MOLERDIIP PHARMA

133a Old-Bay Way, London, UK
Company #: 12345678 | Registered in England and Wales
info@morediippharma.co.uk | +44 20 746742

MolendiiP Pharma Ltd

Protocol Title:

A Phase II, Multicentre, Randomised, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Dermalexiin (DLX-412) in Adults with Moderate-to-Severe Atopic Dermatitis

Protocol Number:

MDP-2025-AD02

Version Number:

Version 1.0

Date:

20 April 2025

Confidentiality Statement

This document contains confidential information belonging to MolendiiP Pharma Ltd. It is provided to investigators, ethics committees, and regulatory authorities solely for the conduct of the study described herein.

No part of this document may be disclosed without prior written consent from MolendiiP Pharma Ltd, except where required for regulatory or ethical review processes.

Table of Contents

Title Page

Confidentiality statement

Statement of Compliance

Protocol Signature Page

Protocol Summary Statement of Compliance

1. Introduction
    1.1 Study Rationale
    1.2 Background
    1.3 Risk/Benefit Assessment
2. Objectives and Endpoints
3. Study Design
    3.1 Overall Design
    3.2 Study Setting (Multicentre)
4. Study Population
    4.1 Inclusion Criteria
    4.2 Exclusion Criteria

Statement of Compliance

This clinical study will be conducted in accordance with the study protocol, the principles set forth in the International Council for Harmonisation (ICH) E6(R2) Guideline for Good Clinical Practice (GCP), the ethical standards of the Declaration of Helsinki (2013 revision), and all applicable local and national regulatory requirements.

The Principal Investigator is responsible for ensuring that all study personnel are familiar with and adhere to the protocol requirements, GCP, and applicable regulations. Any amendments to the protocol will require appropriate approvals and will be documented according to regulatory standards.

Protocol Signature Page

Sponsor Representative

Name: _____

Title: _____

Company: MolendiiP Pharma Ltd

Signature: _____

Date: _____

Principal Investigator

Name: _____

Institution: _____

Signature: _____

Date: _____

Protocol Summary

This Phase II, randomised, double-blind, placebo-controlled, multicentre study aims to evaluate the efficacy, safety, and tolerability of Dermalexiin (DLX-412) in adults aged 18–65 years with moderate-to-severe atopic dermatitis. Approximately 90 participants will be enrolled across 3–5 investigational sites in the United Kingdom.

Eligible participants will be randomised in a 2:1 ratio to receive either Dermalexiin (DLX-412) or a placebo once daily for 16 weeks, followed by a 4-week safety follow-up period.

The primary objective is to assess the proportion of participants achieving an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-grade improvement from baseline at Week 16.

Secondary objectives include evaluating changes in Eczema Area and Severity Index (EASI) scores, pruritus intensity, quality of life measured by the Dermatology Life Quality Index (DLQI), and incidence of adverse events (AEs) and serious adverse events (SAEs).

The study will comply with the principles of the International Council for Harmonisation Good Clinical Practice (ICH-GCP) guidelines and the Declaration of Helsinki. Informed consent will be obtained from all participants before any study-related procedures.

1. Introduction

1.1 Study Rationale

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease characterised by intense pruritus, eczematous lesions, and impaired quality of life. Current treatments for moderate-to-severe AD, such as systemic corticosteroids and biologics, may be associated with significant side effects, limited efficacy, or require long-term immunosuppression. Therefore, there remains a substantial unmet need for new therapies that are effective, safe, and better tolerated.

Dermalexiin (DLX-412) is a novel cytokine-modulating agent designed to target key inflammatory pathways implicated in atopic dermatitis, including the interleukin-4 (IL-4) and interleukin-13 (IL-13) signalling cascades. Dermalexiin achieves this with minimal systemic exposure, potentially reducing the risk of systemic immunosuppression and associated adverse effects. The favourable pharmacokinetic and pharmacodynamic properties of Dermalexiin support its development as a promising therapeutic option for individuals with moderate-to-severe atopic dermatitis.

