CLINICAL TRIAL PROTOCOL

Trial Title:	The ADRO Trial: An Adaptive, 2-Part, Phase 2 Clinical Trial Investigating the Safety and Efficacy of ADX-629 in Adults with Atopic Dermatitis
Protocol Number:	ADX-629-ATD-001
Clinical Trial Phase:	2
Sponsor:	Aldeyra Therapeutics, Inc. 131 Hartwell Avenue, Suite 320 Lexington, MA 02421, United States of America
IND Number:	[redacted]
Protocol Version & Date	Version 2.0, 11 October2023

This trial will be conducted in accordance with the ethical principles that originate from the Declaration of Helsinki and that are consistent with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines on Good Clinical Practice (GCP) and regulatory requirements as applicable.

CONFIDENTIAL

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1 CLINICAL TRIAL PROTOCOL APPROVAL

PROTOCOL TITLE: The ADRO Trial: An Adaptive, 2-Part, Phase 2 Clinical Trial Investigating the Safety and Efficacy of ADX-629 in Adults with Atopic Dermatitis

PROTOCOL NUMBER: ADX-629-ATD-001

The undersigned have reviewed the format and content of and have approved the Clinical Trial Protocol. The undersigned agrees that the trial will be carried out in compliance with the Clinical Trial Protocol, GCP, Declaration of Helsinki (with amendments), and local legal and regulatory requirements.

Any modifications of the Clinical Trial Protocol must be agreed upon by the Sponsor and the Investigator and must be documented in writing.

Sponsor Approval:

[redacted]

2 INVESTIGATOR STATEMENT

PROTOCOL TITLE: The ADRO Trial: An Adaptive, 2-Part, Phase 2 Clinical Trial Investigating the Safety and Efficacy of ADX-629 in Adults with Atopic Dermatitis

I understand that all information concerning ADX-629 in connection with this clinical trial and not previously published is confidential. This confidential information includes the Investigator's Brochure, Clinical Trial Protocol, case report form, clinical methodology, and basic scientific data.

I will not initiate this clinical trial without approval from the IRB/ REB, and I understand that any changes in the protocol must be approved in writing by Aldeyra Therapeutics, Inc., and the IRB/REB before they can be implemented, except when necessary to eliminate immediate hazards to the subjects.

I will use only the informed consent form approved by Aldeyra Therapeutics, Inc., and by my IRB/REB and will fulfil all responsibilities for submitting pertinent information to the IRB/REB responsible for this clinical trial.

By my signature below, I attest that I have read, understand, and agree to abide by all the conditions, instructions, and restrictions contained in Protocol Number ADX-629-ATD-001, and will conduct the clinical trial in accordance with the ICH-GCP guidelines and applicable regulatory requirements.

_____
Site Name

_____
Site Address

_____
Investigator's Printed Name

_____ _____
Investigator's Signature Date

3 PROTOCOL SYNOPSIS

Name of Sponsor: Aldeyra Therapeutics, Inc.

Protocol Number: ADX-629-ATD-001

Title of the Trial: The ADRO Trial: An Adaptive, 2-Part, Phase 2 Clinical Trial Investigating the Safety and Efficacy of ADX-629 in Adults with Atopic Dermatitis

Investigational Product: ADX-629 (250 mg) administered twice daily (BID) for 90 days

Number of Subjects: Approximately 50 Adult Subjects

Number of Sites: Approximately 15 sites in the United States of America (USA)

Objectives and Endpoints

Primary Objective: Evaluate the safety of ADX-629 administered alone and in addition to standard-of-care in adults with atopic dermatitis

Secondary Objective: Evaluate the activity and efficacy of ADX-629 administered alone and in addition to standard-of-care in adults with atopic dermatitis

Primary Endpoint: Incidence and severity of treatment-emergent adverse events and serious adverse events

Key Secondary Endpoint: Proportion of subjects with an IGA score of 0 or 1 at Day 90

Other Secondary Efficacy Endpoints:

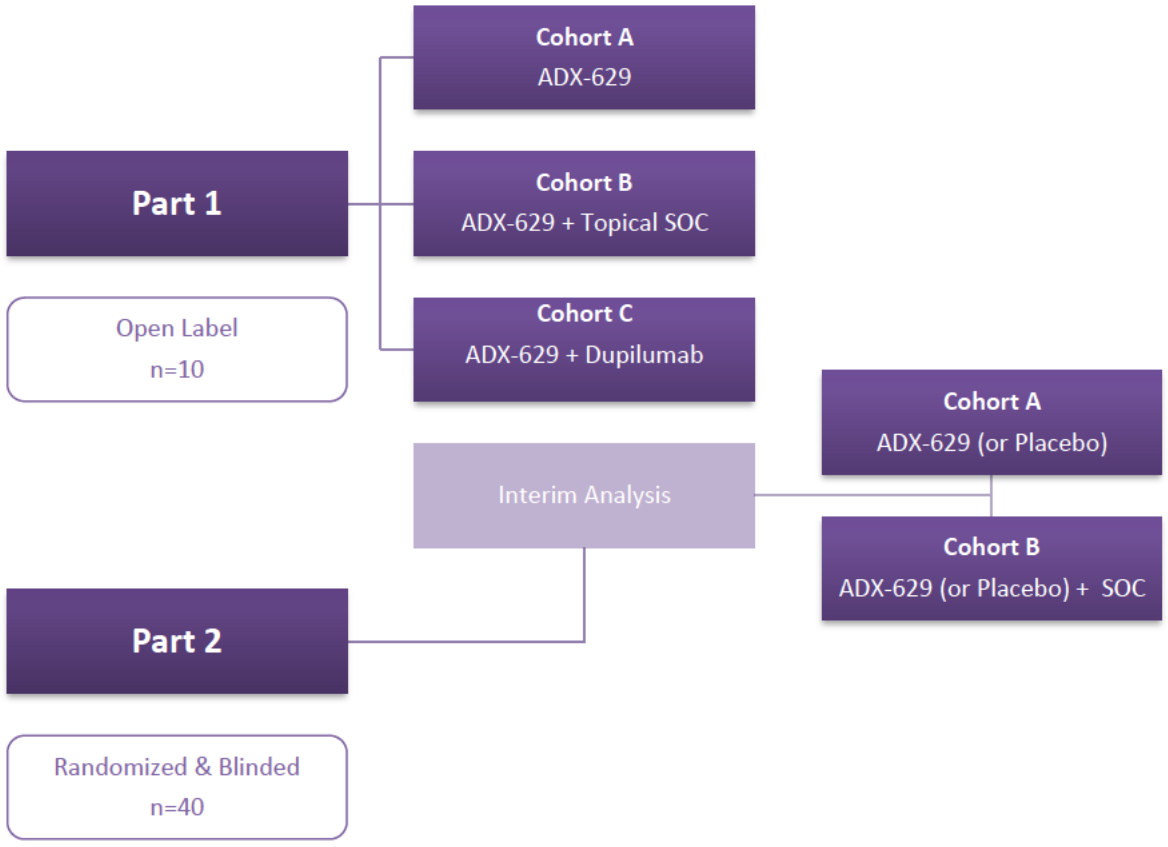
- Proportion of subjects with an IGA score of 0 or 1 and ≥2-grade improvement from Day 1
- Proportion of subjects achieving a ≥50%, 75% and 90% improvement in the EASI
- Proportion of subjects achieving ≥4 points improvement in the Peak Pruritus NRS
- Time to AD flare-up (days), as defined by use of rescue medication
- Proportion of subjects with a 4-point or more improvement in POEM total score at Day 90
- Percent change in HDL-C, LDL-C, and triglycerides from Baseline
- Change from Baseline in IGA Score, EASI Score, HAM-D score, and BAI Score.

Trial Design and Plan:

This Phase 2, multicenter, 2-part clinical trial is designed to evaluate the safety and efficacy of ADX-629 alone and in combination with standard-of-care in subjects ≥ 18 years of age with atopic dermatitis. The trial will enroll approximately 50 adults with mild, moderate, and severe atopic dermatitis, as defined by the inclusion and exclusion criteria. Trial drug will be administered orally, every 12 hours, to eligible subjects for 90 days. Subjects will be enrolled in cohorts based on their standard-of-care treatment (SOC) for AD at baseline. Subjects that are not receiving SOC treatment are assigned to Cohort A and will receive trial drug only (i.e., monotherapy). Subjects receiving SOC AD therapy (i.e., topical therapy or dupilumab) will be assigned to another cohort and will receive trial drug and SOC. The trial will not provide SOC treatment and therefore, must be obtained independently by the subject.

The trial is divided into 2 parts; the first part of the trial (Part 1) is open-label, and the second part (Part 2) is randomized, double-blind, and placebo controlled. In Part 1, approximately 10 subjects will receive open-label ADX-629 twice daily for 90 days alone or in combination with SOC treatment for AD. In Part 2, approximately 40 subjects will be randomized to receive either ADX-629 or matching placebo twice daily for 90 days.

Figure 1 - Schematic of Trial Design:



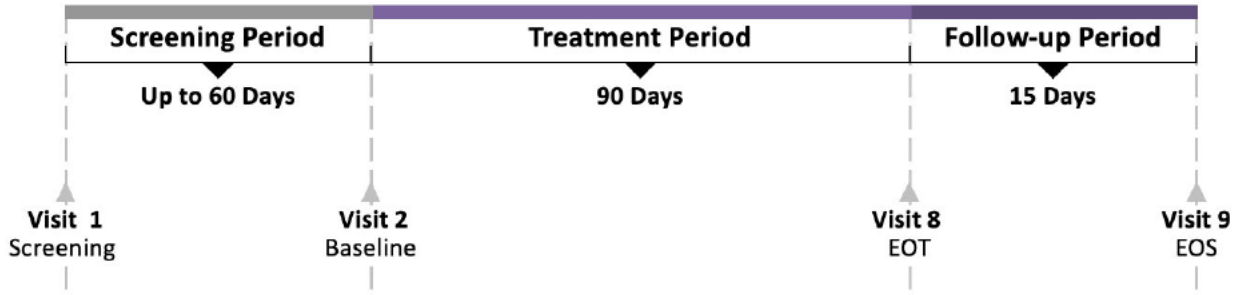
a) An interim analysis may be performed after all subjects complete the treatment period in Part 1.

b) The trial design in Part 2 may be adapted based on the data from Part 1.

The trial duration for each subject is approximately 5 months and involves 9 trial visits. The trial is divided into 3 periods: Screening, Treatment, and Follow-up. The screening period ranges from 3 days to 60 days to and allow for adequate washout of prohibited concomitant medications, as indicated in Table 3. Prior to any trial procedure/assessment, written informed consent will be obtained. Eligibility will be confirmed during screening and prior to dosing at Visit 2 (Day 1). Trial-related assessments and procedures will be performed at the timepoints indicated in the Schedule of Assessments (Table 1)The use of emollients must be stable in the 5 days prior to Visit 2. Eligible subjects will receive the first dose of trial drug at Visit 2 (Day 1) and complete trial visits every 15 days during the 90-day treatment period. Trial can be performed on-site, remotely (i.e., phone call, telehealth visit) or at home. After the treatment period, subjects will undergo a follow-up period and complete an end of trial visit approximately 15 days from the last dose of trial drug. Unscheduled visits or assessments may be performed if clinically warranted, in the opinion by the Investigator. Subjects who require rescue medication for an AD flare-up during the treatment period will be asked to discontinue trial drug and complete remaining scheduled trial visits. A summary of the trial assessment schedule is provided in Table 1.

