing to chronic infections (e.g., bronchiectasis, chronic osteomyelitis); [redacted]

6. Body Mass Index (BMI) ≤40 kg/m^2 at Visit 1;
7. Females may participate if they meet one of the following criteria:
   - Surgically sterile (e.g., hysterectomy or bilateral oophorectomy),
   - At Visit 1, females with a documented history of lack of menses for ≥12 consecutive months with no other reversible medical etiology will be considered postmenopausal.
   - At Visit 1, if positive for lack of menses but onset <12 months, then an FSH >40 will be required to define post-menopausal status, otherwise subject is considered of childbearing potential, or
   - If of childbearing potential, with a negative pregnancy test at Visit 1 and if participates in heterosexual intercourse, agrees to be compliant with the consistent and correct use of acceptable methods of contraception as described below. Acceptable methods of birth control for this study are:
     a) one highly effective contraceptive method of birth control, which includes intrauterine devices, partner sterilization (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate), tubal ligation, bilateral tubal occlusion, intrauterine hormone-releasing systems, **in addition to**
     b) one effective method of birth control, which includes male condom, female condom, cervical cap, diaphragm or contraceptive sponge all with spermicide (hormonal methods are not allowed).

     The above described contraception methods must be maintained for the duration of the study and for at least 30 days after the last dose of study drug.
8. Male subjects must agree to use a barrier contraceptive method with spermicide for the duration of the study and for at least 12 weeks after the last dose of study drug or be sterilized (with appropriate post-vasectomy documentation of the absence of sperm in the ejaculate):

   Male subjects should be informed about the risks involved if pregnancy in female partners occurs while he is taking an investigative product and for at least 12 weeks after the last dose of study drug. Counseling on the appropriate contraception methods for their female partners should be given as follows: female partners of male subjects randomized in this study must be post-menopausal or in case of female partner of childbearing potential, unless surgically sterile, they must agree to use at least one form of an acceptable form of birth control (in addition to the method utilized by the male subject) for the duration of the study and for at least 12 weeks after the last dose of study drug. Please see inclusion criterion # 7 for a list of acceptable forms of birth control for the study (hormonal methods will be allowed for females partners of male subjects);

   Additionally, male subjects must not donate sperm for the duration of the study and within 12 weeks of the last dose of study drug.
9. [redacted]
10. Able and willing to complete an [redacted] questionnaire responses on a mobile device on a daily basis for the duration of the study;
11. Able and willing to give written informed consent.

3.5.6.2 Psoriasis Area and Severity Index

Psoriasis area and severity index (PASI), a quantitative rating score to assess the severity of psoriatic lesions based on the area coverage and plaque appearance will be performed according to the schedule summarized in Table 1.

For a given subject, the PASI assessments should be performed by the same evaluator throughout the study.

The PASI score will be derived as indicated in Table 7.

The head, trunk, upper limbs and lower limbs are assessed separately for erythema, thickening (plaque elevation, induration) and scaling (desquamation). The average degree of severity of each sign in each of the four body regions is assigned a score of 0 to 4. The area covered by lesions on each body region is estimated as a percentage of the total area of that particular body region. Further practical details help the assessment:

1. The neck is assessed as part of the head.
2. The axillae and groin are assessed as part of the trunk.
3. The buttocks are assessed as part of the lower limbs.
4. When scoring the severity of erythema, scales should not be removed.

Because the head and neck, upper limbs, trunk and lower limbs correspond to approximately 10%, 20%, 30% and 40% of the body surface area, respectively, the PASI score is calculated using the following formula:

PASI = 0.1(EH+IH+DH)AH + 0.2(EU+IU+DU)AU + 0.3(ET+IT+DT)AT + 0.4(EL+IL+DL)AL

Where,

The PASI scores can range from 0, corresponding to no signs of psoriasis, up to a theoretic maximum of 72.0, corresponding to maximal signs of psoriasis.

kilograms will be documented to one decimal place and the height in centimeters will be rounded to the nearest whole number.

3.5.6.8 Medical History

A complete medical history will be performed at Visit 1 and will include evaluations for past or present conditions. Specifically, any known history of psoriatic arthritis will be documented.

