STUDY PROTOCOL

ATM-2301

Patient Self-Administered Intralesional Injections of Triamcinolone for Acne Vulgaris

Proof of Concept Study

Version 1.0
31-Jan-2023

Study Sponsor
ACOM Labs Inc.
1 Letterman Dr., Suite C3500
San Francisco, California, USA 94129

Clinical Research Organization
ethica CRO Inc.
3551 St. Charles Blvd, Suite 501
Kirkland, Quebec, Canada H9H 3C4

agreement with the Sponsor, except to other study personnel and to the extent necessary to obtain informed consent from participating subject.

PROTOCOL APPROVAL SIGNATURE PAGE

The following individuals approve this version of Protocol ATM-2301. All changes to this version of the protocol must have a prior written approval and require an amendment or administrative letter.

Approved by Sponsor – ACOM Labs Inc.

Printed Name	Title
Signature	Date

INVESTIGATOR SIGNATURE PAGE

I agree to:

- Implement and conduct this study diligently and in strict compliance with the protocol, good clinical practices and all applicable laws and regulations.
- Maintain all information supplied by ACOM Labs, Inc. in confidence and, when this information is submitted to an Institutional Review Board (IRB) or another group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Principal Investigator *(Printed Name)*	Signature	Date

SYNOPSIS

Version	Version 1.0 (31-Jan-2023)	**Study Device**	Injection Assistance Device
Study Number	ATM-2301		
Phase	Proof of Concept	**Control Product**	Not Applicable
Indication	Inflammatory Acne Lesions	**Study Sites**	~3 sites (US)
Title	Patient Self-Administered Intralesional Injections of Triamcinolone for Acne Vulgaris		
Sponsor	ACOM Labs, Inc.		
Study Duration	14 days per subject	**Sample Size**	~150 subjects
Study Design	This is an open-label, prospective, single-arm study. Approximately 150 subjects will be enrolled at approximately 3 study sites. All subjects will receive standard-of-care intralesional injection with triamcinolone using an Injection Assistance Device (i.e., for self-administered intralesional injections) at Visit 1 (Day 1). Subjects will then submit photos via secure photographic app for asynchronous follow up on Day 2 (24-hours post-injection), Day 3 (48-hours post-injection), Day 4 (72-hours post-injection), Day 7, and Day 14. Efficacy assessments (target lesion assessments) will be conducted remotely by the Investigator at time of each photo submission. Subjects will conduct lesion pain assessments and satisfaction assessments at the time of each remote check-in. Participants will be invited to also have additional photography captured by the study team at the study site or at a location as per participants' convenience.		
Study Objectives	The objective of this proof-of-concept study is to investigate the immediate safety of self-administered intralesional injections of triamcinolone using an Injection Assistance Device.		
Inclusion Criteria	1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Baseline. 2. Diagnosed with facial acne vulgaris. 3. At least one (1) identifiable inflammatory lesion that, in the opinion of the investigator, is clinically indicated for standard-of-care intralesional injection(s) of triamcinolone. 4. Owner of smartphone with capacity for front-facing photography and app download from Apple App Store or Google Play. 5. Able to follow study instructions and likely to comply with virtual follow-up requirements. 6. In good general health as determined by medical history at the time of screening (Investigator discretion). 7. Sign the IRB-approved ICF (including HIPAA authorization) prior to any study-related procedures being performed.		
Exclusion Criteria	1. Female subjects who are pregnant or breast-feeding. 2. Known hypersensitivity or previous allergic reaction to any constituent of triamcinolone injection. 3. Active cutaneous viral infection in any treatment area at Baseline. 4. Have concomitant skin disease or infection (other than acne) or presence of skin comorbidities in the areas of skin where study device will be used. 5. History of poor cooperation or unreliability (Investigator discretion). 6. Subjects who are investigational site staff members or family members of such employees. 7. Exposure to any other investigational device within 30 days prior to Visit 1.		