The trial periods are illustrated in Figure 2.

Figure 2- Schematic of Trial Periods:



Part 1

Part 1 of the trial will include at least 10 subjects with mild, moderate, or severe AD whose disease is not adequately controlled with current standard-of-care treatment. The purpose of Part 1 is to evaluate the safety of ADX-629 and confirm the target patient population and background therapy selection prior to expansion into Part 2. All subjects in Part 1 will receive open-label ADX-629 for 90 days either alone or in combination with SOC treatment. Subjects will be enrolled in either Cohort A, Cohort B, or Cohort C based on their SOC treatment at baseline. Subjects that are not receiving standard-of-care therapy will be assigned to Cohort A, subjects on a stable topical therapy will be assigned to Cohort B, and subjects on a stable dose of dupilumab will be assigned to Cohort C. Subjects in Cohort B must be able to discontinue topical therapy within 14 days of taking trial drug or by Visit 3 (Day 15) or will be discontinued from trial drug. Subjects in Cohorts C must be willing and able to continue background therapy throughout the duration of the clinical trial. The cohorts for Part 1 are described in Figure 3.

Part 2

Part 2 of the trial will be a randomized, double-blind, and placebo controlled and will include at least 40 subjects with AD. Subjects will be assigned to cohorts based on their standard-of-care therapy at baseline. Subjects will be randomized on Day 1 in a 1:1 or 2:1 ratio to receive ADX-629 (250 mg) or matching placebo for 90 days. Investigators, subjects, and the trial team will be blinded to treatment allocation. The purpose of Part 2 is to compare ADX-629 to placebo and standard-of-care treatment(s). The trial design will be adapted after the review of the safety and efficacy data from Part 1 and before any subjects are randomized into Part 2. Adaptations or modifications may include increasing the sample size, adjusting the number of cohorts or allocation of subjects in each cohort, and revising eligibility criteria and endpoints.

Figure 3: - Description of Cohorts for Part 1

Cohort	SOC Treatment	Requirements
Cohort A	**None**	• No topical therapies in the 14 days prior to Day 1 • No oral systemic therapies in the 45 days prior to Day 1 • No injectable systemic therapies in the 90 days prior to Day 1
Cohort B	**Topical therapy**	• Stable dose and consistent use of topical therapy required for at least 30 days prior to Day 1 and through Day 15 of the trial. • No oral systemic therapies in the 45 days prior to Day 1 • No injectable systemic therapies in the 90 days prior to Day 1
Cohort C	**Dupilumab**	• Stable dose and consistent use of dupilumab required for at least 6 months prior to Day 1 and throughout the trial. • No topical therapies in the 14 days prior to Day 1 • No oral systemic therapies in the 45 days prior to Day 1

Inclusion Criteria:

Subjects who fulfil all the following criteria (as applicable) are eligible for enrollment in the trial:

1. Adult subjects ≥18 years of age at the time of signing the ICF.
2. History of atopic dermatitis, according to American Academy of Dermatology criteria, that has been present for at least 6 months prior to screening, as confirmed by the Investigator.

[redacted]

10. Able and willing to provide informed consent, complete trial procedures/assessments and attend scheduled trial visits.
11. Agree to use a highly effective barrier method of contraceptive (as detailed in the trial protocol), and abstain from sperm (or semen) and egg donation for the trial duration and at least 30 days after the last dose of trial drug, if applicable. Women of childbearing potential (i.e., ovulating, pre-menopausal and not surgically sterile) must use a barrier method of contraception, and all

male subjects must use a medically accepted contraceptive regimen during their participation in the study and for 30 days after the last administration of the investigational drug.

Exclusion Criteria:

Subjects who fulfil any of the following criteria (as applicable) are not eligible for enrollment in the trial:

[redacted]

11. Pregnant, intending to become pregnant (or father a child), or breastfeeding during trial.
12. Current or recent participation in another interventional trial within 60 days prior to screening.
13. Previously taken ADX-629 (Active or Placebo); or suspected hypersensitivity to ADX-629.
14. History of any unstable chronic diseases/conditions, clinically significant abnormalities, or findings that, in the opinion of the Investigator, could compromise subject safety, data integrity, or affect the conduct of the trial.

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1 BACKGROUND AND TRIAL RATIONALE

1.1 Atopic Dermatitis

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, non-contagious, relapsing inflammatory skin disease that is characterized by red, flaky skin and pruritus. AD is characterized by clinical signs of erythema, swelling, dryness, lichenification, and pruritus (itch). Itch is a major symptom that severely impacts quality of life and is associated with sleep loss, anxiety, depression, and increased risk for suicidal ideation (**Ronnstad et al., 2018**). Atopic dermatitis affects approximately 5% to 10% of adults in the US with a majority ranging from mild-to-moderate in severity of disease (Barbarot et al2018; Chiesa Fuxench et al 2019). Atopic dermatitis stems from a complex combination of factors including genetic predisposition, immune dysregulation, and skin barrier defect. Pro-inflammatory cells such as Th1, Th2, Th9, Th17 and Th22 cells have been implicated in AD; IL-4, IL-9, IL-13, IL-31, and IL-22 have been reported to be increased in AD patients (Werfel et al 2016). Exposure to environmental allergens such as dust mites, pollens, molds, cigarette smoke, and dander from animals may exacerbate symptoms of AD (Langan et al 2020). Adequate treatment and control of AD is supported by significant reductions in flares, skin symptoms, and sleep problems.

Topical medications including corticosteroids, calcineurin inhibitors, and Phosphodiesterase-4 (PDE4) inhibitors are usually the first line of treatment for patients with mild AD symptoms. Other treatments for AD include emollients, topical corticosteroids, topical calcineurin inhibitors, coal tar preparations, phototherapy (with or without psoralen). Common systemic immunomodulating treatments include short-term corticosteroids, cyclosporin, mycophenolate, and azathioprine. However, these options are not advised for long-term use because of serious side effects. Newer therapies for AD include JAK-inhibitors and biologics, such as dupilumab (Dupixent). Long-term use of current immunosuppressant therapies may have toxic side effects, including skin atrophy, hypertension, reduced bone mineral density, metabolic complications, bladder toxicity, hyperlipidemia, leukopenia, and an increased risk of infection. Long-term use of methotrexate may cause liver damage including the development of fatty liver disease, fibrosis and even cirrhosis. Topical calcineurin inhibitors may include possible risk of skin malignancies. Low-potency topical steroids are recommended when treating sensitive areas including the face, neck, and groin because of potential adverse effects, such as skin atrophy and discoloration (Frazier et al 2020). ADX-629 may potentially represent a valuable treatment option for patients with chronic immune-mediated diseases by reducing dependence on immunosuppressant therapies and offering a safer alternative.

1.2 ADX-629 Background

[redacted]

[redacted]

1.3 Trial Rationale

[redacted]

Despite the approval of recent, innovative therapies in the last few years, there is still a need for a systemic AD therapy for patients with mild atopic dermatitis and residual dermatitis symptoms (Kamata and Yada 2021; Simpson et al 2016; Leigh et al 2021. Patients with mild AD are at an increased risk of developing atopic comorbidities since the impact of skin inflammation may be underestimated. Additionally, AD involvement of the face, neck, and hands has been linked to a significantly higher impact on health-related outcomes and overall quality of life (Abuabara et al 2022). The use of systemic therapy is based on AD extent and severity, which is determined by subjective and arbitrary cut-off points on AD grading scales. Therefore, early and appropriate systemic intervention may prevent mild AD from progressing to more severe, persistent forms and reduce the risk of developing comorbidities (Maintz and Bieber et al 2022runner, et al., 2017). Subjects that are enrolled in trials with long washout periods experience more disease exacerbation and flare-ups than those in trials permitting topical corticosteroids and shorter washout periods (Silverberg et al2022). Additionally, repeated discontinuation and resumption of background therapies, such as dupilumab, may decrease the efficacy of the drug long-term (Kamata and Tada 2021). To prevent worsening of subjects disease status and

[redacted]

[redacted]

[redacted]

2 TRIAL OBJECTIVES AND ENDPOINTS

2.1 Trial Objectives

2.1.1 Primary Objective

- To evaluate the safety of ADX-629 administered alone and in addition to standard-of-care in adults with atopic dermatitis

2.1.2 Secondary Objectives

- To evaluate the activity and efficacy of ADX-629 administered alone and in addition to standard-of-care in adults with atopic dermatitis

2.2 Trial Endpoints

2.2.1 Primary Endpoint

- Incidence and severity of treatment-emergent adverse events and serious adverse events

2.2.2 Key Secondary Endpoint for Efficacy:

- Proportion of subjects with an Investigator's Global Assessment score of 0 or 1 at Day 90

2.2.3 Secondary Endpoints

- Proportion of subjects with an Investigator's Global Assessment score of 0 or 1 and ≥ 2-grade improvement from Baseline (Day 1)
- Proportion of subjects achieving a ≥ 50%, 75%, and 90% improvement in the Eczema Area and Severity Index
- Proportion of subjects achieving ≥4 points improvement from Baseline (Day 1)in the peak pruritus numerical rating scale
- Time to AD flare-up (days), as defined by use of rescue medication
- Proportion of patients with a 4-point or more improvement in Patient Oriented Eczema Measure (POEM) total score at Day 90
- Percent change in High-density lipoprotein Cholesterol (HDL-C), Low-density lipoprotein Cholesterol (LDL-C), and triglycerides from Baseline (Day 1)
- Change from Baseline (Day 1) in the following:
  - IGA Score
  - EASI Score
  - Hamilton Depression Rating Scale (HAM-D) score
  - Beck Anxiety Inventory (BAI) Score