Any pre-existing conditions that are detected at Visit 1 (e.g., abnormalities in ECG, physical examination, vital signs and laboratory tests) are considered to be medical history.

3.5.6.9 Vital Signs

Vital sign assessments including blood pressure, heart rate, respiratory rate and body temperature (°C) will be performed in sitting position according to the schedule summarized in Table 1. Subjects must rest in a sitting position for at least 5 minutes in preparation for blood pressure and heart rate assessments.

3.5.6.10 12-Lead ECG

12-lead ECG recordings and conduction intervals including RR, PR, QRS, QT and Fridericia-corrected QT interval (QTcF) will be obtained according to the schedule summarized in Table 1. The Investigator or designee will review and assess each individual ECG report and the interpretation of the actual findings, rather than the automatic printout, results on the ECG tracing will be documented. Subjects will lay supine without pillows for at least 3 minutes prior to the 12-lead ECG assessment.

3.5.6.11 Hematology

Blood samples to assess complete blood count including erythrocytes, hematocrit (Hct), hemoglobin (Hgb), platelets, leucocytes and differential (percent and absolute [neutrophil, eosinophil, basophil, lymphocyte, monocyte]) will be obtained under fasted conditions according to the schedule summarized in Table 1.

3.5.6.12 Serum Biochemistry

Blood samples to assess ALT, ALB, ALP, AST, bilirubin, blood urea nitrogen (BUN), calcium, carbon dioxide, chloride, creatinine phosphokinase (CPK), creatinine (CRN), gamma-glutamyl transferase (GGT), globulin, glucose, CRP, lactate dehydrogenase (LDH), phosphate, potassium, protein, sodium, urate, will be obtained under fasted conditions according to the schedule summarized in Table 1.

3.5.6.13 Bone Specific ALP

Blood samples to measure bone specific ALP will be obtained according to the schedule summarized in Table 1.

3.5.7 Clinical Institutions and Laboratories

This study will be conducted by:

[redacted]

room visits, same-day/outpatient/ambulatory procedures, and those for pre-planned, elective procedures for a pre-existing condition that did not worsen after the informed consent has been signed (no AE present). However, if the hospitalization was prolonged due to a complication of a pre-existing condition, the complication (diagnosis of same) would qualify as an SAE.

Disability: A substantial disruption of a person's ability to conduct normal life functions.

Life-threatening: Any adverse drug experience that places the patient or subject, in the view of the Investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that had it occurred in a more severe form, might have caused death.

Physical Examination, [redacted], Vital Signs, Laboratory Test and ECG Abnormalities: Any abnormalities fulfilling the criteria for an SAE should be reported as such, in addition to being recorded as an AE in the CRF. Any abnormal vital sign, physical [redacted] finding or laboratory/ECG result which is clinically significant (i.e., meets one or more of the following conditions) should be recorded as a single diagnosis on the AE page in the CRF:

- Accompanied by clinical symptoms
- Leads to permanent discontinuation of study drug
- Requires a change in concomitant therapy (e.g., addition of, interruption of, discontinuation of, or any other change in a concomitant medication, therapy or treatment).

This does not apply to abnormal vital signs, physical finding or laboratory/ECG results that do not meet the clinical significance criteria or those which are a result of an AE which has already been reported.

Pre-existing conditions that are detected at the Screening Visit (Visit 1), including abnormalities in ECG, physical examination, [redacted], vital signs and laboratory tests, are considered to be medical history

3.6.2 Assessing Adverse Events

When completing appropriate forms for reporting the AE, the Investigator will be asked to assess the AE as follows:

Seriousness of Adverse Event:

- Serious: The AE meets a criterion of the SAE definition.
- Not Serious: The AE does not meet a criterion of the SAE definition.

Severity of Adverse Event:

- Mild: No interference with functioning.
- Moderate: No significant interference with functioning.
- Severe: Significant interference with functioning.