Study Treatment	**Delivery System and Injection Assistance Device:** The Delivery System consists of an Injection Assistance Device used with a sterile, single use 32G intradermal safety needle and 1 mL luer lock syringe containing triamcinolone. The Injection Assistance Device is the durable component of the delivery system and is a non-sterile, single patient use, reusable device intended for use by patients to deliver an intradermal injection of 0.1 mL of an FDA-approved drug contained in a commercially-available sterile, single use, 1 mL plastic luer syringe **Triamcinolone for Injection:** A commercial supply of triamcinolone for injection will be used for injection. The site will store triamcinolone as per the conditions described in the package insert. A 1.0mL luer syringe will be loaded with an appropriate volume and concentration of triamcinolone. A total of 0.1 mL of triamcinolone 1.0% will be injected into each target lesion. The syringe will then be installed into the Injection Assistance Device. At least one (1), and up to three (3) inflammatory target lesions will be selected for intralesional injections of triamcinolone using the Injection Assistance Device.
Blinding	Not applicable
Investigator Assessments	• **Global Severity Score (GSS):** A 5-point scale assessing ranging from 0 (Clear) to 4 (Severe). *Note: only Baseline assessments will be conducted.* • **Target Lesion Erythema:** A 5-point scale ranging from 0 (No Erythema) to 4 (Very Severe Erythema). • **Target Lesion Severity:** A 5-point scale ranging from 0 (None) to 4 (Very Severe). • **Target Lesion Improvement:** A 7-point scale ranging from 1 (Clear; 100%) to 7 (Worse). • **Target Lesion Videography:** A video will be taken of each injected lesion starting from just prior to needle penetration and up to 10 seconds after removed of needle from lesion. • **Target Lesion Photography:** Photographs will be taken by study team at Baseline both pre- and post-injection. Participants can elect to have additional photography captured by the trial team at clinic or location of participants' convenience at each study time point, or to use the photography app that can be used outside of the clinic.
Subject Assessments	• **Target lesion time course:** At Baseline, subjects will report approximate length of time (in days) since lesion emerged on face**.** • **Target Lesion Pain:** Target lesion pain will be self-assessed by the subject using a Visual Analog Scale. • **Target Lesion Injection Pain:** Target lesion injection pain will be self-assessed by the subject using a Visual Analog Scale immediately after the injection of the first target lesion and at 5 minutes post-injection. • **Subject Satisfaction:** A 5-point scale ranging from 1 (Very satisfied) to 4 (Very dissatisfied). • **Target lesion Photography:** Participants will take photos of each injected inflammatory lesion at each study time point with the photography app. At Baseline, photographs will be taken by participants both pre- and post-injection. Participants can elect to have additional photography captured by the trial team at clinic or location of participants' convenience. For tracking of lesion number and size, participants will place next to each lesion a numbered adhesive sticker prior to each photography session.
Safety Endpoints	Adverse Events
Sample Size	Approximately 150 subjects will be enrolled. This is a POC study and a formal sample size justification is not provided for this study. It is the opinion of the Sponsor that a total of 150 subjects will be sufficient to achieve the objective of the study.
Statistical Methods	For categorical parameters, the number and percentage of subjects/observations in each category will be presented. The denominator will be based on the number of subjects/observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will

	include n (number of subjects or observations), mean, standard deviation, median, and range. Two-sided 95% CIs will be provided for all study outcomes. The modified Intent-to-Treat (mITT) Population (defined as all subjects who were enrolled and received at least one application with the study device) will be used for analyses of safety and effectiveness endpoints. A Per-Protocol (PP) Population will neither be defined nor analyzed.

SCHEDULE OF EVENTS AND PROCEDURES

Visit Number	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**
Day/Week/Month	**Day 1**	**24hr Post-Inj.**	**48hr Post-Inj.**	**72hr Post-Inj.**	**Day 7** *±1 day*	**Day 14** *±2 days*
Assessment and Procedures						
Informed Consent	X					
Inc/Excl Criteria	X					
Demographics, Med Hx	X					
Intralesional Injection(s)	X					
Investigator Assessments						
Global Severity Score	X					
Target Lesion Assessments	X	X	X	X	X	X
Target Lesion Photography	X *pre-/post- inj.*	X *opt-in*	X *opt-in*	X *opt-in*	X *opt-in*	X *opt-in*
Lesion Injection Videography	X					
Subject Assessments						
Target Lesion Pain	X *pre-inj.*	X	X	X	X	X
Intralesional Injection Pain	X *post- inj.*					
Target Lesion Photography	X *pre-/post- inj.*	X	X	X	X	X
Subject Satisfaction		X	X	X	X	X
Safety Assessments						
UPT (as applicable)	X					
Concomitant Medications	X					
Adverse Events	X	X	X	X	X	X

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11 INTRODUCTION

Intralesional injections are a commonplace, low risk therapy for acne lesions. They are typically dosed with triamcinolone acetonide at concentrations of 0.5 mg/mL to 2.5 mg/mL (i.e., 0.5% to 2.5%) in volumes of 0.05 mL to 0.15 mL.

This proof-of-concept study will investigate the safety of self-administered intralesional triamcinolone injections in patients with acne vulgaris using an Injection Assistance Device.

As intralesional triamcinolone injections are standard-of-care, the purpose of this proof-of-concept study is to test the safety of the Injection Assistance Device, not the safety and efficacy of triamcinolone per-se.

12 STUDY OBJECTIVE

The objective of this proof-of-concept study is to investigate the safety of self-administered intralesional injections of triamcinolone using an Injection Assistance Device.