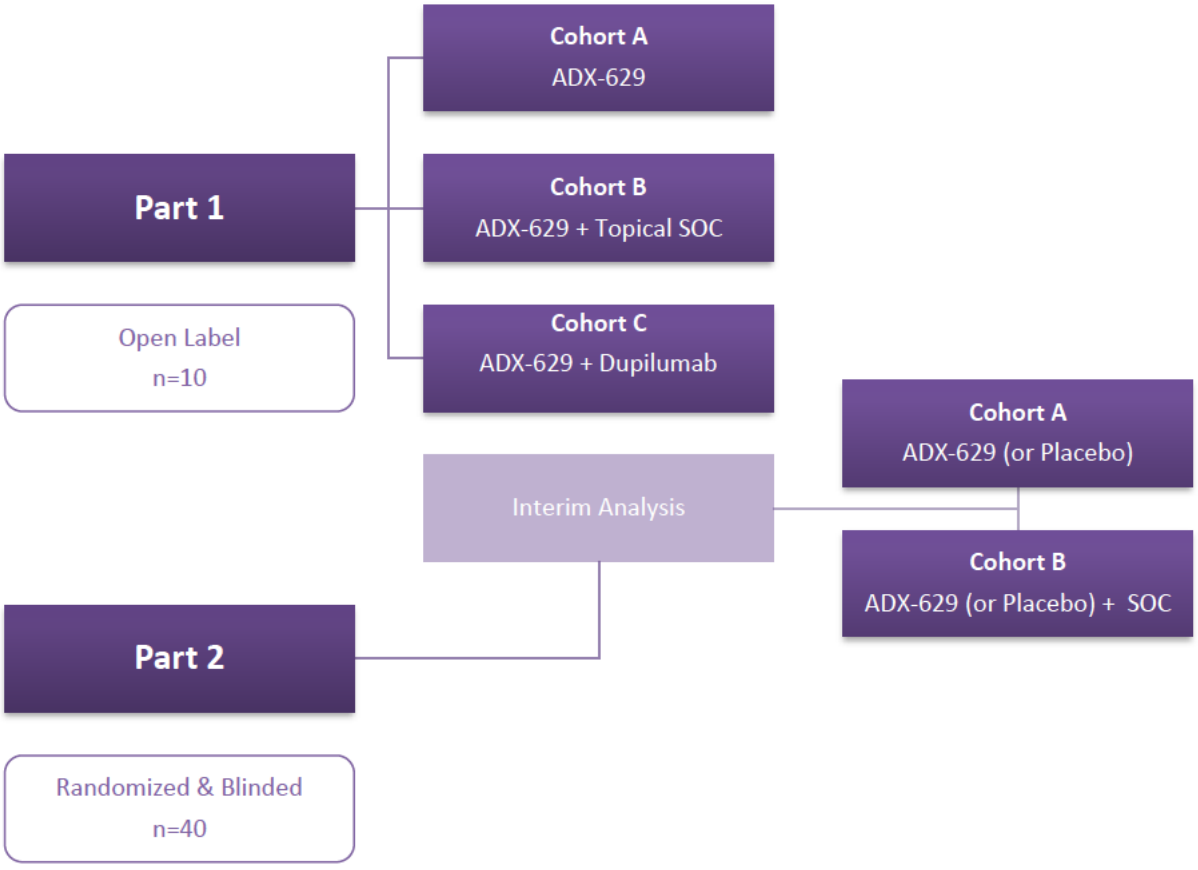
3 TRIAL DESIGN AND DESCRIPTION OF THE TRIAL

3.1 Trial Design and Plan

This Phase 2, multicenter, 2-part clinical trial is a designed to evaluate the safety and efficacy of ADX-629 alone and in combination with SOC in subjects ≥ 18 years of age with atopic dermatitis. The trial will enroll approximately 50 adults with mild, moderate, and severe atopic dermatitis, as defined by the inclusion and exclusion criteria. Trial drug will be administered orally every 12 hours to eligible subjects for 90 days. Subjects will be enrolled in cohorts based on their SOC treatment for AD. Subjects that are not receiving SOC treatment or are able/willing to washout of SOC will be assigned to Cohort A. Subjects in Cohort A will receive trial drug only (i.e., monotherapy). Subjects receiving a SOC AD therapy will be assigned the other cohort(s). The trial will not provide SOC treatment and therefore must be obtained independently by the subject.

The trial is divided into 2 parts; the first part of the trial (Part 1) is open-label, and the second part (Part 2) is randomized, double-blind, and placebo controlled. In Part 1, approximately 10 subjects will receive open-label ADX-629 (250 mg) twice daily for 90 days alone or in combination with SOC treatment for AD. In Part 2, approximately 40 subjects will be randomized to receive either ADX-629 (250 mg) or matching placebo twice daily for 90 days.

Figure 1- Schematic of Trial Design:



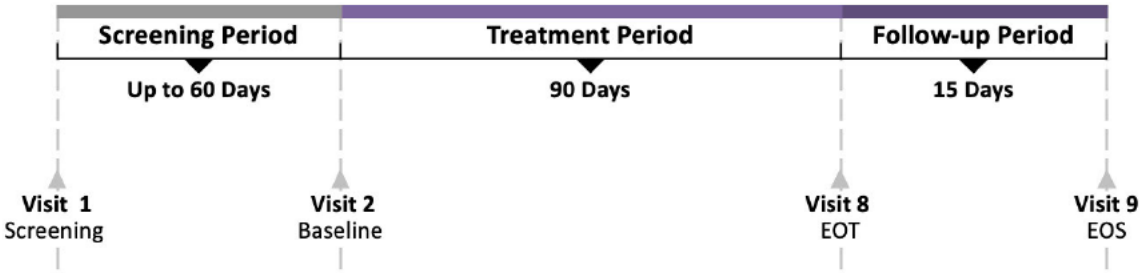
c) An interim analysis may be performed after all subjects complete the treatment period in Part 1.

d) The trial design in Part 2 may be adapted based on the data from Part 1.

The trial duration for each subject will be approximately 5 months and will involve 9 trial visits. The trial is divided into 3 periods (Screening, Treatment, and Follow-up). The screening period will range from 3 days to 60 days to complete screening procedures trial and allow for adequate washout of prohibited concomitant medications, as indicated in Table 3. Prior to any trial procedure/assessment, written informed consent will be obtained. Trial-related assessments and procedures will be performed at the timepoints indicated in the Schedule of Assessments (Table 1). Eligibility will be confirmed during screening and prior to dosing at Visit 2 (Day1). Eligible subjects will receive the first dose of trial drug at Visit 2. Subjects will complete trial visits every 15 days during the 90-day treatment period. Trial visits may be performed in-person or remotely (i.e., phone call, telehealth visit). Subjects will then undergo a follow-up period and complete an end of trial visit approximately 15 days from the last dose of trial drug. Unscheduled visits or assessments may be performed if clinically warranted, in the opinion by the Investigator. Subjects who require rescue medication for an AD flare-up during the treatment period will be asked to discontinue trial drug and complete remaining scheduled trial visits.

The trial periods are illustrated in Figure 2.

Figure 2- Schematic of Trial Periods:



Overview of Part 1:

Part 1 of the trial will include at least 10 subjects with mild, moderate, or severe AD whose disease is not adequately controlled with current standard-of-care treatment. The purpose of Part 1 is to evaluate the safety of ADX-629 and confirm the target patient population and background therapy selection prior to expansion into Part 2. All subjects in Part 1 will receive open-label ADX-629 (250 mg) for 90 days either alone or in combination with SOC treatment. Subjects will be enrolled in either Cohort A, Cohort B, or Cohort C based on their SOC treatment at baseline. Subjects that are not receiving standard-of-care therapy will be assigned to Cohort A, subjects on a stable topical therapy will be assigned to Cohort B, and subjects on a stable dose of dupilumab will be assigned to Cohort C. Subjects in Cohort B must be able to discontinue topical therapy within 14 days of taking trial drug or by Visit 3 (Day 15) or will be discontinued from trial drug. Subjects in Cohorts C must be willing and able to continue SOC throughout the duration of the clinical trial. The cohorts in Part 1 are described in Figure 3.

Figure 3: Description of Cohorts for Part 1

Cohort	SOC Treatment	Requirements
Cohort A	**None**	• No topical therapies in the 14 days prior to Day 1 • No oral systemic therapies in the 45 days prior to Day 1 • No injectable systemic therapies in the 90 days prior to Day 1
Cohort B	**Topical therapy**	• Stable dose and consistent use of a topical therapy required for at least 30 days prior to Day 1 and through Day 15 of the trial • No oral systemic therapies in the 45 days prior to Day 1 • No injectable systemic therapies in the 90 days prior to Day 1
Cohort C	**Dupilumab**	• Stable dose and consistent use of dupilumab required for at least 6 months prior to Day 1 and throughout the trial • No topical therapies in the 14 days prior to Day 1 • No oral systemic therapies in the 45 days prior to Day 1

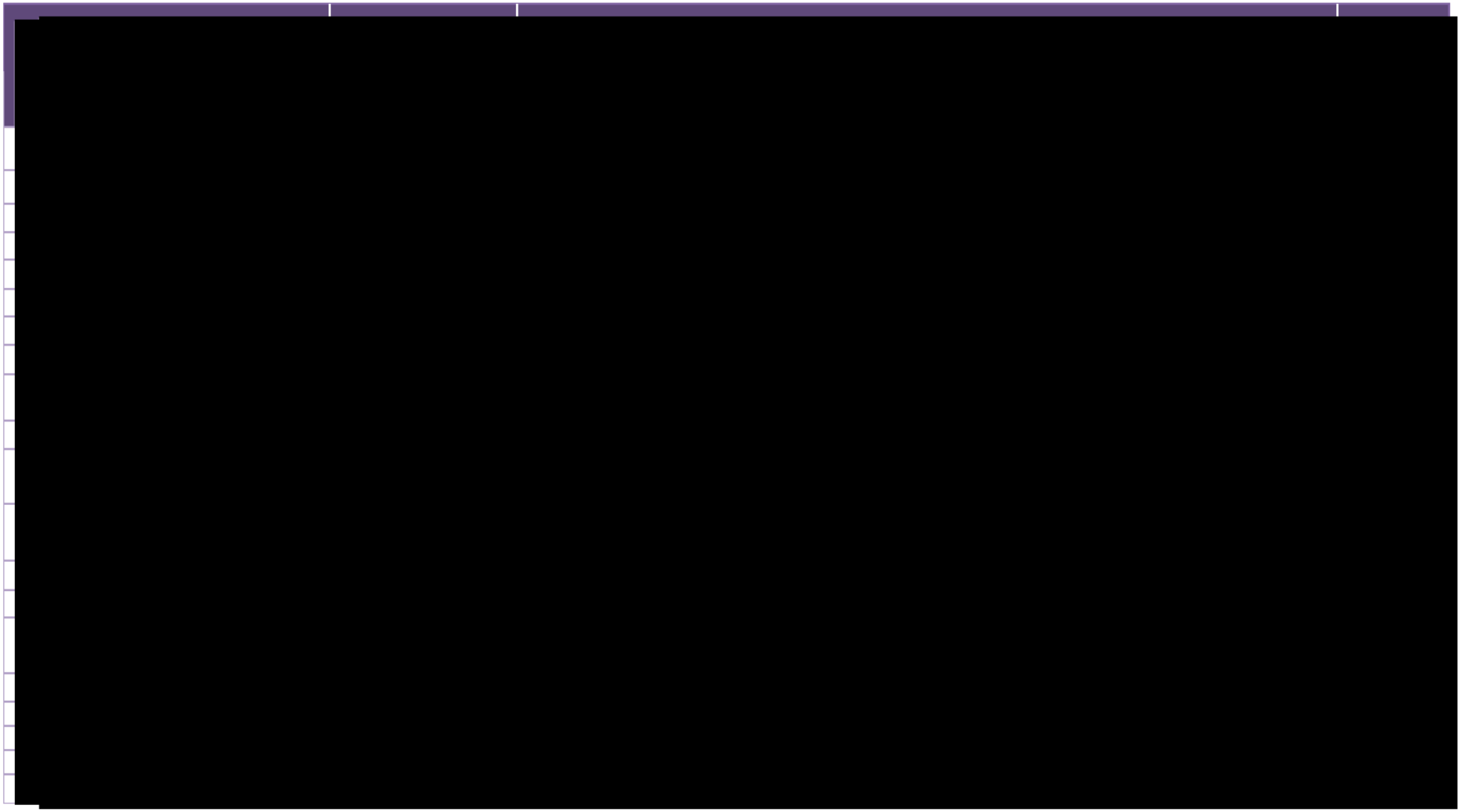
Overview of Part 2:

Part 2 of the trial will be a randomized, double-blind, and placebo controlled and will include at least 40 subjects with AD. Subjects will be assigned to cohorts based on their standard-of-care therapy at baseline. Subjects will be randomized on Day 1 in a 1:1 or 2:1 ratio to receive ADX-629 (250 mg) or matching placebo for 90 days. Investigators, subjects, and the trial team will be blinded to treatment allocation. The purpose of Part 2 is to compare ADX-629 to placebo and standard-of-care treatment(s). The trial design will be adapted after the review of the safety and efficacy data from Part 1 and before any subjects are randomized into Part 2. Adaptations or modifications may include increasing the sample size, adjusting the number of cohorts or allocation of subjects in each cohort, and revising eligibility criteria and endpoints.