Relationship of Adverse Event (Causality):

The Investigator's causality assessment is the determination whether there is a reasonable possibility that the IMP caused or contributed to the adverse event. Generally, the facts (evidence) or arguments to suggest causal relationship should be documented. Factors to be taken into consideration when assessing causality include: subject's underlying and pre-existing conditions, prior/concomitant medications, timing of onset relative to study drug administration, the known PK characteristics of JTE-051, the currently-known safety profile of JTE-051, known class effects of similar MOA drugs and any other information that is considered relevant by the Investigator.

Akros Pharma Inc. evaluates the relationship of an AE to the study drug using the following three categories:

- Not Related
- Possibly Related
- Related

Action Taken with Regard to Study Drug:

Akros Pharma Inc. evaluates the action taken with the treatment product and/or interacting product using the following four definitions:

- Dose Not Changed: The subject was on treatment with the study drug when the AE occurred, and the study drug dosing was maintained at the same dose level
- Drug Interrupted: The subject was on treatment with the study drug when the AE occurred, and the study drug dosing was temporarily discontinued and then re-started
- Drug Withdrawn: The subject was on treatment with the study drug when the AE occurred, and the study drug dosing was permanently discontinued
- Not Applicable: The subject was not receiving treatment with the study drug when the AE occurred (i.e., AE occurred before the first study drug administration or after the last study drug administration)

Other Action Taken:

- None
- Additional Treatment Given for the AE
- Therapeutic/ Diagnostic Procedure
- Other (including discontinuation/reduction of a concomitant medication due to the AE)

Outcome to Date:

- Not Recovered/Not Resolved: The subject has not yet recovered from the AE; the event has not improved (follow-up of all serious AEs will be continued until the overall clinical outcome has been ascertained).
- Recovering/Resolving: The subject has not yet recovered from the AE, however, the event is improving (follow-up of all serious AEs will be continued until the overall clinical outcome has been ascertained).
- Recovered/Resolved: The subject recovered from the AE with no sequelae.
- Recovered/Resolved with Sequelae: The subject recovered from the AE with sequelae.
- Fatal: The subject's death was a result of the AE.

28 days of discontinuing study drug, the Investigator should report the pregnancy to the Sponsor or designee within 24 hours of being notified.

The subject/partner should be followed by the Investigator until completion of the pregnancy. If the pregnancy ends for any reason before the anticipated date, the Investigator should notify the Sponsor or designee. At the completion of the pregnancy, the Investigator will document the outcome of the pregnancy. If the outcome of the pregnancy meets the criteria for immediate classification as an SAE (i.e., spontaneous abortion, stillbirth, neonatal death, or congenital anomaly), the Investigator should follow the procedures for reporting an SAE as described above.

Overdose Reporting:

An overdose is a significant variation from the recommended/scheduled dosage for a product. For the purposes of this study, overdose is defined by any confirmed use of blinded study medication of more than four tablets once a day. If such situations occur, the Investigator should provide additional training to the subject on study drug dosing instructions and emphasize the importance of compliance. Currently there is no known antidote to JTE-051, thus appropriate symptomatic and/or supportive care is to be provided at the Investigator's discretion, as needed. The subject's continued eligibility will be left to the judgment of the Investigator.

Information on overdoses in subjects is collected by the Sponsor or designee. Should a subject experience an overdose during the course of the study, the investigator or qualified designee must report the overdose as soon as possible, but not later than the timeframe requested by the Sponsor or designee after the investigator or qualified designee first becomes aware of the overdose. Instructions will be provided on how to collect this information.

3.7 Identification of Treatments

3.7.1 Method of Assigning Subjects to Treatment Groups

After subject signs the informed consent, each site will assign potential study subjects an eight-character subject number. This number will consist of a four-digit site number (with the first two digits representing the country-specific number and the next two digits representing the site-specific number) and a three-digit subject number assigned in a sequential manner. The hyphen between the site and subject number will account for the eighth character. This number will represent the subject's identifier throughout the study. Following confirmation of eligibility at Visit 2, the Interactive Web Response System (IWRS) will be contacted by the site and it will assign the subject a four-digit randomization number that will correspond to a randomly assigned treatment group.

3.7.2 Identity of Investigational Products

[redacted]

An Investigator shall retain records required to be maintained under this part for a period of two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and the FDA is notified.

For sites in Canada, the Investigator shall retain records required to be maintained under this part for a period of twenty-five years following completion of the clinical trial in accordance with the local regulations.