13 COMPLIANCE STATEMENT

The study will be conducted in accordance with the Clinical Investigation Plan, International Conference on Harmonization (ICH) and Good Clinical Practice (GCP), the Declaration of Helsinki, International Organization for Standardization (ISO) 14155, and the United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312). In addition, the study will be conducted in compliance with all applicable laws and regulatory requirements relevant to the use of new medical devices in the United States.

The sites' Principal Investigator (PI) is responsible for ensuring the privacy, safety and welfare of the subjects during and after the study and must ensure that site personnel are appropriately trained. The PI at each site has the overall responsibility for the conduct and administration of the study at their site, and for contact with study site management, and local authorities.

13.1 Variations to the Protocol

No changes from the final approved (signed) protocol will be initiated without the prior approval by the IRB except 1) when necessary to eliminate immediate hazards to the subjects or when the change involves only logistics or administration, or 2) minor administrative or typographical corrections. The sites' PIs and the Sponsor must sign any protocol amendments.

13.2 Investigational Sites

One (1) to three (3) U.S. investigational site will participate in this study. All sites must obtain written approval from a 21 CFR 56 compliant IRB prior to recruitment and enrollment of any subject into the study. Any changes to the study procedures must be made with the mutual agreement of the PI and the Sponsor, documented in an amendment to the protocol, and approved by the reviewing IRB.

14 OVERVIEW OF STUDY DESIGN

This is an open-label, prospective, single-arm study. Approximately 150 subjects will be enrolled at 1 study site. A full description of the inclusion and exclusion criteria can be found in Section 5.

All subjects will self-administer treatment with the study device (i.e., intralesional injection with triamcinolone) at Visit 1 (Day 1). Subjects will submit photos via app pre- and post-injection at Visit 1 (Day 1) and for remote follow-up at Day 2 (24-hours post-injection), Day 3 (48-hours post-injection), Day 4 (72-hours post-injection), Day 7, and Day 14.

15 STUDY POPULATION

Potential study participants may be identified and recruited into the study through various methods, such as:

- Database of individuals who have agreed to be contacted for future studies;
- In-person recruitment;
- Physician to physician referrals;
- Internet advertisement;
- Print advertisement.

Note that scripts and advertisement fliers will be submitted to the IRB as necessary.

15.1 Inclusion Criteria

1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Baseline.

   A female is considered of childbearing potential unless she is:

   - *postmenopausal for at least 12 months prior to study device administration;*
   - *without a uterus and/or both ovaries; or*
   - *has been surgically sterile for at least 6 months prior to study device administration.*

2. Diagnosed with facial acne vulgaris.
3. At least one (1) identifiable inflammatory lesion that, in the opinion of the investigator, is clinically indicated for standard-of-care intralesional injection(s) of triamcinolone.
4. Owner of smartphone with capacity for front-facing photography and app download from Apple App Store or Google Play.
5. Able to follow study instructions and likely to complete all required visits.
6. In good general health as determined by medical history at the time of screening (Investigator discretion).
7. Sign the IRB-approved ICF (including HIPAA authorization) prior to any study-related procedures being performed.

15.2 Exclusion Criteria

1. Female subjects who are pregnant or breast-feeding.

2. Known hypersensitivity or previous allergic reaction to any constituent of triamcinolone injection.
3. Active cutaneous viral infection in any treatment area at Baseline.
4. Have concomitant skin disease or infection (other than acne) or presence of skin comorbidities in the areas of skin where study device will be used.
5. History of poor cooperation or unreliability (Investigator discretion).
6. Subjects who are investigational site staff members or family members of such employees.
7. Exposure to any other investigational device within 30 days prior to Visit 1.

15.3 Subject Withdrawal

Subjects are free to withdraw from participating in this study at any time and for whatever reason, specified or unspecified, and without prejudice. All premature discontinuations and their reasons must be carefully documented by the PI in the source documents, CRF, and (if applicable), on the AE form.

16 SUBJECT NUMBERING, RANDOMIZATION AND BLINDING

This is an open-label, non-randomized, single-group study. All subjects who are enrolled will receive treatment with the study device. Randomization and blinding are not applicable.

All enrolled subjects will receive a 3-digit subject number, starting at 001. Subject numbers will be assigned in ascending order. The subject number will be used to identify the subject throughout the study. Subjects withdrawn from the study will retain their subject number; new subjects will be allocated a new subject number. Screen Failures will not be entered in the eCRF.

17 CONCOMITANT AND PROHIBITED MEDICATION/PROCEDURES

17.1 Concomitant Medications and Procedures

All treatment/procedures received by the subject throughout the treatment period, including the name of the treatment/procedure, must be recorded in the CRF with end dates, if applicable. Every attempt should be made to keep concomitant therapy dosing constant during the study. Any change to concomitant therapy should be noted in source documents and the CRF.