3.2 Schedule of Assessments

A summary of the trial assessment schedule is provided in Table 1.

Table 1: Schedule of Assessments



[redacted]

3.3 Promoting Diversity and Inclusion

Flexibility in the format of trial visits is built into this protocol to support the health and safety of trial staff and subjects as well as improve enrollment of underrepresented and diverse populations. Throughout the protocol, the term 'visit' is used to indicate interaction between the subject and trial staff. Trial subjects are not required to physically attend the clinic if trial-related assessments/procedures can be adequately performed at another suitable location such as the subject's home or via a telehealth visit. Trial visits may be conducted remotely or at an off-site location provided trained, delegated research staff, and required equipment is available to perform the assessments. Other arrangements are also permitted where these will not interfere with the safety of the subject or challenge the integrity of the data.

3.4 Screening Period

Subjects must be given detailed information about the trial and sign the ICF before any trial-related assessments are performed. The ICF signature is the start of the screening period and will be used as the date of Visit 1. The screening period can range from 3 days to 60 days to allow for adequate washout of prohibited/restricted concomitant medications. Visit 1 may have a duration of more than 1 day to accommodate all screening assessments. Unscheduled assessments or visits may be performed if clinically warranted, in the opinion by the Investigator.

3.4.1 Visit 1 (Screening)

- Obtain written informed consent
- Record visit and assign subject identification number
- Review inclusion and exclusion criteria
- Collect demographic information (date of birth/age, gender, ethnicity, and race), as described in Section 8.2.3
- Collect medical history and medication history
    - Record atopic dermatitis history (i.e., age at onset, triggers, failed medications)
- Record concomitant medications, including current and prior AD medications and emollient use
- Record smoking status and alcohol use
- Record Childbearing status and day of menstrual cycle, if applicable. Collection of menstrual cycle details are optional. Additional details provided in Section 7.4.
- Collect vital signs (blood pressure, heart rate, and body temperature)
- Conduct physical examination, including review of the major body systems
- Record height and weight
- Complete dermatological assessments, including IGA, body surface area (BSA) percentage affected by AD, and EASI

- Option to complete the Scoring Atopic Dermatitis (SCOARD)
- Record subject's peak pruritus score on numerical rating scale
- Perform standard 12-lead ECG
- Collect urine sample for urinalysis and perform dipstick urinalysis
- Collect blood sample for routine laboratory testing, including clinical chemistry, hematology, lipid panel, and serum pregnancy, if applicable. Clinical safety laboratory assessments will be performed locally in Part 1.
- Record any pre-treatment AEs
- Advise subject to apply emollient of their choosing for at least 5 days before the baseline visit and during trial
- Dispense subject diary and instructed subject to complete diary daily, along with peak pruritus numerical rating scale
- If applicable, instruct subject to complete washout of any prohibited medications. Refer to Table 3 for details.

3.4.2 Retesting and Rescreening Procedures

If abnormalities or out-of-range values during screening are considered to be transient by both the Investigator and Medical Monitor, then the procedure may be repeated once during screening. Retesting must occur within one week of the initial procedure. If the retest result is no longer exclusionary, the subject may be enrolled.

Subjects who have screen failed may be re-screened once if their eligibility characteristics have changed, in the opinion of the Investigator. Subjects who are re-screened must be assigned a new subject number and screening procedures must be repeated, as applicable. The retesting and rescreening process must be discussed with the Medical Monitor. The Investigator's rationale for retesting and/or rescreening should be documented.

3.5 Treatment Period

Subject's eligibility for the trial will be confirmed at screening and prior to the first dose of trial drug on Day 1. Eligible subjects will be enrolled into the trial and receive the first dose of trial drug at Visit 2 (Day 1). Trial-related assessments and procedures will be performed at the timepoints indicated in the Schedule of Assessments. All assessments will be performed prior to trial drug administration (pre-dose). Unscheduled assessments or unscheduled visits may be performed if clinically warranted, in the opinion by the Investigator. Trial visits may be conducted remotely or at an off-site location (i.e., subject's home) provided trained, delegated research staff, and required equipment is available.

In Part 1, subjects will be assigned to either Cohort A, Cohort B, and Cohort C Visit 2 (Day 1) based on their use of SOC treatment. All subjects will receive open-label ADX-629 (250 mg) twice daily for 90 days.

In Part 2, subjects will be assigned to a cohort at Visit 2 based on their use of SOC treatment subjects. Subjects will then be randomized to either ADX-629 (250 mg) or matching placebo, according to the randomization plan. Subjects will be randomized via interactive randomization technology (IRT). Investigators, subjects, and the trial team will be blinded to treatment allocation.

3.5.1 Visit 2 (Day 1)

- Review inclusion and exclusion criteria
- Review subject diary and peak pruritus numerical rating scale scores
- Ensure subject completed adequate washout of any prohibited medications (Table 3), if applicable
- Perform an unstructured interview with subject and complete HAM-D questionnaire
- Instruct subject to complete POEM and BAI questionnaire and record subject's score
- Collect vital signs (blood pressure, heart rate, and oral body temperature)
- Conduct physical examination, including review of the major body systems
- Complete dermatological assessments, including IGA, SCORAD, BSA, and EASI
- Record standard 12-lead ECG
- Collect urine sample for urinalysis and perform dipstick urinalysis and pregnancy test (if applicable)
- Collect blood sample for routine laboratory testing, including clinical chemistry, hematology
- Confirm subject meets eligibility criteria
- Assign cohort based on SOC and washout requirements
- Complete randomization of subject via IRT
- Dispense trial drug and record subject details on label
- Administer trial drug and provide instructions for use and storage at home
    - Trial drug will be administered orally, with or without food, every 12 hours with water. trial drug will be taken twice daily at approximately the same time every morning and evening. Subject will record trial drug intake in diary.
    - Subject will store trial drug at room temperature in a secure location at their home in between trial visits.
    - Subject will return all unused trial drug tablets and empty containers at every visit.
- Record any AEs or changes to concomitant medications
- Collect/dispense diary and provide retraining as necessary
- Record emollient details and advise subject to apply stable dose of emollient, of their choosing, during trial

- Instruct subject to continue stable dose of background therapy, if applicable

3.5.2 Visit 3 (Day 15)

- Record any AEs or changes to concomitant medications
- Review subject diary and peak pruritus numerical rating scale scores
- Perform an unstructured interview with subject and complete HAM-D questionnaire
- Instruct subject to complete POEM and BAI questionnaire and record subject's score
- Collect vital signs (blood pressure, heart rate, and oral body temperature)
- Complete dermatological assessments, including IGA, SCORAD, BSA, and EASI
- Collect urine sample for urinalysis to perform dipstick urinalysis and pregnancy test (if applicable)
- For Part 1 - Cohort B: Instruct subjects to discontinue topical therapy
- Dispense trial drug and record subject details on label
- Perform accountability and administer trial drug to subject
- Collect/dispense diary and provide retraining, as needed
- Advise subject to apply stable dose of emollient of their choosing during trial

3.5.3 Visit 4 (Day 30) and Visit 6 (Day 60)

- Record any AEs or changes to concomitant medications
- Review subject diary and peak pruritus numerical rating scale scores
- Perform an unstructured interview with subject and complete HAM-D questionnaire
- Instruct subject to complete POEM and BAI questionnaire and record subject's score
- Collect vital signs (blood pressure, heart rate, and oral body temperature)
- Conduct physical examination, including review of the major body systems
- Complete dermatological assessments, including IGA, SCORAD, BSA, and EASI
- Record standard 12-lead ECG
- Collect urine sample for urinalysis and perform dipstick urinalysis and pregnancy test (if applicable)
- Collect blood sample for routine laboratory testing, including clinical chemistry, hematology
- Dispense trial drug and record subject details on label
- Perform trial drug accountability and record compliance
- Administer trial drug to subject
- Collect/dispense diary and provide retraining, as needed

- Advise subject to continue to apply stable dose of emollient at least twice daily
- Instruct subject to continue stable dose of background therapy, if applicable

3.5.4 Visit 5 (Day 45) and Visit 7 (Day 75)

- Assess and record any adverse events
- Review concomitant medications and record any changes
- Review diary and peak pruritus numerical rating scale scores
- Advise subject to continue to apply stable dose of emollient at least twice daily
- Instruct subject to continue stable dose of background therapy, if applicable

Visits can be performed remotely via telephone or video conferencing. Unscheduled assessments may be performed if clinically warranted, in the opinion by the Investigator.

3.6 End of Treatment

Subjects will complete the end of treatment (EOT) visit approximately 90 days after the first dose of trial drug. The end of trial treatment will also be performed if subject discontinues trial drug before Day 90 and withdraws from the trial prematurely.

3.6.1 Visit 8 (Day 90)

- Record any AEs or changes to concomitant medications
- Review subject diary and peak pruritus numerical rating scale scores
- Perform an unstructured interview with subject and complete HAM-D questionnaire
- Instruct subject to complete POEM and BAI questionnaire and record subject's score
- Collect vital signs (blood pressure, heart rate, and oral body temperature)
- Conduct physical examination, including review of the major body systems
- Complete dermatological assessments, including IGA, SCORAD, BSA, and EASI
- Record standard 12-lead ECG
- Collect urine sample for urinalysis and perform dipstick urinalysis and pregnancy test (if applicable)
- Collect blood sample for routine laboratory testing, including clinical chemistry, hematology
- Administer last dose of trial drug
- Collect all unused trial drug tablets and used trial drug kits
- Perform trial drug accountability and record compliance

- Collect diary and review for completion
- Instruct subject to continue stable dose of background therapy, if applicable

3.7 Follow-up Period

Subjects will complete a 15-day follow-up period after the treatment period. Subjects will complete an End of Trial Visit approximately 15 days after last dose of trial drug. The visit can be performed remotely via telephone or video conferencing. Unscheduled assessments may be performed during this time if clinically warranted (i.e., unresolved AEs), in the opinion by the Investigator.