The Sponsor or designee should inform the Investigator(s)/institution(s) in writing of the need for record retention and should notify the Investigator(s)/institution(s) in writing when the trial related records are no longer needed.

Custody of the records may be transferred to another responsible party, acceptable to the Sponsor, who agrees to abide by the retention policies. Written notice of transfer must be submitted to the Sponsor or designee. The Investigator must contact, and obtain prior written permission of the Sponsor prior to disposing of or transferring any study records.

4.8 Confidentiality

The Investigator, Medical Monitor, the Sponsor and its representatives, agree to protect the privacy and confidentiality of the protected health information in accordance with applicable laws and regulations.

Subject medical information obtained by the study is confidential and disclosure to third parties other than those noted below is prohibited unless required by law. The Investigator shall retain all such information, and any other information designated by the Sponsor as confidential, or is otherwise of reasonably confidential nature, in confidence and shall not use such information for any purpose other than the performance of obligations pursuant to the agreement with the Sponsor and designated affiliates or contractors, as the case may be, without prior written authorization from the Sponsor.

At the subject's request, medical information may be given to his or her personal physician or other appropriate medical personnel responsible for his or her welfare.

Data generated by this study must be available for inspection on request by representatives of regulatory authorities, the Sponsor or designee, and the IRB(s)/IEC(s) if appropriate.

4.9 Publications

The Investigator agrees that all data, calculations, interpretations, opinions and recommendations regarding the study shall be the sole and exclusive property of the Sponsor, and that the Sponsor may make any use thereof at its discretion without obligation to Investigator. The Investigator agrees to consider the results as information subject to confidential and use restrictions.

In the event that the study results are published in the scientific literature by the Sponsor, acknowledgment will be made to the Investigator(s) in the accepted style, as appropriate. The names of the Investigators or their representatives shall not be used by the Sponsor in

Abbreviation	Definition of term
OAT	Organic anion transporter
OATP	Organic anion transporting polypeptide
OCT	Organic cation transporter
OECD	Organization for Economic Co-operation and Development
PASI	Psoriasis area and severity index
P-gp	P-glycoprotein
pH	Logarithmic measure of hydrogen ion concentration
PI	Principal Investigator
PK	Pharmacokinetic(s)
PP	Per protocol
PR	Interval from beginning of the P wave to the beginning of the QRS complex in the frontal plane
PT	Prothrombin time
QD	Once daily
QOL	Quality of life
QTcF	Fridericia-corrected QT Interval
RA	Rheumatoid arthritis
[redacted]	
RR	Interval from beginning of the QRS complex in the frontal plane to the next QRS complex
SAE	Serious adverse event(s)
SAP	Statistical analysis plan
SAS	Statistical analysis system
SD	Standard deviation
Skindex-16	A 16-item, skin-related quality of life questionnaire
SOC	System organ class(es)
SPF	Sun protection factor
sPGA	Static Physician's Global Assessment
SUSAR	Suspected unexpected serious adverse reaction
TB	Tubercle bacillus
TCR	T cell receptor
TEAE	Treatment-emergent adverse event
TG	Triglycerides
TNSn	Total neuropathy score nurse
Treg	Regulatory T cells
[redacted]	
TSH	Thyroid stimulating hormone
TV	Target value
UCL	Upper confidence level
WI-NRS	Worst-Itch Numeric Rating Scale

INVESTIGATIONAL PRODUCT (STUDY DRUG), FORMULATION, DOSAGE, ROUTE AND TIME OF ADMINISTRATION	JTE-051 50 mg tablets 50 mg, 100 mg, 150 mg and 200 mg Oral administration for 12 weeks starting on the day of randomization at Visit 2, QD in the morning, regardless of meals. On study visit days, subjects should take their scheduled study treatment at the clinical research site (site) under the supervision of the investigator or designee after all study-related procedures have been completed (except at Visit 6, when no study drug will be administered).
REFERENCE PRODUCT (STUDY DRUG), FORMULATION, DOSAGE, ROUTE AND TIME OF ADMINISTRATION	Placebo Tablets (identical in appearance to JTE-051 tablets) Not applicable (N/A) Oral administration for 12 weeks starting on the day of randomization at Visit 2, QD in the morning, regardless of meals. On study visit days, subjects should take their scheduled study treatment at the site under the supervision of the investigator or designee after all study-related procedures have been completed (except at Visit 6, when no study drug will be administered).