There are no prohibited medications defined for the study. Any necessary therapies that are deemed appropriate by the Investigator are permitted. Subjects currently taking medications to treat acne should be instructed to maintain their current dosing throughout the study.

18 INVESTIGATIONAL PRODUCT MANAGEMENT

18.1 Delivery System

The Delivery System consists of an Injection Assistance Device used in conjunction with a sterile, single use 32G intradermal safety needle and 1 mL luer lock syringe containing triamcinolone. A schematic of the Delivery System is provided below in Figure 1.

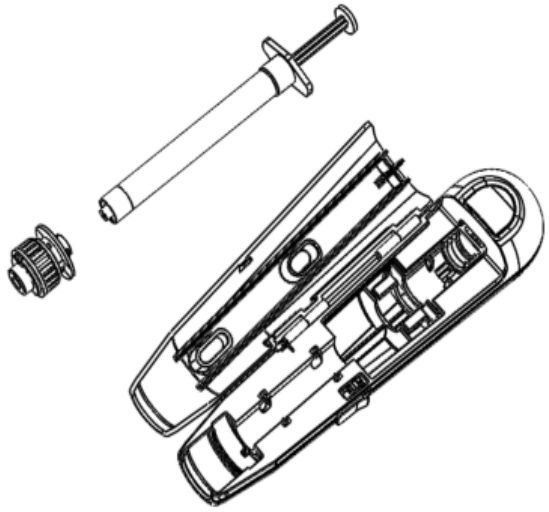

Figure 1. Delivery System

18.2 Injection Assistance Device

A commercial supply of triamcinolone 10% for injection will be provided to the site and diluted with saline to the appropriate concentration. The site will store triamcinolone as per the conditions described in the package insert.

A standard 32G 0.5" needle will be fixed to a 1.0 mL luer syringe and the syringe will be loaded with an appropriate volume and concentration of triamcinolone. A total of 0.05 mL to 0.15 mL of triamcinolone 0.5% to 2.5% will be injected into each target lesion. The choice of volume and concentration for each individual lesion will be at the discretion of the Investigator as per his clinical judgement. The needle will then be installed into the Injection Assistance Device.

At least one (1), and up to three (3) inflammatory target lesions will be selected for intralesional injections of triamcinolone using the intradermal needle adapter.

The Injection Assistance Device is the durable component of the delivery system. It is a non-sterile, single patient use, reusable device intended for use by patients to deliver an intradermal injection of 0.1 mL of an FDA-approved drug contained in a commercially available sterile, single use, 1mL plastic luer lock syringe.

18.3 Triamcinolone for Injection

A commercial supply of triamcinolone 10% for injection will be provided to sites and diluted with Saline to the appropriate concentration. Sites will store triamcinolone as per the conditions described in the package insert.

A 1.0 mL luer lock syringe will be loaded with an appropriate volume and concentration of triamcinolone by the study team. An intradermal safety needle will be affixed to the loaded syringe. A total of 0.1 mL of triamcinolone 1.0% will be injected into each target lesion.

18.4 Assembly of Delivery System and Injection delivery

The subject will load assembled, filled needle-syringe into the Injection Assistance Device and close the access door of the device. The subject then delivers the injection by depressing the tip of the Injection Assistance Device on the skin, at a 90-degree angle to the skin, then pressing the button to activate the device. The Injection Assistance Device then delivers a fixed volume (0.1 mL) into the dermis. The user then lifts the device from the injection site and the needle safety shield is engaged.

At least one (1), and up to three (3) inflammatory target lesions will be selected for intralesional injections of triamcinolone using the Injection Assistance Device.

19 DATA COLLECTION

19.1 Electronic Data Capture

Treatment and follow-up of subjects will be recorded with an app specifically designed for facial dermatologic photography (i.e., the "Appiell app"). This app enables subjects to take consistent, serial photographs of the lesion(s) treated at Visit 1.

Subjects will download the app at time of study enrollment and use the app to take photos and complete surveys throughout the study.

Participants will be trained regarding app use at Visit 1. Functionality of the app will be maintained by the Appiell engineering team, and any issue with app technical functionality will be reported promptly to the study team.

19.2 Photography

Target lesion photography (pre- and post-injection) will be performed at Visit 1 by the study coordinator at the sites using high-quality digital cameras. The same cameras will be used to take a video recording of the injection process. Stickers will be placed next to each lesion to identify lesions in all photos. Addition stickers will be placed on the face that indicate size and dimension.

Subjects will download the Appiell app to their smartphones at Visit 1 and, after training by the study coordinator, will take photographs (pre- and post-injection) of their target lesions.

The subject will be asked to sign a separate photography release form to specify whether he/she allows other uses of the photographs (e.g., publications, promotion). The subject's decision will be then tracked in a separate photography release log kept at the site.

