Efficacy and Safety of Stapokibart for Primary Cutaneous Amyloidosis: A Randomized, Double-blind, Placebo-controlled Study

I. Background of the Study

Amyloidosis is a group of diseases characterized by the abnormal deposition of amyloid substances in tissues and organs, which can be classified into primary and secondary forms, or focal and systemic types. Primary cutaneous amyloidosis (PCA) refers to a chronic metabolic skin disorder in which amyloid proteins are deposited only in the dermis without involvement of internal organs [1]. This condition is more common in middle-aged and elderly individuals and generally shows no gender predilection. Skin lesions are frequently found on the back, anterior tibia, and thighs, and may also be distributed on the upper lip, nasolabial folds, and penis. PCA comprises three basic types: lichen amyloidosis (LA), macular amyloidosis (MA), and nodular amyloidosis. In addition, it includes special types such as dyschromatosis-like amyloidosis and bullous amyloidosis. Clinically, LA and MA are the most common types.

PCA is generally a chronic condition,with the main clinical manifestations including papules,macules,scales,lichenification,pigmentation,dryness and roughness of the affected skin,excoriations,and in some cases,local pruritus.There are currently no guidelines or expert consensus to direct the standard treatment of PCA,and topical corticosteroid ointments are the most commonly used empirical therapeutic means in clinical practice.In addition to

this,depending on the clinical manifestations and therapeutic expectations of the patients,some may be treated with oral medications such as antihistamines in combination.Overall,the existing traditional treatment options are relatively limited.The need to use medications daily leads to poor patient compliance,and the therapeutic effects are often poor and prone to relapse[2].Because PCA shares certain similarities with another common dermatological condition—atopic dermatitis—in terms of clinical manifestations and traditional treatments,there have been a few case reports in recent years on the use of novel drugs for atopic dermatitis(biologics represented by IL-4 receptor antagonists and small-molecule drugs represented by JAK pathway inhibitors)to treat PCA,all of which have shown good therapeutic effects[3-4].Currently,clinical trials of JAK pathway inhibitors for the treatment of PCA are being conducted in China.However,there is still a lack of large-scale clinical studies exploring the efficacy and safety of novel drugs in PCA.Therefore,this trial is planned to investigate the efficacy and safety of Stapokibart Injection (an IL-4 receptor antagonist that has been marketed and is currently approved for moderate-to-severe atopic dermatitis)in patients with PCA.

References：

[1]Guillet C, Steinmann S, Maul JT, Kolm I. Primary Localized Cutaneous Amyloidosis: A Retrospective Study of an Uncommon Skin Disease in the Largest Tertiary Care Center in Switzerland. Dermatology. 2022;238(3):579-586. doi: 10.1159/000518948. Epub 2021 Sep 15. PMID: 34525472; PMCID: PMC9153345

[2] Zhang Zihui, Du Dan, Jiang Xian. Current Status and Prospects of Physical Therapy for Primary Cutaneous Amyloidosis. Journal of Clinical Dermatology, 2018, 47(9):3.DOI:CNKI:SUN:LCPF.0.2018-09-024.

[3]Zhang, Y., et al. (2024). Successful treatment of primary cutaneous amyloidosis with dupilumab: a case report. Journal of the American Academy of Dermatology.

[4] Shahriari, N., et al. (2023). JAK inhibitors as rescue therapy in dupilumab-refractory severe atopic dermatitis: A case series. JAAD Case Reports, 32 , 1-5.

II.Aims and Expected Outcomes of the Study

Research Objective: To clarify the efficacy and safety of the IL-4 receptor antagonist Stapokibart in primary cutaneous amyloidosis.

Expected Outcome: Publication of 1 SCI (Science Citation Index) article.

III.Design and Methods of the Study

1. Study Period: Sep 15, 2025 – December 31, 2026

2. Randomized, Double-Blind, Placebo-Controlled Trial

3. Two Groups: Placebo group and treatment group

4. Enrollment: A total of 40 participants are planned to be enrolled, with 20 participants in each group, assigned randomly.。

Randomization Process:This study employs a randomized design.A fixed investigator(Investigator A)will use SAS software to generate the randomization tables for subjects and study medications using a stratified block randomization method.Subjects who meet the inclusion criteria will be stratified by baseline IGA(Investigator's Global Assessment)score(3 or 4)and randomly assigned to either the Stapokibart group or the placebo group in a 1:1 ratio.After successful screening of the subjects,the investigators will obtain the randomization numbers from Investigator A.At each study visit when medications are dispensed,the investigators and their designated personnel will obtain the drug identification numbers from Investigator A and assign the study medications according to these numbers.Investigator A,who is responsible for randomization,will record the seed and other parameters used to generate the random numbers in the blind code,which can be unblinded in case of emergency.After signing the informed consent form,subjects will be assigned a unique enrollment number in the order of their successful screening,and this enrollment number will serve as their randomization number.