3.7.1 Visit 9 (Day 105)

- Record any AEs and changes in concomitant medications
- Instruct subject to continue stable dose of background therapy, if applicable, and resume prohibited medications once their participation in the trial is complete.

4 END OF TRIAL DEFINITION

The end of the trial is defined as the date of the last visit or scheduled procedure for the last subject.

At the end of the clinical trial, treatment with ADX-629 in an optional extension study (under a separate study protocol) may be offered to all eligible subjects, provided Independent Ethics Committee IEC)/Institutional Review Board (IRB) and Competent Authority approvals for such an extension are granted.

5 SELECTION OF TRIAL POPULATION

5.1 Description of Trial Population

The trial population will be adults ≥ 18 years of age with a history of atopic dermatitis that has been present for at least 6 months and is not adequately controlled by standard-of-care treatment.

Enrolled subjects will have mild, moderate, or severe atopic dermatitis, defined by an IGA score of ≥ 2, with an afflicted body surface area of ≥ 2%. The trial population in Part 2 may be revised based on the results from Part 1. Subjects that have been enrolled into Part 1 of the trial will not be eligible to participate in Part 2.

5.2 Number and Source of Subjects

Approximately 50 subjects will be enrolled across 10 trial sites in the United States of America. 10 subjects are planned for enrollment in Part 1 and 40 subjects are planned for enrollment in Part 2. The sample size in Part 2 may increase based on the results of Part 1. Potential subjects will be identified from clinical databases, medical records, physician referrals, and digital advertising. Remote visits and adaptive trial design increases subject diversity and inclusion.

5.3 Inclusion Criteria

Subjects who fulfil all the following criteria (as applicable) are eligible for enrollment in the trial:

1. Adult subjects ≥ 18 years of age at the time of signing the ICF.
2. History of atopic dermatitis, according to American Academy of Dermatology criteria, that has been present for at least 6 months prior to screening, as confirmed by the Investigator.

[redacted]

10. Able and willing to provide informed consent, complete trial procedures/assessments and attend scheduled trial visits.
11. Agree to use a highly effective barrier method of contraceptive (as detailed in the trial protocol); and abstain from sperm (or semen) and egg donation for the trial duration and at least 30 days after the last dose of trial medication, if applicable.

5.4 Exclusion Criteria

Subjects who fulfil any of the following criteria (as applicable) are not eligible for enrollment in the trial:

[redacted]

[redacted]

11. Pregnant, intending to become pregnant (or father a child), or breastfeeding.
12. Current or recent participation in another interventional trial within 60 days prior to screening.
13. Previously taken ADX-629 (Active or Placebo); or suspected hypersensitivity to ADX-629.
14. History of any unstable chronic diseases/conditions, clinically significant abnormalities, or findings that, in the opinion of the Investigator, could compromise subject safety, data integrity, or affect the conduct of the trial.

5.5 Early Discontinuation

Participation in the trial is strictly voluntary. A subject has the right to discontinue their participation in the trial at any time for any reason (or no reason at all). The Investigator has the right to terminate participation of any subject at any time if it is in the subject's best interest. The date, reason and circumstances for premature discontinuation will be documented in the subject's electronic case report form (eCRF).

5.5.1 Withdrawal of Consent

A subject may withdraw from the primary interventional component of the trial (trial medication) or all components of the trial. If a subject chooses to withdraw from the trial or stop the trial medication, they must inform the Investigator immediately. The Investigator is encouraged to request a written statement from the subject confirming which components of the trial they wish to discontinue. The Sponsor may retain and continue to use any data collected before withdrawal of consent. If the subject wishes to discontinue the trial early, they will be asked to complete an EOT visit.

5.5.2 Early Treatment Discontinuation

Treatment with the investigational product will be discontinued by the Investigator if safety concerns arise. The Investigator is required to discontinue a subject from trial drug if one or more of the criteria below is met.

[redacted]

[redacted]

Safety concerns should be discussed with the Medical Monitor immediately upon awareness to determine if the subject should discontinue trial treatment. Subjects that discontinue trial drug early will be requested to complete the non-interventional components of the trial and attend trial visits as scheduled, if safe to do so. If unable to complete trial visits as planned, subject will be asked to complete an End of Treatment Visit, as indicated in the Schedule of Assessments. The date and reason for premature trial drug discontinuation will be recorded in the subject's electronic case report form (eCRF).

5.5.3 Lost to Follow-up

A subject may be considered lost to follow-up if they repeatedly miss scheduled visits and are unable to be contacted by the investigative site. If a subject misses a trial visit, the investigative site must contact the subject and reschedule as soon a visit as possible. The subject will be counseled on the importance of maintaining the assigned visit schedule and completing the required trial procedures/assessments. The Investigator or designee must make every effort to regain contact with the subject and reschedule any missed visits.

The following actions must be taken by the investigative site to declare a subject lost to follow-up:

- Contact subject by telephone at least twice
- Contact subject by an alternative method at least once, including email or a certified letter to the subject's last known address
- Request subject to return any unused IP
- Contact subject's emergency contact, if available

Should the subject continue to be unreachable, they will be considered to have withdrawn from the trial. All attempts to contact the subject should be documented in the subject's chart.

5.6 Replacement Policy

Subjects who discontinue or are withdrawn from the trial before taking any trial treatment may be replaced with Sponsor approval. Subjects who discontinue or are withdrawn from the trial after taking one or more doses of trial treatment will not be replaced.

5.7 Stopping or Suspending the Trial

The trial may be discontinued or suspended if there is insufficient accrual of subjects, or if new information arises that has an adverse impact on the benefit/risk assessment.

6 INVESTIGATIONAL PRODUCT

6.1 Description of Investigational Product

ADX-629 is a small molecule drug with a quinoline core that acts as a RASP sequestering agent by irreversibly binding aldehydes. The ADX-629 drug substance is a white to pale yellow crystalline solid that is stable under both refrigerated and ambient conditions. ADX-629 will be manufactured and supplied as 250 mg tablets. Placebo tablets to match ADX-629 will be manufactured using the same excipients as the active product. The Sponsor will be responsible for ensuring that ADX-629 and placebo tablets are manufactured in accordance with applicable current Good Manufacturing Practice regulations and requirements.

ADX-629 tablets or placebo will be provided in treatment kits. The trial drug kit will be labeled according to the requirements of local law and legislation. Each kit includes 1 bottle of 30 tablets. Eligible subjects will either receive ADX-629 or placebo depending on the timing of their enrollment into the trial and the randomization schedule.

An overview of the treatment groups and trial drug is available in Table 2.

Table 2: Description of Investigational Product

[redacted]

6.2 Investigational Product Administration, Storage, and Handling

[redacted]

[redacted]

Further details regarding trial drug administration, storage, and handling are provided in the pharmacy manual.

6.2.1 IP Accountability

The Investigator must keep an accurate accounting of the number of trial drug units delivered to the investigative site, dispensed to subjects, returned to the Investigator by the subject, and returned to the Sponsor or other disposition during and at completion of the trial. The trial drug must be dispensed to subjects only by an appropriately qualified person. The trial drug is to be used in accordance with the protocol by subjects who are under direct supervision of the Investigator. The Investigator should maintain records that adequately document that the subjects were provided the doses specified by the protocol and reconcile all trial drug received at the investigative site before final disposition. At the end of the trial or as directed, all IP, including unused, partially used, and empty containers, will be returned to the Sponsor, and destroyed, according to instructions provided in the appropriate trial manual.

6.2.1.1 Treatment Compliance

The prescribed dosage, timing, and mode of administration of trial treatment should not be changed from the protocol schedule. Departures from the intended regimen will be reported as protocol non-compliance. Subjects must return empty containers and unused trial treatment as compliance will be assessed by tablet counts.

The Investigator or designee will assess the subject's compliance by performing a tablet count on return of unused trial treatment. Subjects who exhibit poor compliance, i.e., not 100% compliant without adequate explanation, should be counseled on the importance of good compliance with the dosing regimen. Severe lack of compliance is defined as <80% or >120% of the correct dosing and is a reason for discontinuation of the subject from the trial.

6.3 Method of Assigning Subjects to Treatment Groups

Subjects who meet all the inclusion criteria and none of the exclusion criteria will be enrolled into the trial. Subjects will be assigned to Part 1 or Part 2 based on the timing of their participation.

Part 1: Part 1 will be open to enrollment first. Subjects will be assigned to Cohort A, Cohort B, or Cohort C based on their prior and concomitant AD medications, as indicated in Figure 3. All subjects will receive ADX-629 open-label for 90 days.

Part 2: Subjects will be randomized in Part 2 once all the subjects in Part 1 complete the treatment period in Part 1 and adaptations/modifications for Part 2 have been implemented.

Subjects will be assigned to a cohort based on their prior and concomitant AD medications Cohorts may be added or dropped in Part 2, based on the data from Part 1. In Part 2, eligible subjects will undergo randomization at Visit 2 (Day 1), after eligibility has been confirmed. Subjects will be randomized in a 1:1 or 2:1 ratio to receive ADX-629 or placebo, either alone or in combination with SOC treatment. The treatment assignments will be allocated via IRT. Treatment assignment will be blinded to Investigator, subjects, and study team. The randomization plan will be followed. Blinded kit dispensation to eligible subjects will be managed by investigative site staff.

6.3.1 Limiting Bias

Bias is limited by adherence to the inclusion and exclusion criteria, the use of a randomization schedule, and a randomized, double-blinded, placebo-controlled trial design in Part 2 of the trial. All measurement procedures will be defined in advance and will be consistently and precisely applied.

6.3.2 Blinding and Unblinding Procedures

Part 1 of the trial is open-label and not blinded. Part 2 of the trial is double-blinded. The trial blind in Part 2 will not be broken until the clinical trial is complete and the database has been locked. Unblinding of a subject's treatment assignment is only permitted in emergency situations where the identification of treatment group is required for further management of the subject's condition by the Investigator. In case of emergency in which neither the Principal Investigator nor the sub-Investigator are available, the Medical Monitor may, as a last resort, perform the unblinding.

In any case of unblinding, the date, time, and reason for breaking the blind will be recorded, and the Sponsor and Medical Monitor will be notified. This information will be stored in the subject's source files with as few of the investigative site staff unblinded as is clinically reasonable.

6.4 Rationale for Selection and Timing of Dose

[redacted]

7 PRIOR MEDICATIONS AND CONCOMITANT THERAPY

All medications taken for atopic dermatitis at any time and any medication taken in the 12 weeks prior to screening (includes over-the counter and prescription drugs) must be recorded in source and eCRF. All concomitant medications and significant non-drug therapies (including physical therapy and blood transfusions) administered after the subject has signed the ICF must be listed in the eCRF and source documents. The drug name, start date, and dose will be recorded in the eCRF and source documents. Subjects will be asked at each visit if they have had any changes in their medications since the previous visit.