2 STUDY OBJECTIVES

- To evaluate the efficacy of JTE-051 administered for 12 weeks in subjects with moderate to severe plaque psoriasis.
- To evaluate the safety and tolerability of JTE-051 administered for 12 weeks in subjects with moderate to severe plaque psoriasis.
- To evaluate the pharmacokinetics (PK) of JTE-051 administered for 12 weeks in subjects with moderate to severe plaque psoriasis.

3 INVESTIGATIONAL PLAN

3.1 Number of Sites and Subjects

Multiple sites will be employed to ensure screening of sufficient number of subjects to randomize (in a 1:1:1:1:1 ratio) approximately 85 subjects (17 subjects per treatment group).

3.2 Study Design

This is a 12-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study in subjects with moderate to severe plaque psoriasis.

Eligible subjects will be randomized at Visit 2 to receive JTE-051 50 mg, 100 mg, 150 mg, 200 mg or placebo QD for 12 weeks. Approximately 85 subjects are planned to be randomized into 5 treatment groups. A follow-up visit will take place approximately 4 weeks after the last dose of study drug. Randomization will be stratified based on prior exposure of subjects to biologic therapy (i.e., biologic treatment-naïve vs. biologic treatment-experienced subjects).

The study duration will be of approximately 20 weeks per subject:

- Up to a 28-day Screening Period
- A 12-week double-blind Treatment Period
- A 4-week Follow-up Period

3.3 Selection of Study Population

Written informed consent must be obtained prior to performing any study-related procedures. A copy of the informed consent will be provided to the subject.

3.3.1 Inclusion Criteria

To qualify for the study, the subject must satisfy the following criteria:

1. Male or female, ≥18 and ≤70 years of age at the time of Visit 1 (Screening Visit);
2. Have had a diagnosis of moderate to severe plaque psoriasis for at least 6 months prior to Visit 1;
3. Plaque-type psoriasis covering ≥10% of Body Surface Area (BSA) at Visit 1 and Visit 2 (Baseline);
4. Psoriasis Area and Severity Index (PASI) score ≥12 at Visit 1 and Visit 2;
5. Static Physician's Global Assessment (sPGA) score ≥3 at Visit 1 and Visit 2;

3.3.2 Exclusion Criteria

The following criteria will exclude a subject from participating in the study:

1. Medical history of treatment failure to any systemic agents (including biologic and non-biologic systemic agents) for plaque psoriasis;
2. Presence of erythrodermic psoriasis, pustular psoriasis, guttate psoriasis, medication-induced psoriasis or other skin conditions at (e.g., clinically-significant eczema or severe acne) that could interfere with study evaluations at Visit 1;
   Note: Subjects with psoriatic arthritis will not be excluded from the study provided that criteria for cutaneous severity of psoriasis, as well as all other study restrictions required by the protocol are met.
3. Presence or history of any itch due to underlying conditions other than plaque psoriasis which cause or influence pruritus of the skin (e.g., drug induced pruritus, significant other systemic diseases with itch) within 12 months prior to Visit 1;
4. Does not meet all study restrictions, including previous/concomitant medication restriction criteria, as described in Section 3.5.4.1;
5. Leucocyte count of <3.0 X 10^9/L (<3000/mm^3), absolute neutrophil count of <1.5 X 10^9/L (<1500/mm^3) or absolute lymphocyte count <0.8 X 10^9/L (<800/mm^3) at Visit 1; Hemoglobin <11 g/dL or platelet count <100,000/mm^3 at Visit 1;
6. ALT >2.0 X the upper limit of normal (ULN) or AST >2.0 X the ULN at Visit 1;
7. Evidence of renal impairment; serum creatinine >1.5 X the ULN at Visit 1;
8. Hemoglobin A1c (HbA1c) >8.5% at Visit 1;
9. Serum triglycerides >400 mg/dL at Visit 1;
10. Positive viral serology at Visit 1 for:
    - Human immunodeficiency virus (HIV): positive HIV antibodies (Ab) or
    - Hepatitis B virus (HBV): positive total hepatitis B core (HBc) Ab or positive hepatitis B surface antigen (HBsAg) or
    - Hepatitis C virus (HCV): positive HCV Ab;
11. Positive drug of abuse test results at Visit 1;
    Note: Non-abusive use of prescription drugs, according to the Investigator's judgment is permitted, provided that the concomitant medications restrictions required by the protocol are met.
12. Positive Purified Protein Derivative (PPD) test or QuantiFERON®-TB Gold-In-Tube test , positive chest radiographic findings for tubercle bacillus (TB) or any other evidence of active or latent TB;
    - For subjects with a history of Bacille Calmette-Guérin (BCG) vaccination or in case PPD test fails, the QuantiFERON®-TB Gold-In-Tube test should be performed;
    - A PPD test is considered positive if, at 48 to 72 hours of administration, the induration (not erythema) obtained is ≥5 mm. The reaction must be read between 48 and 72 hours after administration (a subject that does not return after 72 hours must be rescheduled for a repeat PPD test);