5. For quantitative data, statistical descriptions are provided using mean, median, standard deviation,maximum value, and minimum value. For categorical or ordinal data, frequency and proportion are used to describe the data. Homogeneity comparisons between groups are performed using analysis of variance (ANOVA), chi-square (χ^2) test, or rank-sum test.

IV. Process of Study Implementation

Objective	**Primary Objectives:** ➢ To evaluate the efficacy of Stapokibart in adult subjects with Primary Cutaneous Amyloidosis (PCA). ➢ To evaluate the safety of Stapokibart in adult subjects with Primary Cutaneous Amyloidosis (PCA).
Evaluation Criteria	**Primary Evaluation Criteria:** a.The percentage of subjects achieving AASI-75 at Week 16 of treatment. **Secondary Evaluation Criteria:** a.The percentage of subjects with a weekly average reduction of≥4 points in PP-NRS score at Week 16 of treatment compared to baseline. b.The percentage of subjects achieving AASI-75 at other evaluation visits. c.The percentage of subjects with an IGA score of 0 or 1 and a reduction of≥2 points compared to baseline at each evaluation visit. d.The percentage of subjects achieving AASI-50 at each evaluation visit. e.The percentage of subjects achieving AASI-90 at each evaluation visit. f.Changes and change rates in AASI scores from baseline at each evaluation visit. g.The percentage of subjects with a weekly average reduction of≥3 points in PP-NRS score compared to baseline. h.Changes and change rates in weekly average PP-NRS scores compared to baseline. i.Change rates in BSA involvement from baseline at each evaluation visit. j.Changes in DLQI scores from baseline at each evaluation visit. k.Changes in absolute eosinophil counts in complete blood counts from baseline at each evaluation visit. l.Changes in IgE levels in complete blood counts from baseline at each evaluation visit. m.Changes in histopathology of skin lesions at Week 16 of treatment compared to baseline in some subjects. Safety Endpoints:Including the occurrence of AEs(Adverse Events),and abnormalities in laboratory tests,physical examinations,and vital signs. (For detailed scoring tables,please refer to the appendix.)
Subjects	Adult subjects with Primary Cutaneous Amyloidosis
Sample size	40 cases
Trial Design	This study is a randomized,double-blind,placebo-controlled trial designed to evaluate the efficacy and safety of Stapokibart in adult subjects with Primary Cutaneous Amyloidosis(PCA).A total of 40 subjects are planned to be enrolled and will be randomized in a 1:1 ratio to receive either Stapokibart Injection at a dose of 300 mg

every two weeks(Q2W)(with an initial loading dose of 600 mg) or matching placebo.

The study will consist of a screening period of up to 4 weeks,a 16-week treatment period,and a 12-week post-treatment follow-up period.The treatment period will begin with drug administration on Day 1(D1)and continue with dosing every 2 weeks until Week 16.

After providing informed consent,subjects will enter the screening period.During the screening period,subjects will discontinue any ongoing PCA treatments according to the inclusion criteria.For subjects who do not meet the inclusion/exclusion criteria due to transient laboratory abnormalities or clinical conditions,up to two re-screenings are allowed.At least 7 days before randomization,subjects must apply a moisturizing cream once daily,and this same moisturizing cream must be continued throughout the study period.To objectively assess skin dryness,subjects should avoid applying moisturizing cream on non-lesional skin within 8 hours prior to visits.