7.1 Standard-of-Care Therapies for Atopic Dermatitis

An AD topical therapy or treatment is defined as a medicinal product that is applied to the skin (affected area) and contains an active pharmaceutical ingredient indicated for the treatment of AD, regardless of if it is available over-the counter or by prescription. An AD systemic therapy or treatment is defined as a medicinal product that is administered orally, or as an injection or infusion, and contains an active pharmaceutical ingredient indicated for the treatment of AD, that is available by prescription only. The drug name, dose, start/stop and reason for discontinuation (if applicable) will be recorded in the eCRF and source documents for any medication taken for atopic dermatitis.

Standard-of-care treatments for atopic dermatitis include, but are not limited to:

- Topical corticosteroids
- Crisaborole (Eucrisa), Topical Phosphodiesterase 4 inhibitor
- Pimecrolimus (Elidel), Topical Calcineurin inhibitor
- Ruxolitinib (Opzelura), Topical JAK inhibitor
- Tacrolimus (Protopic), Topical Calcineurin inhibitor
- Cyclosporine (Neoral), Oral Immunosuppressant
- Abrocitinib (Cibinqo), Oral JAK inhibitor
- Azathioprine (Imuran), Oral Immunosuppressant
- Upadacitinib (Rinvoq), Oral JAK inhibitor
- Mycophenolate (Myfortic), Oral Immunosuppressant
- Dupilumab (Dupixent), Injectable IL-4 receptor antagonist
- Omalizumab (Xolair), Injectable Monoclonal antibody
- Tralokinumab (Adbry), Injectable IL-13 antagonist

7.2 Prohibited and Restricted Medications

Disallowed and restricted medications and other products are summarized in Table 3. The screening period allows for washout of medications. Investigators are encouraged to contact the trial Medical Monitor if they need to discuss any concomitant medications.

Table 3: Prohibited and Restricted Medications and Non-drug Therapies

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

7.3 Rescue Medication

If prohibited immunomodulating therapies are required for an AD flare-up, the subject will be discontinued from trial drug. The use of rescue medication, including drug name and dose, will be documented in the subject chart.

7.4 Contraceptive Guidance

The effect of ADX-629 on embryos, female eggs, and male sperm is unknown. Therefore, pregnancy must be avoided during the trial. Highly effective barrier contraception is required for all subjects engaging in sexual activity that could lead to pregnancy. Subjects who are of childbearing potential or have a partner of childbearing potential must agree to use a highly effective method of contraceptive for the trial duration and at least 30 days after the last dose of trial treatment.

- A subject of childbearing potential is defined as any female who has experienced menarche (menstruation) and any male who has not undergone surgical sterilization (i.e., vasectomy). Highly effective barrier contraception as having a failure rate of ~ 1% when used consistently and correctly. Occasional abstinence, the rhythm method, and the withdrawal method are not highly effective and are not acceptable methods of contraceptives during this trial.

[redacted]

Acceptable, highly effective contraceptive methods include:

- Hormonal contraception, associated with inhibition of ovulation (if used in addition to barrier contraception).
- Double-barrier method, defined as a combination involving 2 or more of the following: Spermicide, Condom, Sponge, Diaphragm, and/or Cervical Cap.
- Intrauterine device (if used in addition to barrier contraception).
- Sexual abstinence, if preferred and typical lifestyle choice.
- Sterilization of subject or their monogamous partner (tubal ligation, vasectomy, hysterectomy, bilateral salpingectomy, bilateral oophorectomy, etc.).

Male subjects must abstain from donating sperm or semen and female subjects must abstain from donating egg or ova during their participation in the trial and for 30 days after the last dose of trial treatment.

Subjects are advised to notify the Investigator immediately should they suspect that they or their partner may be pregnant.

8 TRIAL ASSESSMENTS AND PROCEDURES

8.1 Subject Information and Informed Consent

Informed consent is a process that is initiated prior subjects agreeing to participate in the trial and continues throughout their trial participation in the trial. Before any subject enters the trial and any trial-related assessments are performed, the subject will be given detailed information about the trial. The information given to each subject will be both oral and written. The Investigator will explain the nature of the trial, its purpose and associated procedures, the expected duration, and potential benefits, constraints and risks associated with the trial. The subject will be given written information, which has been approved by the IRB/REB. The subject must be given sufficient time (preferably at least 24 hours) to consider their participation and all their questions answered. The subject will also be informed of their right to withdraw from the trial at any time for any reason, or no reason at all. If the subject agrees voluntarily to participate in the trial, he or she will sign and date the ICF. The same form will be signed and dated by the Investigator or designee, who will file the original form in the Investigator site file. A copy or duplicate of the ICF will be given to the subject.

If new information becomes available that potentially affects the subject's safety or willingness to continue in the trial, or if a protocol amendment is issued that affects the subject's safety, trial procedures or any aspects of the trial that may influence the subject's decision to participate in the trial, the ICF will be revised. After the new documents have received approval from the IRB/REB and competent authorities, the subject will be asked to sign the new ICF to confirm their willingness to continue in the trial. In obtaining and documenting informed consent, the Investigator must comply with applicable regulatory requirements (e.g., 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and should adhere to ICH GCP.

8.2 Safety Assessments

Safety assessments will be performed to assess the subject's health status and medical condition during the trial. Safety assessments include collection of medical history and demographic data, physical examinations, laboratory safety tests, vital signs, standard 12-lead ECGs, monitoring of AEs, and review concomitant medication changes. Unscheduled assessments or visits may be performed if clinically warranted by the Investigator.

8.2.1 Demographic Data, Baseline Characteristics, and History of the Disease

The following information will be recorded during screening:

- Date of birth, gender, ethnicity, and race
- Medical history
- Concomitant medications, including current and prior AD medication(s)
- AD history, including date of diagnosis, age at onset, potential triggers, and disease severity

- Smoking status, includes the categories of current smoker, former smoker, and never smoked
- Alcohol use, includes type of alcohol and frequency of use
- Childbearing status

8.2.2 Physical Examination

A full physical examination, including review of the major body systems will be conducted throughout the trial at the time points outlined in (Table 1). Height and weight will only be captured during screening. The physical examination will include examination of the major organ systems, and includes the heart, lungs, abdomen, lymph nodes, extremities, and skin. Physical exams must be performed by a Doctor of Medicine, Doctor of Osteopathy, Physician Assistant, or Nurse Practitioner. Clinically significant abnormal findings should be recorded as AEs.

8.2.3 Vital Signs

Vital signs will be conducted throughout the trial at the time points outlined in (Table 1). Vital signs will be collected prior to the intake of trial medication. Vitals will be taken after subject has been seated for at least 5 minutes. Clinically significant abnormal findings should be recorded as AEs.

Vital signs include the following:

- Heart rate
- Oral body temperature
- Systolic and diastolic blood pressure

8.2.4 Electrocardiogram

12-lead ECG will be obtained at the time points outlined in (Table 1). ECGs will be performed after subject has rested in the supine position for at least 5 minutes and prior to the intake of trial medication at each visit. In the case of abnormal findings, a repeat ECG will be performed. ECG abnormalities will be interpreted by the Investigator for clinical significance. A prolongation of QTc >500ms or an increase from baseline of >60ms will be considered a threshold of concern and require subject to discontinue IP. All Clinically significant abnormal findings should be recorded as AEs.

8.2.5 Subject Diary

Subjects will be required to complete a daily diary during screening and throughout the trial. The Investigator or designee will dispense the diary and provide instructions. Subjects will use the diary to record peak pruritus rating, background therapy use (if any), trial medication intake, rescue medication use, as well as any changes in their lifestyle, including smoking status or alcohol intake, if applicable. Providing details on menstrual cycle or date of last menstrual period is optional. Subjects will be instructed to complete the diary every day and return it at their next schedule trial visit. At each visit, new diary entries will be reviewed (remotely or on-site) by Investigator or designee. Retraining will be performed as deemed necessary.

8.2.6 Clinical Laboratory Analysis

Instructions on urine and blood sample collection, processing, and shipping as well as reference ranges are available in the laboratory manual. Retesting is allowed once during screening.

Clinical laboratory assessments will be performed locally in Part 1 and centrally in Part 2. The following clinical laboratory assessments will be performed at the times indicated in the schedule of assessments (Table 1).

Hematology	hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red blood cell count, white blood cell count with differential (neutrophils, lymphocytes, monocytes, eosinophils, and basophils), and platelet count
Clinical Chemistry	ALT, AST, alkaline phosphatase, gamma-glutamyl transferase, bilirubin, sodium, potassium, chloride, glucose, blood urea nitrogen, serum creatinine, albumin, amylase, uric acid, creatine kinase, calcium, magnesium, bicarbonate, lactate dehydrogenase, High-sensitivity C-reactive protein, and eGFR/1.73 m^2 Lipid Panel: Cholesterol (total), triglycerides, HDL-C, and LDL-C
Urinalysis	Urine Dipstick: Albumin, creatinine, bilirubin, glucose, ketones, blood, nitrite, pH, protein, and specific gravity will be measured at the trial site during scheduled visits Microscopic examination will be performed if indicated by dipstick (Investigator discretion)
Pregnancy	A serum pregnancy test will be performed at screening for all female subjects A urine pregnancy test will be performed at all subsequent visits, indicated in Table 1, for all female subjects. In the case of a positive confirmed pregnancy, the subject will discontinue investigational product immediately

A subject with out-of-range value(s) may be re-tested once; retesting must occur promptly. Instructions on urine and blood sample collection, processing, and shipping as well as reference ranges are available in the laboratory manual. All out-of-range results, if clinically significant, should be recorded as AEs.

The following laboratory results will be considered a threshold of concern and require subject to discontinue trial drug early:

- ALT or AST >3 × ULN
- Bilirubin >2 × ULN
- eGFR of <30 ml/min/1.73 m^2

8.3 Efficacy Assessments

8.3.1 Investigator Global Assessment

The IGA is a five-point scale that provides a global clinical assessment of AD severity ranging from 0 to 4, where 0 indicates clear and 4 indicates severe AD. A decrease in score relates to an improvement in signs and symptoms. The clinical evaluator of atopic dermatitis will perform an assessment of the overall appearance of the lesions at the timepoints indicated in the schedule of assessments (Table 1). The IGA score is determined using descriptors that best describe the affected area. It is not necessary that all characteristics under the morphological description be present. The evaluator that completes the IGA at baseline must complete all subsequent IGA for the same subject, to the extent that is possible. The IGA score will be documented in subject's source and recorded in eCRF.

8.3.2 Scoring Atopic Dermatitis

The SCORAD is a validated, clinical scoring index for atopic dermatitis, which provides a total score based on the area affected or extent of disease (0-100), severity/intensity (0-18), and subjective symptoms based on pruritus and sleep loss (0-20). A total score of under 25 represents mild AD, score between 25 and 50 represents moderate AD, and a score over 50 represents severe AD. The SCORAD will be completed at the timepoints indicated in the schedule of assessments (Table 1).