Table 7. The PASI Scoring

Body region	Erythema (E)	Thickening (plaque elevation, induration, I)	Scaling (desquamation, D)	Area score (based on true area %, A)*
Head (H)†	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0 = 0% 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%
Trunk (T)‡	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0 = 0% 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%
Upper limbs (U)	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0 = 0% 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%
Lower limbs (L)§	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0=none 1=slight 2=moderate 3=severe 4=very severe	0 = 0% 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%

* Percentage (not score) of body region (not whole body) affected will be entered in the CRF.

† Neck is assessed as part of the Head (H) body region.

‡ Axillae and groin are assessed as part of the Trunk (T) body region.

§ Buttocks are assessed as part of the Lower limbs (L) body region.

3.5.6.14 Lipid Panel

Blood samples to measure cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides will be obtained according to the schedule summarized in Table 1.

3.5.6.15 Serum Immunoglobulins

Blood samples to measure Serum IgG, IgM and IgA will be obtained according to the schedule summarized in Table 1.

3.5.6.16 25-hydroxyvitamin D

Blood samples to measure 25-hydroxyvitamin D will be obtained according to the schedule summarized in Table 1.

3.5.6.17 Coagulation

Blood samples to assess thromboplastin time (PT) and activated partial thromboplastin time (aPTT) will be obtained as measures of blood coagulation according to the schedule summarized in Table 1. International normalized ratio will also be calculated.

3.5.6.18 Viral Serology

Blood samples to assess HbcAb (HBsAg), HCV Ab and HIV Ab will be obtained at the Visit 1.

3.5.6.19 Drugs of Abuse and Alcohol Screen

Urine samples to assess amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine metabolites, opiates, ethanol, methadone, methylenedioxymethamphetamine and oxycodone will be obtained at Visit 1.