Subjects who meet the inclusion criteria and do not meet the exclusion criteria will proceed to the baseline/D1 visit.Subjects will be stratified by baseline IGA score[3(moderate),4(severe)]and randomly assigned to either the Stapokibart group or the placebo group in a 1:1 ratio,to receive the following treatments:

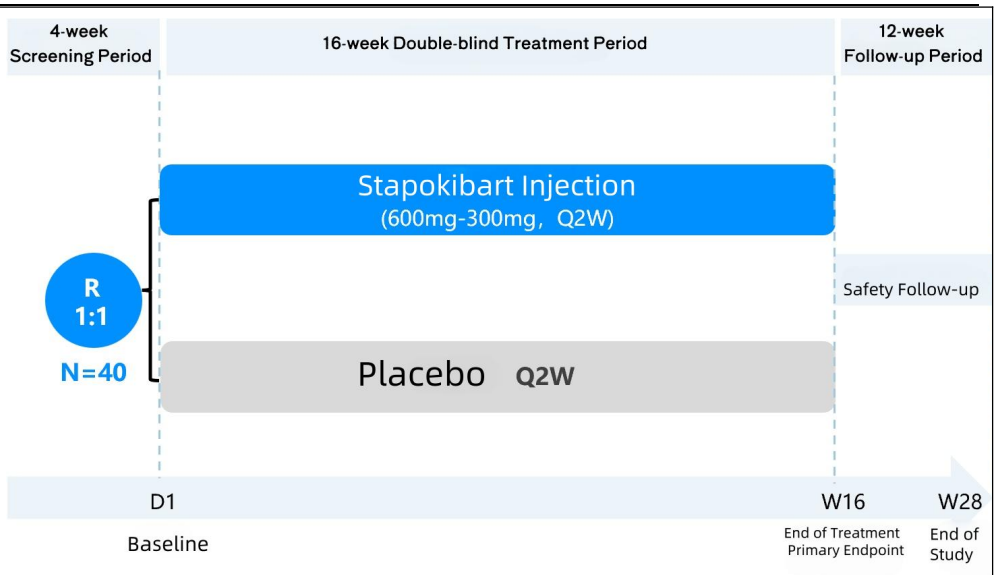
• Stapokibart group:Stapokibart Injection,300 mg,Q2W,with an initial dose of 600 mg.

• Placebo group:Matching placebo injection with the same dosage and regimen as above.

Subjects will follow the visit schedule and receive study drug/placebo injections every 2 weeks during the study period from V2(D1)to V10(D113).

During the study,subjects will undergo the following assessments:Complete blood counts,biochemical tests,and urinalysis will be performed at V1,V2,V10,and V12.An electrocardiogram(ECG)and pregnancy test will be conducted at V1,and ECGs will also be performed at V10 and V12.A subset of subjects will undergo skin biopsies for histopathological examination at V1 and V12.(For details,see Table 1:Subject Visit Schedule and Table 2:Laboratory Tests Checklist)

The study design is illustrated in the figure below.：



Estimated Target

The primary clinical question of this study is: Among PCA patients randomly enrolled and treated with Stapokibart or placebo, regardless of whether they terminated treatment or used prohibited medications (live attenuated vaccines) that do not affect efficacy assessment for reasons other than disease progression or use of prohibited medications during the study period (including within D1–D28 days or before 16 weeks of treatment), to evaluate the percentage of subjects achieving AASI-75 at Week 16. The difference in the AASI-75 response rate between the treatment group and the control group will be used as the effect size at the population level to assess the efficacy of the study drug.Primary Estimation Target:• Target Population: Adult PCA subjects randomly enrolled.• Treatment: Stapokibart Injection/Placebo 300 mg Q2W (with an initial loading dose of 600 mg).• Target Variable: The percentage of subjects achieving AASI-75 at Week 16.

Concomitant Events and Management Strategies：

Concomitant Events	**Management Strategies**	**Notes**
Rescue therapy is used only during the treatment period from Day 1 to Day 28.	Therapeutic Strategy	If this event occurs during th treatment period, the subjec will still follow the planne follow-up schedule, and actua observed data will be used.
Discontinuation of treatment due	Composite	After the occurrence of thi