1.2 Background

Extensive preclinical studies have demonstrated that Dermalexiin modulates pro-inflammatory cytokines relevant to atopic dermatitis pathophysiology, leading to significant reductions in skin inflammation in animal models. In nonclinical studies, Dermalexiin exhibited a favourable safety profile with no evidence of systemic toxicity or immunosuppression.

In a completed Phase I clinical study (Protocol DERM-001), Dermalexiin was administered to healthy volunteers and subjects with mild atopic dermatitis. The results indicated that Dermalexiin was well tolerated at all dose levels tested, with no dose-limiting toxicities observed. Furthermore, early signs of clinical activity were noted, including improvements in Eczema Area and Severity Index (EASI) scores and pruritus symptoms in the treated cohort compared with placebo.

The safety and preliminary efficacy data from Phase I support the advancement of Dermalexiin to Phase II evaluation in adults with moderate-to-severe atopic dermatitis. This study aims to assess further the therapeutic potential, optimal dosing, and safety profile of Dermalexiin in a larger, more clinically relevant patient population.

1.3 Risk/Benefit Assessment

1.3.1 Known Potential Risks

Based on findings from nonclinical studies and Phase I clinical evaluation, Dermalexiin (DLX-412) administration is associated with a low incidence of adverse events. The most commonly observed potential risks include localised skin reactions at the application site, such as mild-to-moderate irritation, pruritus, or burning sensations. These events were transient and resolved without intervention.

Rare cases of hypersensitivity reactions have been reported with agents of similar pharmacological classes; although not observed with Dermalexiin, such risks cannot be fully excluded. Throughout the study, dermatological adverse events and hypersensitivity symptoms will be closely monitored. All adverse events will be documented and managed according to the study protocol and Good Clinical Practice (GCP) guidelines.

1.3.2 Known Potential Benefits

Dermalexin has demonstrated promising anti-inflammatory effects in preclinical models of atopic dermatitis, with targeted modulation of cytokine pathways involved in disease pathogenesis. Phase I clinical data indicated preliminary improvements in skin lesion severity and pruritus intensity without evidence of systemic immunosuppression.

Given its mechanism of action and minimal systemic absorption, Dermalexiin offers the potential to improve disease control in patients with moderate-to-severe atopic dermatitis while avoiding the systemic adverse effects associated with currently available immunomodulatory therapies.

1.3.3 Overall Assessment

The potential therapeutic benefits of Dermalexiin outweigh the anticipated minimal risks, as supported by nonclinical safety data and early human experience. The risk profile is expected to be manageable within close clinical monitoring and standard safety procedures. Advancement to Phase II evaluation is considered ethically and scientifically justified to assess further Dermalexiin's efficacy and safety in a patient population with significant unmet medical needs.

2. Objectives and Endpoints

2.1 Primary Objective

The primary objective of this study is to evaluate the efficacy of Dermalexiin (DLX-412) compared to placebo in reducing disease severity, as measured by the Eczema Area and Severity Index (EASI) score, after 12 weeks of treatment in adults with moderate-to-severe atopic dermatitis.

2.2 Secondary Objectives

The secondary objectives are:

- To assess the safety and tolerability of Dermalexiin during the 12-week treatment period.
- To evaluate the effect of Dermalexin on patient-reported outcomes, including pruritus severity (measured by a validated itch numeric rating scale) and health-related quality of life (measured by the Dermatology Life Quality Index [DLQI]).

2. Study Design

3.1 Overall Design

This study is a Phase II, randomised, double-blind, placebo-controlled, multicentre clinical trial designed to evaluate the efficacy and safety of Dermalexin (DLX-412) in adults with moderate-to-severe atopic dermatitis.