9.3 Sponsor Follow-up

Subjects will be asked to sign a separate Sponsor contact release form to specify whether he/she allows the Sponsor to access contact information (name, phone number, email) for follow-up after completion of the study. Subject may select as many or as few of the following permissions as desired: 1) follow-up about study experience, including use of injection assistance device 2) user interviews about personal experience with acne 3) invitations to participate in future acne research

trials and 4) information about Sponsor's products, including the injection assistance device. The subject's decision will be then tracked in a separate Sponsor-contact release log kept at the site.

110 STUDY EVALUATIONS

110.1 Visit Procedures

110.1.1 Visit 1 (Baseline; Day 1)

- Written informed consent (incl. HIPAA and California Bill of Rights)
- Inclusion / exclusion criteria
- UPT (if female subject of childbearing potential)
- Medical history and demographics
- Concomitant medications/treatments
- Investigator Assessments
  - *Global Severity Score (GSS)*
  - *Target Lesion Assessments: lesion erythema, lesion severity*
  - *Target Lesion Photography (pre- and post-injection)*
  - *Target Lesion Injection Videography*
- Subject Assessments
  - *Target lesion time course (pre-injection)*
  - *Target lesion pain (pre-injection)*
  - *Intralesional injection pain (post-injection)*
  - *Target Lesion Photography (pre- and post-injection)*
- Intralesional injection(s)
- AE Assessment

110.1.2 Remote Follow-Up Visits 2 to 6 (24hr, 48hr, 72hr, 7 days±1 day, 14 days±2 days)

- Investigator Assessments of Submitted Photographs
  - *Target Lesion Assessments: lesion erythema, lesion severity, improvement*
  - *Target Lesion Photography (if opt-in)*
- Subject Assessments
  - *Target lesion photography*
  - *Target lesion pain*
  - *Target lesion improvement*
  - *Subject Satisfaction*
- Concomitant medications/treatments
- AE Assessment

110.2 Investigator Assessments

110.2.1 Global Severity Score (GSS)

The Investigator will use the GSS scale to determine subjects' Baseline acne severity (Table 1).

Table 1: Global Severity Score

Score	Grade	Description
0	**Clear**	Normal, clear skin with no evidence of acne vulgaris
1	**Almost Clear**	Rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red
2	**Mild**	Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
3	**Moderate**	Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may or may not be one nodulocystic lesion
4	**Severe**	Inflammatory lesions are more apparent, many comedones and papules/pustules, there may or may not be up to 2 nodulocystic lesions

110.2.2 Target Lesion Assessments

Up to 3 inflammatory lesions on the face will be chosen for intralesional injections of triamcinolone using the Injection Assistance Device as per Section 8. Days since lesion eruption will be also be reported by the participant for each lesion.

Each injected lesion will be individually assessed as per the following methods.

110.2.2.1 Target Lesion Erythema

The Investigator will use the following scale to determine the severity of erythema for each target lesion (Table 2).

Table 2: Target Lesion Erythema

Grade	Description
0	No Erythema
1	Mild Erythema
2	Moderate Erythema
3	Severe Erythema
4	Very Severe Erythema

110.2.2.2 Target Lesion Severity

The Investigator will determine the severity of each target lesion as per the scale in Table 3.

Table 3: Target Lesion Severity

Grade	Description
0	None
1	Mild
2	Moderate
3	Severe
4	Very Severe

110.2.2.3 Target Lesion Improvement

The Investigator will determine the improvement seen with each target lesion as per the scale in Table 4. Lesion improvement will not be assessed at Baseline.

Table 4: Target Lesion Improvement

Grade	Description
1	Clear (100%)
2	Almost clear (90% to <100%)
3	Marked improvement (75% to <90%)
4	Moderate improvement (50% to <75%)
5	Fair improvement (25% to <50%)
6	No change
7	Worse

110.3 Subject Assessments

110.3.1 Target Lesion Pain

For each inflammatory lesion injected, lesion pain will be assessed by the subject using a 10 cm Visual Analog Scale (VAS) Scale. Lesion pain at Baseline will be recorded prior to injection(s). The occurrence of inflammatory lesion pain is expected and will not be considered an AE.

110.3.2 Target Lesion Injection Pain

Injection pain will be assessed at each study timepoint by the subject using the VAS. Lesion pain at Baseline will be recorded prior to injection(s). Injection Site Pain during injection will be assessed immediately after the injection of the first target lesion and at 5 minutes post-injection. The occurrence of injection site pain is expected and will not be considered an AE.

110.3.2.1 Target Lesion Improvement

The subject will assess subjective improvement seen with each target lesion compared to Baseline as per the scale in Table 4. Lesion improvement will not be assessed at Baseline.