	to lack of efficacy	Variable Strategy	event during the treatmer period, the primary endpoir will be considered as "nc achieved."
	Discontinuation of treatment for reasons other than the use of prohibited medications or disease progression	Therapeutic Strategy	If this event occurs during th treatment period, the subjec will continue to follow th planned follow-up schedule and actual observed data will b used.
	Use of prohibited medications or treatments that affect the efficacy assessment during the study period (excluding rescue therapy used from Day 1 to Day 28).	Composite Variable Strategy	After the occurrence of thi event during the treatmer period, the primary endpoir will be treated as "nc achieved."
	Use of prohibited medications that do not affect efficacy assessment during the study period (live attenuated vaccines).	Therapeutic Strategy	If this event occurs during th treatment period, the subjec will continue to follow th planned follow-up schedule and actual observed data will b used.
	Population-level Summary: The difference in the AASI-75 response rate between the treatment group and the control group.。		
Inclusion Criteria	1) Males or females aged 18 to 75 years, with a diagnosis of PCA confirmed by skin biopsy, and an IGA score of ≥3, a AASI score of ≥5, and a BSA involvement of ≥5%. 2) Subjects who have received at least 4 weeks of mid-to-high potency or at least 2 weeks of very high potency topical corticosteroids (TCS) or an adequate course of systemic corticosteroids within the 6 months prior to screening, but with an inadequate response; or subjects who are unable to receive the above treatments due to adverse reactions or potential risks. 3) Prior to the first dose, subjects must have used a moisturizer continuously for at least 1 week, once daily, and must continue to use it throughout the study period. 4) Able to understand and complete study-related questionnaires. 5) Able to read, understand, and are willing to sign the informed consent form. 6) Willing and able to comply with study visits and related procedures. 7) Women of childbearing potential must agree to use contraception (such as		

	intrauterine devices, oral contraceptives, or condoms) during the study and for 6 months after the study ends; must have a negative serum pregnancy test within 7 days before the first dose and must not be breastfeeding; male subjects must agree to use contraception during the study and for 6 months after the study ends.
Exclusion Criteria	Subjects meeting any of the following criteria will be excluded from the trial:1) Use of any of the following treatments within 4 weeks prior to randomization: a. Immunosuppressants or immunomodulators, such as systemic corticosteroids, cyclosporine, mycophenolate mofetil, interferon gamma (IFN-γ), azathioprine, methotrexate, and Janus kinase (JAK) inhibitors; b. UV phototherapy; c. Systemic traditional Chinese medicine (TCM) treatment.2) Use of topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), TCM, or phosphodiesterase 4 (PDE-4) inhibitors within 2 weeks prior to randomization.3) Receipt of anti-IL-4R monoclonal antibodies, anti-IgE monoclonal antibodies, or other biologics within 12 weeks or 5 half-lives (whichever is longer) prior to randomization.4) Receipt of live attenuated vaccines within 12 weeks prior to randomization or planned vaccination during the study period.5) Use of antihistamines within 1 week prior to randomization (subjects who have been on a stable dose of antihistamines for at least 7 days prior to randomization and plan to continue during the study period may be included).6) Receipt of allergen-specific immunotherapy (desensitization therapy) within 6 months prior to randomization.7) Presence of any skin comorbidities that may interfere with study assessments, including but not limited to scabies, cutaneous T-cell lymphoma, psoriasis, etc.8) Previous receipt of at least 12 consecutive doses of anti-IL-4Rα or IL-13 monoclonal antibodies with inadequate clinical response (defined as failure to achieve AASI 50 during treatment).9) Presence of any other significant medical history that the investigator deems would pose a risk to the subject's safety or be poorly controlled if the subject participates in the study, in addition to PCA.10) History of known or suspected immunosuppression (immunodeficiency), including a history of invasive opportunistic infections (such as histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, and aspergillosis), even if the infection has resolved; or unusual frequency, recurrence, or chronicity of infections (at the investigator's discretion).11) Subjects with any type of active malignancy or a history of malignancy (except for cervical cancer that has been cured for more than 5 years prior to the screening period, or non-metastatic squamous cell carcinoma of the skin, basal cell carcinoma, and papillary thyroid cancer).12) Presence of active Mycobacterium tuberculosis infection.13) Subjects with severe liver or kidney function impairment during the screening period, such as aspartate aminotransferase or alanine aminotransferase >2 times the upper limit of normal (ULN), total bilirubin >1.5 times ULN, serum creatinine >1.2 times ULN, etc.14) Presence of active hepatitis during the screening period, or positive for hepatitis B surface antigen (HBsAg), or positive for hepatitis B core antibody (HBcAb) and HBV-DNA, or positive for hepatitis C virus (HCV) antibody and HCV-RNA.15) Positive for HIV antibody during the screening period, or history of HIV infection.16) Positive for Treponema pallidum antibody during the screening period (subjects who have undergone standard treatment and have a negative non-treponemal antigen serological test may participate in the study).17) Participation in another clinical trial of a drug or