3.5.6.20 Urinalysis

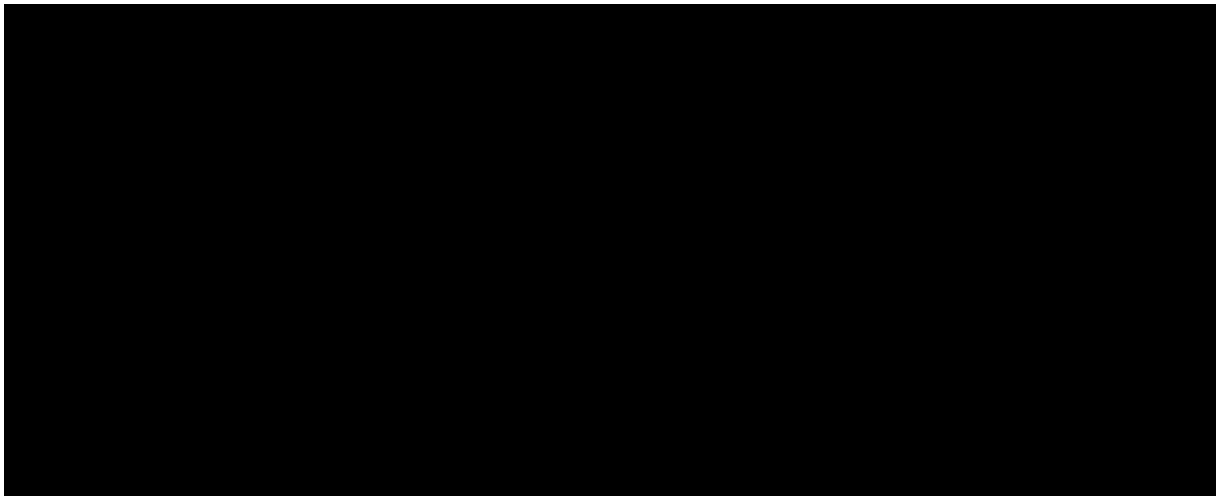
Urine samples to assess bilirubin, occult blood, color, glucose, ketone, leukocyte esterase, nitrite, pH, protein, specific gravity, turbidity and urobilinogen, as well as for a microscopic exam (to be performed only if the macroscopic exam is abnormal), including bacteria, cast, crystals, epithelial cells, mucus threads, erythrocytes, leukocytes and budding yeast will be obtained under fasted conditions according to the schedule summarized in Table 1.

3.5.6.21 Glycosylated Hemoglobin

Blood samples to measure glycosylated hemoglobin will be obtained at Visit 1.

3.5.6.22 Pregnancy Test

Blood samples will be collected at Visit 1 for a serum pregnancy test to assess human chorionic gonadotropin (βHCG) levels for all female subjects. At Visits 2 through 7, urine pregnancy tests will be performed only for female subjects of childbearing potential.



3.6.3 Reporting Adverse Events

Adverse Events Reporting

Adverse events occurring (initial occurrence or a worsening of a pre-existing condition) after the informed consent has been signed and up to 4 weeks (28 days) after the last dose of study drug will be reported and included in the study database. However, pre-existing conditions detected as part of the screening procedures should be documented as medical history. Worsening of the underlying condition (i.e., plaque psoriasis) or signs/symptoms associated with this condition should not be reported as an AE unless they meet at least one serious criterion; in such case when they would be reported as both an AE and an SAE. Adverse events will be reported on the AE CRF page.

Serious Adverse Event Reporting

Reporting by Investigators
Detailed instruction regarding SAE reporting will be provided in the appropriate documents outside of this protocol. A brief, non-all-inclusive summary is provided below.

Any SAE experienced by a study subject after signing the informed consent up to 28 days after the last dose of study drug will be reported to the Sponsor or designee. Additionally, SAEs that occur after this period will also be reported to the Sponsor or designee if the Investigator considers the SAE possibly related or related to the study drug.

Serious adverse events (both initial reports and follow-up information) must be reported to the Sponsor or designee within 24 hours of the Investigator's (site's) awareness or notification of the event.

The Investigators should make every effort to provide complete information when reporting the SAE (both for initial reports, as well as for follow-ups).

The Investigator must continue to follow the subject until the SAE has subsided, the condition becomes chronic in nature, stabilizes (in the case of persistent impairment), or the subject dies. Within 24 hours of receipt of follow-up information, the Investigator must submit it to the Sponsor or designee.

The Investigator is also required to submit SAE reports to the IRB/IEC in accordance with local requirements. All investigators involved in studies using the same IMP will receive any Suspected Unexpected Serious Adverse Reaction (SUSAR) reports for onward submission to their local IRB/IEC as required. All reports sent to investigators will be blinded.

Reporting by the Sponsor
Competent authorities and IRBs/IECs will be informed by the Sponsor or designee of SUSARs according to the local requirements. Additionally, all SUSARs will be reported by the Sponsor or designee into the EudraVigilance system, as appropriate. Cases will be unblinded by designated personnel for reporting purposes as required.

Exposure *in Utero* Reporting:

If a female subject becomes pregnant or the female partner of a male subject participating in the study becomes pregnant after the subject receives the first dose of study drug, or within

3.7.3 Storage and Handling Procedures

The JTE-051 and placebo tablets should be stored at room temperature between 20 and 25°C (United States Pharmacopeia [USP]) and in a secure location with restricted access.