Table 4: Target Lesion Improvement

Grade	Description
1	Clear (100%)
2	Almost clear (90% to <100%)
3	Marked improvement (75% to <90%)
4	Moderate improvement (50% to <75%)
5	Fair improvement (25% to <50%)
6	No change
7	Worse

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110.3.3 Subject Satisfaction

Subject Satisfaction will be assessed by the subject using the following subjective 5-grade scale as detailed in Table 5. Subject will be instructed: “Rate your level of satisfaction with the effect of study treatment on inflammatory acne lesions by using the following scale”:

Table 5. Subject Satisfaction Scale

Grade	Description
1	Very satisfied
2	Satisfied
3	Neither satisfied nor dissatisfied
4	Dissatisfied
5	Very dissatisfied

110.3.3.1 Target Lesion Videography

A video will be taken of the entire injection process, including preparation, application of device to skin, needle penetration, and up to 30 seconds after removed of needle from lesion.

110.3.3.2 Target Lesion Photography

Photographs will be taken at each study time point of each injected inflammatory lesion. At Baseline, photographs will be taken both pre- and post-injection. At Baseline, photographs will be taken by the study team and by subject. At other timepoints, photographs will be taken by subject with the option to participate in further photography by the study team. Prior to each photographic session, numbered stickers will be placed on the face next to each lesion selected for treatment.

110.4 Safety

110.4.1 Adverse Events

All observed or volunteered AEs regardless of suspected causal relationship to the study device will be recorded in the CRF. Subjects will be questioned for the occurrence of any new or worsening signs or symptoms at each visit.

110.4.1.1 Definition of Adverse Event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a study device and which does not necessarily have a causal relationship with the study device. AEs include any unfavorable and unintended illness, sign, symptom, clinically significant laboratory test abnormality, or disease temporally associated with the use of a study device that has appeared or worsened during the course of the clinical trial, regardless of causal relationship to the study device under study.

The collection of non-serious AEs and serious adverse events (SAEs) will begin following the subject's exposure to study device.

110.4.1.2 Documenting Adverse Experiences

The PI is responsible for documenting all Treatment-Related AEs (TRAEs) and SAEs that occur at the study visits. AEs should be documented as a single medical diagnosis. When this is not possible, AEs should be documented in terms of signs/symptoms observed by the PI or reported by the subject at each study visit. Each AE that appears to be independent of any prior event will be reported separately.

All TRAEs occurring after the subject first exposure to study device through the last study visit must be reported. AEs that are not related to study treatment will not be recorded. All SAEs will

be recorded.

At the first study visit, the subject will be assessed for the occurrence of TRAEs. The following data will be collected on all TRAEs and recorded on the appropriate eCRF:

- Event name (diagnosis preferred, if unknown, record the signs/symptoms)
- Onset date and end date
- Maximum intensity (severity)
- Seriousness
- Action taken regarding study device
- Corrective treatment, if given
- Outcome
- Investigator assessment of causality

110.4.1.3 Serious Adverse Events

All AEs will be assessed as either serious or non-serious.

An SAE is defined as any untoward medical occurrence that at any dose:

- Results in death
- Is immediately life threatening, (the term "life threatening" in the definition of "serious" refers to an event in which the subject is at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization for elective surgery for a Baseline condition is not considered an AE)
- Results in persistent or significant disability/incapacity (permanent or substantial disruption of a person's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect
- Is a medically important event that may not be immediately life threatening or result in death or hospitalization but may jeopardize the subject and may require medical or surgical intervention to prevent one of the above listed outcomes. Examples of such events include, but are not limited to, allergic bronchospasm requiring intensive treatment in an emergency room or at home; blood dyscrasias or convulsions that do not result in inpatient hospitalization.

Note: A spontaneous abortion will be considered an SAE and must be reported per Reporting of SAEs under Section 10.4.1.6.

110.4.1.4 Assessment of Severity

The severity assigned to an AE should be determined by the maximum severity of the AE. The categories described below should be used to estimate the severity of AEs:

- **Mild:** Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required
- **Moderate:** Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required
- **Severe:** Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization or prolongation of current hospitalization

possible; may be incapacitating or life threatening

110.4.1.5 Assessment of Causality

The PI should assess the relationship of the AE to the study device as either "Related" or "Not Related". The following should be considered when assessing AE causality:

- **Related:** There is at least a reasonable possibility that the AE/SAE is related to the study device. Reasonable possibility means that there is evidence to suggest a causal relationship between the study device and the AE.
- **Not Related:** There is little or no reasonable possibility that the AE/SAE is related to the study device. This assessment implies that the AE/SAE has little or no temporal relationship to the study device and/or a more likely or certain alternative etiology exists.

110.4.1.6 Reporting of Serious Adverse Events

Adverse events classified as "serious" require expeditious handling and reporting to ethica CRO within 24 hours of investigational center notification.