	medical device within 12 weeks prior to randomization.18) Presence of chronic active or acute infection requiring systemic treatment with antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 4 weeks prior to randomization. After resolution of the infection, the subject may be re-screened once.19) Subjects who plan to undergo major surgical procedures during the study period.20) Pregnant or breastfeeding women.21) Subjects with a history of alcoholism, drug abuse, or known drug dependence.22) History of atopic keratoconjunctivitis involving the cornea.23) Any medical or psychiatric conditions that the investigator deems would pose a risk to the subject, interfere with participation in the study, or confound the interpretation of study results.
Investigational Medicinal Product	Investigational Medicinal Product: Stapokibart Injection, Specification: 300mg (2ml) per vial Control Medication: Stapokibart Placebo, Specification: 0mg (2ml) per vial
Dosage Regimen	Subjects will receive dosing starting from Day 1 (D1), once every 2 weeks, continuing until Visit 10 (Day 113), for a total of 9 doses. The treatment period will end after Visit 10. Any changes in the subject's condition that require communication with the investigator or the need for rescue therapy* will necessitate an unscheduled visit. If the trial is discontinued early, the Early Termination (ET) visit should be initiated as soon as possible.
Safety Evaluation Criteria	The severity of adverse events will be assessed using the NCI-CTC AE 5.0 criteria. During the trial, the Adverse Event Record Form should be completed accurately, including the time of occurrence of the adverse event, its severity, its relationship to the study treatment, its duration, measures taken, and its outcome.
Efficacy Evaluation Criteria	AASI score, PP-NRS score, IGA score, DLQI score, BSA score (for details, see the appendix).
Data Analysis and Statistical Methods	**Efficacy Analysis** The primary efficacy endpoint will be analyzed using the Cochran-Mantel-Haenszel test, adjusted for randomization stratification, and the 95% confidence interval for the difference in response rates (Stapokibart group - Placebo group) will be calculated.For secondary efficacy endpoints, binary variables will be analyzed using the same method as the primary efficacy endpoint. Continuous variables will be analyzed using a mixed-effects model for repeated measures

	(MMRM), incorporating relevant baseline covariates into the model, and the 95% confidence interval for the difference between the treatment group and the placebo group will be calculated **Safety Analysis** Adverse events will be coded using MedDRA (Medical Dictionary for Regulatory Activities). The incidence, number of cases, and rate of each type of adverse event in the treatment group and the control group will be calculated separately. Adverse events will be classified and summarized at two levels: System Organ Class (SOC) and Preferred Term (PT). Safety assessments will also include vital signs, 12-lead electrocardiograms (ECGs), and laboratory test results.
Estimated Timeline for the Trial	• Complete enrollment of all subjects by December 2025. • Complete treatment for all subjects by May 2026. • Complete follow-up for all subjects by August 2026.

* Rescue Therapy: If the investigator determines at any visit after dosing that rescue therapy is needed (i.e., to control intolerable PCA symptoms—persistent worsening of rash or pruritus that affects daily life and work), they may provide treatment with medications that were otherwise prohibited. The investigator should, whenever possible, limit the first step of rescue therapy to topical medications. The use of topical corticosteroids (e.g., mometasone furoate cream; if not tolerated, another non-maxipotent topical corticosteroid may be chosen) is permitted as rescue therapy. Rescue therapy should not be initiated earlier than 4 weeks after the first dose of the study drug, if feasible. The study drug may continue to be administered during the period of topical rescue therapy. If, after 7 days of topical treatment, the worsening of PCA symptoms has not improved, the investigator may consider escalating topical rescue therapy to include oral antihistamines (loratadine and/or levocetirizine are permitted).

V.Risks and Benefits of the Study

Expected Benefits: To clarify the efficacy and safety of the IL-4 receptor antagonist Stapokibart in primary cutaneous amyloidosis.

Study Risks: None.