8.3.3 Eczema Area and Severity Index and Affected Body Surface Area

The Eczema Area and Severity Index quantifies the severity of a subject's atopic dermatitis based on both severity of lesion clinical signs and the percent of BSA affected. The EASI score is a composite score, and scores the degree of erythema, edema/papulation, excoriation, and lichenification for 4 separate body regions on a 4-point scale (0 to 3). The evaluator that completes the EASI at baseline must complete all subsequent IGA for the same subject, to the extent that is possible. The EASI and BSA assessment will be completed at the timepoints indicated in the schedule of assessments (Table 1).

The number of handprints, or unit of measurement using the size of the subject's hand with closed fingers, of skin afflicted with atopic dermatitis in a body region can be used to determine the extent (%) to which a body region is involved with atopic dermatitis. 1% BSA is equal to the palm plus 5 digits, with fingers tucked together and thumb tucked to the side (handprint) and the thumb is equal to 0.1% BSA. The BSA ranges from 0 to 100%, with higher values representing greater severity of atopic dermatitis. The scalp, palms, and soles may be included in the BSA assessment.

8.3.4 Hamilton Depression Rating Scale

The HAM-D is a widely used clinician-administered depression assessment scale. The questionnaire contains items relating to symptoms of depression experienced in the past week (Williams JB 1988). The questionnaire is completed by the Investigator, after an unstructured interview with the subject to determine their symptoms. A total score is calculated by summing the individual scores from each question. The HAM-D rating scale will be completed at the timepoints indicated in the schedule of assessments (Table 1).

8.3.5 Patient-Reported Outcomes

Subjects will complete the self-administered patient-reported outcome assessments and questionnaires as indicated in the schedule of assessments. Subjects should be instructed to follow the instructions provided with the instrument and to provide the best possible response to each item. Subjects who are functionally unable to read the instruments may have site personnel read the questionnaire to them. The subject should complete the questionnaires at the timepoints indicated in the schedule of assessments (Table 1) and before site personnel perform any clinical assessments to avoid biasing the subject's response.

8.3.5.1 Patient-Oriented Eczema Measure

The POEM is a 7-item PRO measure used to assess the impact of AD over the past week.

8.3.5.2 Beck Anxiety Inventory Questionnaire

The Beck Anxiety Inventory questionnaire is a 21 item self-reported scale measuring anxiety (Beck et al., 1988). The total score is calculated by finding the sum of the 21 items. A score of 0 – 21 equates to low anxiety, a score of 22 – 35 equates to moderate anxiety, and a score of 36 and above equates to potentially concerning levels of anxiety.

8.3.5.3 Peak Pruritus Numerical Rating Scale

The Peak Pruritus NRS is an assessment tool that subjects used to report the intensity of their pruritus (itch) during a 24-hour period. Subjects will be asked to rate their itch daily, on a horizontal scale from 0 to 10, at the worst moment in the previous 24-hour period.

8.4 AD Flare-up

An atopic dermatitis flare-up is defined as worsening of disease by extent or severity, for which requires escalation or intensification of treatment, in the opinion of the Investigator. Flare-ups may induce or exacerbate skin inflammation and pruritus. Flares may be triggered by several factors including exposure to allergens, stress, hormonal changes, irritating clothing, or fabric, change in weather (hot or cold), or change in medications. Start and stop dates, as well as possible triggers for flare-ups will be documented in source and captured in eCRF.

9 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

All AEs occurring during the trial, from the time the subject signs informed consent until the subject completes the trial, will be reported. Any SAEs that occur within 30 days of the end of treatment will also be reported. SAEs will be reported to the regulatory authorities and IRBs/REBs according to local regulations and will be followed up until the event is resolved or stabilized.

9.1 Definitions

Adverse Event: an adverse event is any untoward medical occurrence or worsening of a pre-existing medical condition in a trial subject. Adverse events include unfavorable, or unintended signs or symptoms and worsening of pre-existing diseases that may or may not be related to the investigational treatment administered. Adverse events may be caused by something other than the investigational product, and therefore, do not necessarily have to have a causal relationship to IP.

Abnormal laboratory values or vital signs abnormalities are considered to be AEs, only if they are medically relevant or clinically significant. In the case of chronic disease, if the disease is known and present when the subject enters the trial, only worsening of the disease (i.e., increased frequency or intensity) will be considered as an AE.

Serious Adverse Event: a serious adverse event is an adverse event that meets one of the following criteria:

- Results in death
- Life-threatening, (i.e., immediate risk of death)
- Requires in-patient hospitalization, or prolongation of existing hospitalization
- Results in residual or significant disability or incapacity
- A congenital anomaly/birth defect
- An important medical event, requiring intensive treatment (i.e., bronchospasms, blood dyscrasias, convulsions, development of cancer, or drug abuse).

The following are not considered to be SAEs: elective procedures that require admission to the hospital, in-patient procedures planned prior to signing the inform consent form (e.g., angioplasty), or emergency room visits for less than 24 hours that are an event that is not medically important or life-threatening.

9.2 Adverse Event Assessment and Reporting

Adverse events can be spontaneously reported by the subject, elicited during open-ended questioning, or observed during examination or evaluation of the subject. Adverse events will be collected by non-leading questions (i.e., "Have you experienced any change in your health since your last visit?"), direct observations, or spontaneously reports by the subject. To prevent reporting bias, subjects should not be questioned regarding the specific occurrence of one or more AEs.

Clinically significant signs, symptoms, and abnormal diagnostic procedures should be grouped together and recorded as a single diagnosis or syndrome, whenever possible. Adverse event details including start/stop date, severity, seriousness, relationship to trial drug and action taken, and outcome should be documented in source and recorded in the eCRF.

9.2.1 Severity

Severity of an AE is defined as a qualitative assessment of the degree of intensity of an AE as determined by the Investigator or reported by the subject. The assessment of severity is made irrespective of relationship to trial procedures or seriousness of the event and should be evaluated according to the following scale:

- **Grade 1 (Mild)** - asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
- **Grade 2 (Moderate)** - minimal, local, or noninvasive intervention indicated, limiting age-appropriate instrumental activities of daily living (ADL)

- **Grade 3 (Severe)** - medically significant but not immediately life-threatening; hospitalization indicated; disabling; limiting self-care ADL
- **Grade 4 (Life-threatening)** - serious consequences; urgent intervention indicated
- **Grade 5 (Death)** - AE resulting in death

9.2.2 Relationship to Trial Treatment

Assessment of causality is based on the following considerations: associative connections (time or place), pharmacological explanations, previous knowledge of the drug, presence of characteristic clinical or pathological phenomena, exclusion of other causes, or absence of alternative explanations.

The Investigator will assess the causal relationship to the trial treatment according to the following classifications:

- **Definite:** A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (de-challenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically using a satisfactory re-challenge (the drug is readministered to determine if the same reaction occurs) procedure if necessary.
- **Probable:** A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (de-challenge) should be clinically plausible.
- **Possible:** A clinical event, including laboratory test abnormality, with a reasonable time sequence to the drug administration, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.
- **Unlikely**: A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable and in which other drugs, chemicals or underlying disease provide plausible explanations.
- **Not related**: Any event that does not meet the above criteria; there is sufficient information that etiology of the event is in no relation to the trial treatment.

9.2.3 Action Taken with Investigational Product

The Investigator will be asked to record action taken in relation to the trial or trial treatment and to other treatments. The categories in relation to the trial or trial treatment are:

- No action taken
- Investigational product dose reduced
- Investigational product discontinued temporarily
- Investigational product discontinued permanently

- Not applicable

9.2.4 Outcome

The Investigator will be asked to record the outcome by choosing one of the following alternatives:

- Recovered
- Recovering
- Not recovered
- Recovered with sequelae
- Unknown

9.3 Reporting of Serious Adverse Events

The Investigator must report all SAEs, regardless of the causal relationship to IP, immediately and within 24 hours of having notified of the event to the Sponsor's representative. Any new and unexpected SAEs must be reported to the IRB/REB as required by local regulations. Suspected unexpected serious adverse reactions (SUSARs) are AEs that are considered by the Investigator and Sponsor to be related to trial treatment and are both unexpected (i.e., the nature or severity is not expected from the information provided in the Investigator Brochure) and serious. ADX-629 is at an early stage of development, therefore, any SAE deemed related to the trial treatment will be considered unexpected and will be reported as a SUSAR.

Suspected unexpected serious adverse reactions are subject to expedited reporting to the Regulatory Authorities and IRB/REB as appropriate. Investigators should provide written documentation of IRB/REB notification for each report to the Sponsor or CRO. The Sponsor or CRO will ensure that the appropriate regulatory authorities are notified of all reportable SAEs. The Sponsor or Sponsor's representative may make expedited reports of all SAEs that are expected and causally related to the trial drug to the Competent Authorities, according to local regulations.

Safety Contact Information - SAE Reporting :



The initial report can be followed by a follow-up report as soon as the Investigator obtains more specific information on the event. Every effort should be made to document further any SAE that is fatal or life-threatening within 1 week (7 days) after the initial notification. The Investigator must also send copies of all examinations carried out and the dates on which these

examinations were performed. Laboratory reference ranges should be included for all laboratory results. Care should be taken to ensure that the subject's identity is protected and the subject's identifiers in the clinical trial are not included on any copy of source documents provided to the Sponsor.

9.3.1.1 Initial Reports

All SAEs occurring from the time of informed consent until the completion of End of Trial Visit must be reported within 24 hours of the knowledge of the occurrence. After the End of Trial Visit, any SAE that the Investigator considers related to trial drug must be reported to the Sponsor or the designee.

9.3.1.2 Follow-up Reports

The Investigator must continue to follow the patient until the SAE has subsided or until the condition becomes chronic in nature, stabilizes (in the case of residual impairment), or the patient dies. Within 24 hours of receipt of follow-up information, the Investigator must update the SAE form electronically in the EDC system for the trial and submit any supporting documentation (e.g., patient discharge summary or autopsy reports) via fax or email. If it is not possible to access the EDC system, refer to the procedures outlined above for initial reporting of SAEs. Refer to Sponsor contact list for additional contact details.

9.3.1.3 Discontinuation Due to Serious Adverse Events

The onset of an SAE is a reason for premature discontinuation of trial treatment. If the trial treatment is permanently discontinued because of an AE, this must be documented in the eCRF. Refer to Section 5.5.2 for more details.

9.3.2 Pregnancy

In the event of pregnancy, the trial drug must be discontinued, and the Sponsor informed immediately (i.e., within 1 working day). Pregnancy in a female trial subject, or in a female partner of a male trial subject, during the trial period or within 4 weeks after the last dose of IP, must be reported to the Sponsor within 24 hours of knowledge of its occurrence by the investigative site staff. The pregnancy will be followed up until the outcome has been determined. Any SAE experienced during pregnancy, or if the outcome of the pregnancy is a congenital anomaly or birth defect, the procedure for reporting SAEs (Section 9.3) will be followed.