3.7.4 Clinical Supplies Packaging

Each site will receive a supply of double-blind study drug packaged as blister cards corresponding to 8 days of QD dosing. Each blister card will contain a total of 32 JTE-051 tablets.

Study drug blister cards may be labeled with the following information, as appropriate:

- Sponsor identity and protocol number
- Card number
- Dosing instructions
- Spaces for site personnel to add subject number and subject initials
- Spaces for site personnel to add visit number, site number and Investigator name
- Spaces for site personnel to add the card identifier, as appropriate
- Quantity and identity of contents
- Lot number and storage conditions
- Expiration date
- For investigational use only statement

The planned blister card allocation of tablets for each dose, broken down by treatment group, is provided below.

Treatment Group	Tablet 1	Tablet 2	Tablet 3	Tablet 4
JTE-051 50 mg	JTE-051 50 mg	JTE-051 Placebo	JTE-051 Placebo	JTE-051 Placebo
JTE-051 100 mg	JTE-051 50 mg	JTE-051 50 mg	JTE-051 Placebo	JTE-051 Placebo
JTE-051 150 mg	JTE-051 50 mg	JTE-051 50 mg	JTE-051 50 mg	JTE-051 Placebo
JTE-051 200 mg	JTE-051 50 mg	JTE-051 50 mg	JTE-051 50 mg	JTE-051 50 mg
Placebo	JTE-051 Placebo	JTE-051 Placebo	JTE-051 Placebo	JTE-051 Placebo

3.7.5 Administration of Study Drug

During the Treatment Period, beginning on the day of Visit 2, subjects will self-administer one dose of study drug (4 tablets) daily for 12 weeks. Study drug will be taken QD in the

publications, for advertising, for other commercial purposes, or otherwise, without appropriate written permission, unless required by law or government regulation.

Individual study center manuscript(s) for publication, text for talks, abstracts of papers, poster presentations, and similar material will be submitted to the Sponsor for review and comment prior to publication or disclosure. In order to ensure that the Sponsor will be able to make comments and suggestions where pertinent, material for public dissemination will be submitted to the Sponsor for review at least sixty (60) days prior to submission for publication, public dissemination, or review by a third party committee. The Sponsor will have sixty (60) days from receipt of such information to review and comment on and discuss the contents thereof with the Investigator. If the Sponsor requests, the Investigator will remove any and all confidential information (other than study results) prior to submitting or presenting the materials. Upon the Sponsor's request, the Investigator will delay submitting or presenting the materials for a further sixty (60) days to permit the Sponsor to take necessary actions to protect its confidential information, including the filing of patent applications thereon.

5 STUDY MANAGEMENT

5.1 Monitoring

Monitoring visits will be conducted by the Sponsor or designee according to applicable regulations and guidelines for GCP. The Investigator will permit the Sponsor and/or designated representative(s) to make regular site visits during the study. The frequency of monitoring visits will be agreed upon by the Sponsor and/or designee. At each visit, the Investigator and staff will be expected to cooperate with the Sponsor or designee for the review and verification of protocol compliance, AE reporting, CRFs, source documents, clinical supplies and inventory records, and any additional records as may have been previously arranged between the Investigator and Akros or designated representative(s).

The Investigator and/or other designated study personnel are expected to contact the monitor of the Sponsor or designee as needed regarding study concerns and/or questions.

5.2 Management of Protocol Amendments and Deviations

With the exception of emergency situations, implementation of any change in the protocol that affects the safety of the subjects, the scope of the investigation, or the scientific quality of the study will not be permitted until the Sponsor and the Investigator have approved the protocol amendment and the IRB/IEC responsible for review and approval of the study has reviewed and approved the protocol change.

Implementation of changes that do not affect the safety of the subjects, the scope of the investigation, or the scientific quality of the study cannot be made until the protocol changes are reviewed and approved by Akros and the Investigator. The IRB/IEC must be notified of these protocol changes.

The Investigator will not deviate from the protocol without prior written approval from the Sponsor or designee.