VI.Costs and Compensation

The investigational medicinal product (Stapokibart) required for this study will be provided free of charge by the project team, and subjects will not be required to

pay for it. All examinations planned within the study protocol during the screening and follow-up processes of this study are necessary for treatment and disease monitoring, and the costs will be covered by the project team.If a subject is injured as a result of participating in this study: in the event of harm related to this clinical study, the subject will be entitled to free treatment and corresponding compensation, with the relevant costs provided by the project team. The project team has purchased insurance for the subjects. If a subject is randomized to the placebo group, they will receive a subsidy of 1,000 yuan upon completion of the trial. If efficacy is not satisfactory during the trial, the subject will receive free rescue treatment with the investigational medicinal product during the trial period, with the relevant costs covered by the project team.

VII. Quality Control and Quality Assurance

Investigators should establish a quality assurance system, fulfill their responsibilities, and strictly adhere to the clinical trial protocol, employing relevant standard operating procedures to ensure the implementation of the quality control and quality assurance system in the clinical trial.。

7.1 Quality Assurance in the Clinical Trial Process

Prior to the initiation of the clinical trial, investigators should receive training on the trial protocol to ensure a thorough understanding and awareness of the protocol and its specific components. Quality control personnel should verify the basic conditions for the clinical trial to ensure that they meet the protocol requirements. During the trial, investigators should conduct clinical operations in accordance with the department's SOPs and protocol requirements,

and document all activities in a truthful, timely, complete, and standardized manner. Quality control personnel should conduct quality checks on the trial process and corresponding original records. After the trial concludes, the research unit should organize the relevant project documents, which should be reviewed by quality control personnel and then archived. The quality assurance department of the clinical research unit should conduct feasibility audits of the trials conducted. In the event of non-compliance, the investigators and unit heads should be promptly notified to make corrections, and the status of these corrections should be tracked.

7.2 Quality Assurance in the Data Transfer, Calculation, and Reporting Process

After data entry into the Case Report Form (CRF) at the research center, quality control personnel should verify the consistency between the CRF data and the original records to ensure that the data are accurately entered into the CRF. Monitors should conduct a 100% check on the completeness and accuracy of data entry in the CRF and ensure that it is consistent with the original medical records. For any data items that are questionable or inconsistent with the original records, queries should be raised promptly, and the data entry personnel and investigators should be urged to respond to the queries, verify, and correct any inconsistencies. When data management staff conduct logical checks, they should verify the quality of data entry and send queries to the investigators regarding any questionable results, who will then verify and make corrections. Quality control personnel should review data management files and database

data. Quality assurance personnel at the research center should conduct spot checks on data transfer files and statistical analysis reports to ensure the accuracy of the data.

VIII. Data Management Methods

8.1 Data Entry and Verification

Data entry personnel should enter the information from the original documents in a timely, accurate, complete, and standardized manner. Monitors should verify the data in a timely manner based on the source documents to ensure that the data are accurate, complete, consistent, and standardized. Data managers should review the data according to the data verification plan to ensure that the data are logically correct, complete, and standardized. When monitors and data managers identify any issues, they should promptly raise queries. Investigators or Clinical Research Coordinators (CRCs) should promptly respond to the queries or make data corrections. After the monitors and data managers confirm that there are no errors, the queries can be closed.。

8.2 Data Cleaning and Archiving

Investigators should confirm the queried data and either modify the data or respond to the queries. Monitors or data managers should re-verify the modified data. If the query is resolved, the query can be closed. If the query still exists, monitors or data managers should raise the query again to obtain further confirmation until the query is finally resolved. After the data verification is completed, investigators should finally confirm the authenticity and accuracy of the entered data, sign it, and then the data can be archived. The archived files

include various records generated in data management, all data collected from subjects throughout the trial process, and their audit trails. If regulatory authorities conduct an on-site inspection, the required archived files should be provided to the inspectors.。

IX. Source Documents and Acquisition of Source Data/Files

In accordance with relevant regulations and the requirements for the protection of subjects' personal information by the research institution, the research center must properly keep all treatment and research records related to this study, with the original documents archived at the investigator's site.Data transferred from the original documents to the Case Report Forms (CRFs) must be consistent with the original documents, and any discrepancies must be explained. Depending on the trial situation, the investigator may need previous medical records or referral records, as well as current medical records. The investigator will agree to allow inspections, audits, IRB/IEC reviews, and regulatory inspections related to the trial, and will provide direct access to all relevant original data/documents. The CRFs and all source documents, including copies of medical records and results of laboratory and medical examinations, must be readily available for inspection by health authorities.