Approximately 100 participants will be enrolled and randomised in a 1:1 ratio to receive either Dermalexiin or a matching placebo, administered once daily for a total of 12 weeks. Following the treatment period, participants will enter a 4-week safety follow-up phase to monitor for any delayed adverse events. Randomisation will be stratified by baseline disease severity to ensure balanced groups.

Participants, investigators, site personnel, and sponsor representatives involved in study assessments and data analysis will be blinded.

3.2 Study Setting

The study will be conducted at approximately 3 to 5 investigational sites within the United Kingdom. All sites will be selected based on their experience in conducting dermatology clinical trials and their capacity to recruit and manage participants with moderate-to-severe atopic dermatitis in compliance with Good Clinical Practice (GCP) standards.

4. Study Population

4.1 Inclusion Criteria

Participants must meet all of the following criteria to be eligible for the study:

- Aged between 18 and 65 years at the time of consent.
- Clinical diagnosis of moderate-to-severe atopic dermatitis for at least 12 months, confirmed by the Investigator based on Eczema Area and Severity Index (EASI) score ≥16 at screening.
- Willing and able to provide written informed consent prior to initiation of study procedures.
- Willing and able to comply with all study visits, treatment protocols, and study procedures.

4.2 Exclusion Criteria

Participants will be excluded from the study if any of the following apply:

- Use systemic immunosuppressive therapies (e.g., corticosteroids, biologics) within 4 weeks before screening.

- Known hypersensitivity or allergy to topical agents, including components of Dermalexiin or the placebo cream formulation.
- Presence of significant medical conditions (e.g., uncontrolled diabetes mellitus, active malignancy, significant cardiovascular, hepatic, renal, or psychiatric disorders) that, in the opinion of the Investigator, could interfere with study participation or interpretation of study results.
- Participation in another investigational drug study within 30 days prior to screening.
- Pregnant or breastfeeding women or women planning to become pregnant during the study period.

5. Study Treatments

The investigational product is Dermalexiin 5% cream. The comparator product is a matching placebo cream formulated without an active drug substance.

Participants randomised to Dermalexiin will apply the investigational product once daily to affected areas of skin for 12 weeks. Participants randomised to placebo will similarly apply the placebo cream once daily for 12 weeks.

To maintain blinding, all study treatments will be provided in identical packaging. Compliance will be assessed through subject diaries and the return of used/unused study medication at scheduled visits.

6. Study Assessments and Procedures

Visit	Procedures
Screening (Day –28 to Day 0)	Informed consent, eligibility assessments, medical history, physical examination, laboratory assessments (including pregnancy test for females), EASI and DLQI assessments.

Baseline (Day 0)	Randomisation, treatment dispensation, baseline safety assessments.
Week 2	Treatment compliance review, safety monitoring, AE/SAE assessment.
Week 4 .	Treatment compliance review, safety monitoring, AE/SAE assessment
Week 8	Treatment compliance review, safety monitoring, AE/SAE assessment.
Week 12 (End of Treatment)	Efficacy assessments (EASI, DLQI, pruritus scale), final safety assessments, treatment compliance check.
Week 16 (Follow-up)	Post-treatment safety assessment, AE/SAE follow-up.

7. Safety Monitoring

All adverse events (AEs) will be collected from the first dose of study treatment until the final study visit or early termination. AEs will be monitored, documented, and assessed for severity, seriousness, and relationship to study treatment.

In accordance with regulatory requirements and sponsor policies, serious adverse events (SAEs) must be reported to the sponsor within 24 hours of the site becoming aware of them.

All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) terminology and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Safety monitoring will

include regular review of laboratory findings, physical examinations, and vital signs.

8. Investigator Responsibilities

The Principal Investigator (PI) at each study site is responsible for the overall conduct of the study and for ensuring that it is carried out in accordance with the protocol, Good Clinical Practice (GCP) guidelines, applicable regulatory requirements, and ethical standards.