10 DATA MANAGEMENT

10.1 Case Report Forms

Data will be collected on eCRFs that are specifically designed for this trial. The Investigator or person designated by him or her will record subject data as accurately as possible in the eCRFs.

The Investigator must provide an electronic signature to attest to the accuracy and completeness of all the data. If any changes are made to an eCRF after a form has been locked and electronically signed, the Investigator will be required to perform an additional electronic signature authorizing agreement with any new information or changes to the eCRF.

All corrections on the eCRF will be automatically tracked and a reason for change is always required.

10.2 Data Management Plan and Database Design

Detailed information on data management will be provided in a data management plan (DMP) that will be written specifically for this trial. All plans and deviations will be documented in the DMP, unless a trial-specific plan, guideline, or specification is created.

The trial database will be defined according to the corresponding eCRFs and the trial protocol. Standard design templates will be used, and trial-specific items will be created as required. Data validation or data cleaning procedures are designed to assure validity and accuracy of clinical data. They consist of reviewing data entered, and computerized edit checks and queries for identifying data values that are out of range, protocol violations, incomplete or inconsistent. The DMP will specify the checks that are to be performed on subject data to raise data discrepancies or queries and will define the electronic edit checks and data validation queries to be created for the trial.

Queries will be raised for all errors discovered in the clinical data, when information is missing, or needs further clarification.

10.3 Handling of External Data

External data consists of data that is not recorded on eCRFs. Data may be received in electronic format or paper printout. Key variables will be defined to uniquely identify each sample record. File and data formats will be agreed with the external data provider. Any data transferred between the external data provider and data management must contain the origin, date created, date sent and number of records at minimum. The source of all external data will be specified in the DMP.

10.4 Database Lock

All data entry, verification, medical encoding, and data validation activities will be finalized before the database is locked. Quality control activities will be completed to acceptable error

rates. All unnecessary user privileges to the trial will be removed, except for the Data Manager who will perform the database lock.

In exceptional circumstances, when critical reasons are justified, there may be a need to perform updates to the database after it has been locked. A database that is locked and released for analysis will only be unlocked if an error is identified that will significantly affect the statistical outcome of the analysis of the efficacy parameters or change the safety profile of the trial.

11 STATISTICAL ANALYSES

11.1 General Statistical Considerations

A formal Statistical Analysis Plan (SAP) will be developed and finalized prior to locking and unblinding the trial database. The full details of data presentations and analyses will be provided in the SAP. The SAP will rule over any statistical language in the protocol. Additional statistical analyses other than those described in this section may be performed if deemed appropriate and included in the SAP. Any deviations from the final SAP will be discussed in the final trial report.

11.2 Protocol Deviations

Deviations from the protocol will be categorized as 'minor' or 'major'. A protocol deviation plan will include the definition of major and minor protocol deviations and the identification of major protocol deviations which will be excluded from the per-protocol analysis. Protocol deviations will be assessed regularly and finalized prior to database lock and unblinding.

11.3 Populations for Analyses

11.3.1 Screened Population

All subjects who signed the ICF and underwent screening assessments

11.3.2 Intent-to-Treat Population

All subjects who were met eligibility criteria and were enrolled into the trial

11.3.3 Safety Population

All subjects in the intent-to-treat (ITT) Population who received at least one dose of IP

11.3.4 Per-Protocol Population

All subjects in the safety population who completed the trial, excluding subjects/data points with one or more major deviations which impacts the efficacy results

11.4 Determination of Sample Size and Statistical Hypotheses

[redacted]

[redacted]

11.5 Analysis of Safety Data

All safety analyses will be based upon the safety population. Subjects will be analyzed by background therapy and treatment group. Frequency distributions and individual listings of all adverse events will be generated. Treatment-emergent adverse events (TEAE) will be summarized by treatment group and by system organ class and preferred term, in accordance with the latest MedDRA coding dictionary. A TEAE is defined as an adverse event that emerges during the treatment period (having been absent pre-treatment) or worsens relative to the pre-treatment period. Safety variables will be summarized descriptively by treatment and background therapy. The number of subjects reporting each AE preferred term will be tabulated for all TEAEs and separately for those considered as at least possibly related to trial treatment by the Investigator.

11.6 Interim Analysis

[redacted]

11.7 Analysis of Efficacy Data

The ITT Population will be the primary analysis population for efficacy. Subjects will be analyzed by planned treatment, disease severity at baseline, and background therapy. The PP set will be used for a sensitivity analysis of the efficacy data. Efficacy data will be summarized by treatment group, AD severity at baseline, and background treatment. The analysis for Part 2 will be performed once all subjects complete the end-of-study visit or discontinue prematurely. The double-blind analysis for Part 2 will include the analysis of the primary efficacy endpoint and all other efficacy endpoints.

12 REGULATORY, ETHICAL, AND TRIAL OVERSIGHT CONSIDERATIONS

12.1 Clinical Monitoring

Clinical monitoring is conducted to ensure that the rights and well-being of subjects are protected, that the reported trial data is accurate, complete, and verifiable, and that the conduct of the trial follows the approved protocol/amendment(s), ICH GCP, and applicable regulatory requirement(s). The trial will be monitored regularly, according to a monitoring plan that will be written specifically for this trial. The monitoring plan will define the nature of monitoring (e.g., on-site, central, or remote), monitoring frequency, and detailed procedures. In general, during monitoring visits, the monitor will ensure that the trial is being conducted according to the protocol, ICH GCP guidelines, other applicable regulations, and will compare the eCRF entries to original source data. The monitor will also make sure that the informed consent procedure has been carried out correctly and will ensure that all SAEs have been reported within the required timeframes. The monitor will check that trial drug accountability has been

maintained and will, after completion of the trial, perform final accountability and arrange for the return or destruction of IP.

12.2 Audits and Inspections

The Sponsor has the right to perform an audit of the trial site and the CRO.

The regulatory authorities, both national and foreign, may inspect the investigative site at any time. The Investigator is responsible for notifying the Sponsor of such an inspection immediately after gaining knowledge of it.

During the audit or inspection, the Investigator will permit the auditor, IRB/REB reviewer, and regulatory inspector(s) direct access to all relevant medical records and other source data, trial-related files, and eCRFs.

12.3 Future Use of Stored Specimens and Data

Biological samples and specimens are not intended to be stored after the trial is complete.

12.4 Record Keeping and Archiving

Essential documents must be retained for at least a period of 2 years following the date a marketing application is approved for the trial 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 2 years after the investigation is discontinued and Food and Drug Administration (FDA) is notified. The Investigator must take measures to prevent accidental or premature destruction of any essential documents. The Investigator must not destroy any trial-specific documentation before receiving written permission for this from the Sponsor.

12.5 Ethics

12.5.1 Institutional Review Board/Research Ethics Board

The trial will not commence until favorable opinion has been obtained from the appropriate IRB/REB and the Competent Authority.

If any alterations, other than changes of an administrative nature, are made to the trial protocol, a formal protocol amendment will be issued and submitted to relevant IRB/REB for approval. The amendment will not be implemented until approval has been received from the IRB/REB, except in cases where immediate implementation is necessary to eliminate or prevent imminent hazard to the subjects. In such a case, the deviation will be reported to the IRB/REB as soon as possible.

12.5.2 Guidelines and Regulations

The trial will be conducted in accordance with the principles of the Declaration of Helsinki and in compliance with FDA Code of Federal Regulations Part 312, Section 21, ICH GCP E6 (R2), and the regulations on electronic records and electronic signature (21 CFR 11).

12.5.3 Subject Confidentiality

The Investigator(s) will respect and protect the confidentiality of the subject in all possible ways. Subject identification, other than the subject's trial number and age, will not appear in any eCRF pages or other documents given to the Sponsor. Only the Investigator and the persons authorized to verify the quality and integrity of the trial will have access to subject records where the subject can be identified.

12.6 Financing and Insurance

12.6.1 Financial Issues

Financial contracts will be signed between the Sponsor and the Investigator or a representative of the investigative site before commencement of the trial.

12.6.2 Insurance

The Sponsor will provide Product Liability insurance for all subjects included in the clinical trial.

12.7 Trial Report and Publications

A final clinical trial report will be prepared according to the ICH guideline on structure and contents of clinical trial reports on completion of the trial. The trial will be considered to have finished after the last subject has completed the last trial visit.

A final clinical trial report will be prepared where any subject has signed the ICF, regardless of whether the trial is completed or prematurely terminated. Where appropriate, an abbreviated report may be prepared. The clinical trial report will be in compliance with any applicable regulatory requirements, national laws in force and will be in English.

The publication of trial results will be agreed upon between the Sponsor and the Investigator(s). The Sponsor is interested in publishing the results of the trial but to prevent publication of any confidential information, the Sponsor retains the right to review all publications and presentations before they are made public and may delay any publication if necessary for reasons of intellectual property protection. However, the Sponsor will not have the right to prevent publication of the trial results indefinitely.

12.8 Trial Committees

No committees are associated with this trial.

12.9 Contact Information

Sponsor:



13 ABBREVIATIONS

%CV	Percent coefficient of variation
AD	Atopic Dermatitis
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BAI	Beck Anxiety Inventory
BID	Twice daily (*bis in die*)
CKD-EPI	Chronic Kidney Disease Epidemiology
C_{max}	Maximum plasma concentration
CRO	Contract Research Organization
CYP	Cytochrome P450
DMP	Data management plan
EASI	Eczema Area and Severity Index
ECG	Electrocardiogram
EDC	Electronic Data Capture
eCRF	Electronic case report form
eGFR	Estimated glomerular filtration rate
EOS	End of Study
EOT	End of Treatment
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HAM-D	Hamilton Rating Scale for Depression
HDL-C	High-density lipoprotein Cholesterol
HNE	Hydroxynonenal
ICF	Informed consent form
ICH	International Council for Harmonisation
IL	Interleukin
IP	Investigational product
IGA	Investigator's Global Assessment
IRB	Institutional Review Board

ITT	Intent-to-Treat
IUD	Intrauterine device
LDL-C	Low-density lipoprotein Cholesterol
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MDA	Malondialdehyde
MedDRA	Medical Dictionary for Regulatory Activities
NRS	Numerical Rating Scale
PASI	Psoriasis area and severity index
POEM	Patient-Oriented Eczema Measure
QTcF	QT interval corrected for heart rate using Fridericia's formula
RASP	Reactive aldehyde species
RBC	Red blood cell
REB	Research Ethics Board
SAE	Serious adverse event
SAP	Statistical analysis plan
SCORAD	Scoring Atopic Dermatitis
SOC	Standard-of-Care
SUSAR	Suspected unexpected serious adverse reaction
TEAE	Treatment-emergent adverse event
TNFα	Tumor necrosis factor alpha
ULN	Upper limit of normal
UV	Ultraviolet

14 REFERENCES

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Table 4: 1 Version 2.0 Summary of Changes Table

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[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]