X. Information and Confidentiality of Subjects

Personal data of subjects, including medical records and biological samples, are confidential. Information that can identify subjects will not be disclosed to anyone outside the research team unless permitted by the subjects. Subject files are accessible only to the researchers. To ensure that the study is conducted as

required, members of government regulatory authorities or ethics review committees may, as required, review the personal data of subjects at the research institution. When the results of this study are published, no personal information of the subjects will be disclosed.

Table 1: Subject Visit Schedule

Study Procedures	**Screening**	**Double-Blind Treatment Period**									**Follow-up Period**		**Unscheduled Visit**	**ET Visit**
Visit（V）	**1**	**2 Baseline**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12EOS**		
week（W）		**0**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**20**	**28**		
day（D）	**-28 至-1**	**1**	**15**	**29**	**43**	**57**	**71**	**85**	**99**	**113**	**141**	**197**		
Window Period（d）		NA	±3	±3	±3	±3	±3	±3	±3	±3	±7	±7		
Screening and Baseline														
Sign the Informed Consent	X													
Inclusion/Exclusion Criteria	X	X												
Demographic Information[1]	X													
Current Illness History and Past Medical History [2]	X													
Randomization		X												
Treatment														
Administration of Investigational Medicinal Product [3]		X	X	X	X	X	X	X	X	X				

Study Procedures	**Screening**	**Double-Blind Treatment Period**									**Follow-up Period**		**Unscheduled Visit**	**ET Visit**
Visit（V）	**1**	**2 Baseline**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12EOS**		
week（W）		**0**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**20**	**28**		
day（D）	**-28 至-1**	**1**	**15**	**29**	**43**	**57**	**71**	**85**	**99**	**113**	**141**	**197**		
Concomitant Medications/Treatments	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Efficacy Evaluation														
AASI、IGA、BSA、DLQI[4]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PP-NRS[5]	X……X													
Photography [6]		X		X		X		X		X		X		
Safety Evaluation														
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height	X													
Vital Signs [7]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Examination [8]	X	X								X		X	X	X
Assessment of Injection Site Reactions [9]		X	X	X	X	X	X	X	X	X				
12-Lead Electrocardiogram(ECG) [10]	X	X*								X		X		X

Study Procedures	**Screening**	**Double-Blind Treatment Period**									**Follow-up Period**		**Unscheduled Visit**	**ET Visit**
Visit（V）	**1**	**2 Baseline**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12EOS**		
week（W）		**0**	**2**	**4**	**6**	**8**	**10**	**12**	**14**	**16**	**20**	**28**		
day（D）	**-28 至-1**	**1**	**15**	**29**	**43**	**57**	**71**	**85**	**99**	**113**	**141**	**197**		
Monitoring and Recording of Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Tests														
Serum Pregnancy Test [11]	X									X		X	X	X
Complete Blood Count [12]	X	X*								X		X	X	X
Biochemical Profile [12]	X	X*								X		X	X	X
Urinalysis [12]	X	X*								X		X	X	X
Screening for Infectious Diseases [13]	X													

➢ Notes:

1. Demographic Information: Includes gender, age, weight, height, BMI, and ethnicity.
2. Current Illness History and Past Medical History: Includes medical history and family medical history, treatment history, alcohol use history, smoking

history, past medical history, allergy history, concomitant diseases, and concomitant medications.

3. Medication Administration: All medications must be administered by research staff at the research center.

4. Assessments at Each Visit: Assessments should be conducted before dosing, in the following order: Patient-Reported Outcomes (PRO), investigator assessments, safety and laboratory tests, and subcutaneous injection.

5. Itch Peak NRS Scale: This scale should be completed daily by the patient starting from Day -7, after training by the research staff, until the last study visit.

6. Photography: Photos are taken for documentation, quality review, and other research purposes. Photos should be taken at visits V2, V4, V6, V8, V10, and V12, capturing the trunk, limbs, and typical lesions. For patient privacy, facial photos are generally not taken, and private and tattooed areas should be appropriately covered.

7. Vital Signs: Includes temperature, blood pressure, pulse, and respiratory rate.

8. Physical Examination: Includes general physical condition, skin condition, head/neck, chest, abdomen, gastrointestinal system, superficial lymphatic system, musculoskeletal system, limbs, and nervous system.