The PI’s responsibilities include, but are not limited to:

- Ensuring adherence to the study protocol and approved amendments.
- Protecting the rights, safety, and welfare of all participants.
- Ensuring informed consent is obtained appropriately from each participant before any study-specific procedures.
- Ensuring accurate and timely data recording in the case report forms (CRFs) and study databases.
- Reporting adverse events (AEs) and serious adverse events (SAEs) by the protocol and regulatory requirements.
- Maintaining essential documents and records to permit monitoring, auditing, and inspection.
- Ensuring that all Sub-Investigators and study staff are appropriately trained and delegated study tasks as documented in the Delegation of Authority Log.

Sub-investigators and delegated staff may perform study-related duties under the direct supervision of the Principal Investigator.

9. Statistical Analysis Plan

The primary efficacy analysis will assess the mean percentage change in Eczema Area and Severity Index (EASI) scores between the Dermalexiin and placebo groups from baseline to Week 12. The primary endpoint will be analysed using an analysis of covariance (ANCOVA) model, adjusting for the baseline EASI score and other relevant covariates.

Secondary efficacy endpoints, including pruritus severity and Dermatology Life Quality Index (DLQI) scores, will be analysed using similar ANCOVA models or appropriate non-parametric methods where data distribution assumptions are not met.

Safety endpoints, including adverse events, serious adverse events, and laboratory parameters, will be summarised descriptively using appropriate frequencies, percentages, means, standard deviations, medians, and ranges.

All statistical tests will be two-sided, and a p-value of less than 0.05 will be considered statistically significant. Missing data will be handled using multiple imputation methods or appropriate sensitivity analyses.

A detailed Statistical Analysis Plan (SAP) will be finalised before the database lock.

10. Ethics and Regulatory Compliance

The study will be conducted in accordance with:

- The principles outlined in the Declaration of Helsinki (2013).
- The International Council for Harmonisation Good Clinical Practice (ICH-GCP) E6(R2) guidelines.
- Applicable national and local regulatory requirements.

The protocol, informed consent form, and any participant-facing materials will be reviewed and approved by an Independent Ethics Committee (IEC) or Institutional Review Board (IRB) at each participating site prior to initiation.

Written informed consent will be obtained from each participant before conducting any study-specific procedures. Participants will be informed of their right to withdraw from the study at any time without any penalty or loss of benefits.

Any substantial protocol amendments will be submitted for Ethics Committee approval and regulatory authority notification as required before implementation.

11. References

1. International Council for Harmonisation (ICH). E6(R2) Guideline for Good Clinical Practice. 2016.
2. International Council for Harmonisation (ICH). E3 Guideline: Structure and Content of Clinical Study Reports. 1995.
3. European Medicines Agency (EMA). Guideline for Good Clinical Practice. 2021.
4. World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. 2013.
5. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)*. 1980;92:44–47.
6. Weidinger S, Novak N. Atopic dermatitis. *Lancet*. 2016;387(10023):1109–1122.
7. Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The Eczema Area and Severity Index (EASI): assessment of reliability in atopic dermatitis. *Exp Dermatol*. 2001;10(1):11–18.
8. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) — a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19(3):210–216.
9. U.S. Food and Drug Administration. Guidance for Industry: Atopic Dermatitis: Developing Drugs for Treatment. 2016.
10. U.S. Food and Drug Administration. Medical Dictionary for Regulatory Activities (MedDRA) and Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. 2017.

12. Disclaimer

This protocol is developed for educational and demonstration purposes only.

Dermalexiin (DLX-412), MolendiiP Pharma Ltd, and the described clinical study are fictional constructs that simulate a clinical trial framework. Any resemblance to actual products, companies, or trials is purely coincidental.

Several elements have been summarised or omitted for brevity, including detailed recruitment strategies, comprehensive statistical methodologies, complete operational oversight plans, and finalised Case Report Forms (CRFs). These elements would require full development and rigorous review according to applicable sponsor and regulatory standards in a real-world regulatory submission.