All SAEs, whether related or unrelated to study device, must be immediately reported to the ethica CRO Clinical Project Manager (or designate) within 24 hours of the PI's awareness of the event. All SAEs must be reported via confirmed facsimile or email transmission and must be submitted on a written SAE report form signed by the PI within 24 hours of the PI's awareness of the event.

PIs should not wait to receive additional information to fully document the event before notifying ethica CRO of an SAE. If only limited information is initially available, follow-up reports are required. Additional relevant information such as hospital records and autopsy reports should be provided to the Sponsor as soon as they are available.

The PI should take all appropriate measures to ensure the safety of the subjects, notably he/she should follow a subject with an SAE until the event has resolved or the condition has stabilized. This may imply that follow-up will continue after the subject has left the study, and that additional investigations may be requested by the Sponsor. When an SAE persists at the end of the study, the PI will conduct follow-up contacts with the subject until the PI/Sponsor agree the event is satisfactorily resolved and/or stabilized.

110.4.1.7 Pregnancy

During the study, all female subjects of childbearing potential should be instructed to contact the PI immediately if they suspect they might be pregnant (e.g., missed or late menstrual period).

If a subject or PI suspects that the subject may be pregnant prior to study enrolment, the study device must be withheld until the results of laboratory pregnancy testing are available. If pregnancy is confirmed, the subject must not receive study device and must not be enrolled in the study.

If pregnancy is suspected while the subject is receiving study device, the study device must immediately be withheld until the result of pregnancy testing is known. If pregnancy is confirmed, the study device will be permanently discontinued, and the subject will be followed until the pregnancy comes to term.

All confirmed pregnancies must be reported via confirmed facsimile or email transmission and must be submitted on an Unanticipated Problems Reporting Form within 24 hours of the PI's

awareness of the pregnancy using the same reporting as procedure for an SAE under Section 10.4.1.6.

111 STATISTICS

There is no inferential statistical testing conducted for this study. Descriptive data summaries will be prepared for all outcome variables.

For categorical parameters, the number and percentage of subjects/observations in each category will be presented. The denominator will be based on the number of subjects/observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n (number of subjects or observations), mean, standard deviation, median, and range. Two-sided 95% CIs will be provided for all study outcomes.

111.1 Sample Size Determination

Approximately 150 subjects will be enrolled. This is a POC study and a formal sample size justification is not provided for this study. It is the opinion of the Sponsor that a total of 150 subjects will be sufficient to achieve the objective of the study.

111.2 Assessment of Safety

111.2.1 Adverse Events

All TRAEs occurring during the study will be recorded and classified on the basis of MedDRA terminology. Descriptions of TRAEs will include the date of onset, the date the TRAE ended, the severity of the TRAE, the action taken regarding study medication usage, the action taken to treat the TRAE, and the outcome. All reported TRAEs will be summarized by the number of subjects reporting AEs, system organ class, severity, and seriousness.

111.3 Analysis Populations

111.3.1 Intent-to-Treat (ITT) Population

The modified Intent-to-Treat (mITT) Population is defined as all subjects who were enrolled and received at least one application with the study device. The mITT Population will be used for analyses of safety and effectiveness endpoints.

111.3.2 Per-Protocol (PP) Population

A Per-Protocol (PP) Population will neither be defined nor analyzed.

111.3.3 Subject Disposition

A tabulation of subject disposition will be provided which will include the numbers of subjects who enter, complete, and discontinue the study. The reasons for discontinuation will be included.

111.3.4 Protocol Deviations and Violations

All protocol deviations and violations will be reported to the Sponsor and recorded throughout the study. A tabulation of protocol deviations will be included in the final study report.

111.3.5 Missing Data Imputations

Data will be analyzed as observed; no imputations will be made for missing data.

111.3.6 Statistical Hypothesis Testing and Control of Multiplicity

Not Applicable.

111.3.7 Interim Analyses

An interim analysis will be conducted after approximately 125 injections (projected to be 50 to 65 participants). As this is a proof-of-concept study, no statistical or sample size adjustments are applicable.

112 QUALITY CONTROL AND QUALITY ASSURANCE

112.1 Study Monitoring

An initiation webinar will be conducted with the PI and study coordinator(s) by Sponsor and/or its designee. During this meeting, an extensive review and discussion of the protocol, all study procedures, source documents, and CRFs will be conducted. Evaluation scales will be reviewed extensively.

The Clinical Project Manager(s) and Clinical Trial Associate(s) will be trained prior to study initiation.