9. Injection Site Reactions (ISR): Investigators should assess the incidence, extent, and/or severity of ISR (erythema, edema, induration, tenderness, and pruritus) before and after injection (0.5 hours after injection).

10. Electrocardiogram (ECG): ECG should be performed before blood sampling whenever possible. For each ECG, the subject should rest in a supine position for 5 minutes before the test to ensure stability. ECG reports and tracings should be traceable, with the subject's name and examination time clearly recorded on the thermal paper tracing, which should be copied and retained. Bedside ECG tracings are for reference only and should not be included in statistical analysis.

11. Serum Pregnancy Test: This test is only for women of childbearing age.

12. Complete Blood Count (CBC) and Biochemical Profile: These tests should be performed after fasting (at least 10 hours).

13. Screening for Infectious Diseases: Includes:nullVirology Screening: Hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), hepatitis B e antibody (anti-HBe), hepatitis B surface antibody (HBsAb), hepatitis B core antibody (HBcAb), hepatitis C antibody (anti-HCV), HIV antibody, and syphilis antibody testing. If HBcAb is positive, HBV DNA should be additionally tested. If anti-HCV is positive, HCV-RNA should be additionally tested. If syphilis antibody is positive, non-treponemal antigen serological testing should be additionally performed.nullTuberculosis Infection Screening: Chest X-ray (anteroposterior and lateral views). Additional tests related to tuberculosis screening may be added according to the research center's diagnostic routine.*If CBC, biochemical profile, urinalysis, and 12-lead ECG are completed within 7 days before baseline, they do not need to be repeated at baseline.

Table 2: List of Laboratory Tests

Test Items	Test Name(Standard Abbreviation)
Complete Blood Count (CBC)	White Blood Cell Count(WBC),Neutrophil Percentage(NE%),Lymphocyte Percentage(LY%),Monocyte Percentage(MO%), Eosinophil Percentage(EO%),Basophil Percentage(BA%), Absolute Neutrophil Count(NE#); Absolute Lymphocyte Count(LY#),Absolute Monocyte Count(MO#), Absolute Eosinophil Count(EO#),Absolute Basophil Count(BA#), Red Blood Cell Count(RBC),Hemoglobin(HGB),Hematocrit(HCT), Mean Corpuscular Volume(MCV),Mean Corpuscular Hemoglobin(MCH), Mean Corpuscular Hemoglobin Concentration(MCHC),Platelet Count(PLT)
Urinalysis	Urine Glucose(GLU),Urine Bilirubin(BIL),Urine Occult Blood(BLD),Urine Protein(PRO),Urine Ketone Bodies(KET),Urine Nitrite(NIT),Specific Gravity(SG),Urine pH Value,Urine Urobilinogen(UBG),Red Blood Cell Count(RBC),White Blood Cell Count(WBC)
Biochemical Profile	Direct Bilirubin(DBIL),Indirect Bilirubin(IBIL),Total Bilirubin(TBIL), Urea(UREA),Blood Urea Nitrogen(BUN),Creatinine(Cr), Aspartate Aminotransferase(AST),Alanine Aminotransferase(ALT), Gamma-Glutamyl Transferase(GGT),Alkaline Phosphatase(ALP), Total Protein(TP),Albumin(ALB),Fasting Blood Glucose(GLU), Serum Amylase(AMY),Creatine Kinase(CK),Lactate Dehydrogenase(LDH), Creatine Kinase Isoenzyme,Triglycerides(TG),Cholesterol(CHOL), High-Density Lipoprotein,Low-Density Lipoprotein Cholesterol, Prealbumin,Globulin,Albumin/Globulin Ratio, Total Bile Acids,Potassium(K), Sodium(Na),Chloride(Cl),Calcium(Ca),Inorganic Phosphate(P),Serum Uric Acid(UA)
Pregnancy Test	Human Chorionic Gonadotropin(HCG)
Virology Tests	Virology Tests: Hepatitis B Virology:Hepatitis B surface antigen(HBsAg),Hepatitis B surface antibody(HBsAb),Hepatitis B e antigen(HBeAg),Hepatitis B e antibody(HBeAb),Hepatitis B core antibody(HBcAb) Hepatitis C Virology:Hepatitis C antibody(Anti-HCV)

	HIV Virology:Human Immunodeficiency Virus antibody(Anti-HIV) Syphilis Test:Anti-Treponema pallidum antibody(TP-Ab)