The conduct of the study will be closely monitored by the Sponsor (or designate) following GCP guidelines. The reports of these verifications will also be archived with the study report. In addition, inspections or on-site audits may be carried out by local and/or federal authorities. The PIs will allow the Sponsor's representatives and any regulatory agency to examine all study records, corresponding subject medical records, clinical dispensing records and storage area, and any other documents considered source documentation. The PIs agree to assist the representative, if required.

112.2 Audits and Inspections

The study will be conducted under the Sponsorship of the Sponsor in conformation with all appropriate local and federal regulations, as well as ICH guidelines.

112.3 Protocol Deviations

The PIs must read the protocol thoroughly and must follow the instructions exactly.

A deviation from the protocol is an unintended and/or unanticipated departure from the procedures and/or processes approved by the Sponsor and the IRB and agreed to by the PI. Deviations usually have an impact on individual subjects or a small group of subjects and do not involve inclusion/exclusion or tolerability and cosmetic endpoint criteria.

A protocol violation occurs when there is non-adherence to the protocol that results in a significant, additional risk to the subject, when the subject or PI has failed to adhere to significant protocol requirements (inclusion/exclusion criteria) and the subject was enrolled without prior Sponsor approval, or when there is non-adherence to ICH GCP guidelines.

The issue of noncompliance may be either on the part of the subject, the PI, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

All protocol deviations and violations must be addressed in study subject source documents. A completed copy of the ethica CRO Inc. Protocol Deviation Form must be maintained in the regulatory file, as well as in the subject's source document. Protocol deviations must be sent to the IRB per its guidelines.

113 ETHICS AND ADMINISTRATIVE ISSUES

113.1 Ethical Conduct of the Study

This study will be conducted in accordance with the ethical principles originating from the Declaration of Helsinki, ICH guidelines, GCP, and in compliance with local regulatory requirements. The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of GCP.

113.2 Ethics Review

The study protocol, informed consent form and other information to subjects, and all appropriate amendments will be reviewed and approved by an Institutional Review Board (IRB). A signed and dated notification of the IRB approval will be provided to the Sponsor and PI prior to study initiation. The name and occupation of the chairman and members of the IRB will be supplied to the Sponsor to the extent allowable by the IRB. The PI will provide required progress reports and report all SAEs to the IRB as required by the IRB.

113.3 Written Informed Consent

This study will be conducted in compliance with 21 CFR Part 50 for informed consent. The subject's willingness to participate in the study will be documented in writing on a consent form, which will be signed by the subject with the date and time of that signature indicated.

The study coordinator will obtain written informed consent from each subject before any procedures or assessments are done and after the aims, methods, anticipated benefits, potential hazards, compensation and/or honoraria, and insurance arrangements in force are explained. It will also be explained to the subject that they are free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment. The Investigator will be available to respond as needed to questions raised by the participant.

Written and/or oral information about the study in a language understandable by the subject will be given to all subjects. The subjects will be given the opportunity to discuss the procedure, risks, benefits, alternative therapies and the study requirements with the Investigator (or qualified designee) and have any and all questions answered to the subject's satisfaction.

The site will keep the original consent forms and copies will be given to the subjects.

113.4 Subject Data Protections

Subject data will be protected by ensuring that no captured data contain subject names, addresses, telephone numbers, email addresses, or other personally identifying information will be included in the study datasets. Subjects' email addresses and phone numbers will entered into the Appiell app and will be used for communication purposes and app functionality; however, email addresses and phone numbers will not be included in the study datasets and will be purged from the system at study completion.

It is acknowledged that subject initials, demographics (including birthdates), medical histories, and prior concomitant medication uses. Other than where necessary to meet regulatory requirements, all data collected in this study will be presented in tabulated (i.e., aggregate) form and listings containing information that could be used to identify an individual subject will not be included in any public disclosures of the study data or the study results.

As part of the study database, study data will be stored at Equinix and Amazon Web Services facilities in Germany and Ireland that are SOC 1, SOC 2, ISO 27001, and FISMA examined and certified. Security monitoring includes biometric scanning protocols, continuous surveillance, and 24x7 production environment management. Data privacy complies with Canadian and US standards, as well as the European Union's General Data Protection Regulation (GDPR).

The study database utilizes encryption to safeguard data and all data is durably stored with National Institute of Standards and Technology (NIST) approved ciphers, transport layer security (TLS) technology, and AES 256-bit at-rest encryption.

113.5 Data Monitoring Committee

Not applicable.

113.6 Investigator Obligation

The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of Good Clinical Practice (GCP).

113.7 Changes to the Protocol

The PIs must read the protocol thoroughly and must follow the instructions exactly. Whenever possible, any planned deviations should be agreed to by prior discussion between the Sponsor and the PI, with appropriate documentation of Sponsor approval prior to effecting the changes agreed upon. Any amendment to the protocol containing major modifications (particularly if it may involve an increased risk to the subjects) will be approved by the IRB before it may be implemented. No change in the conduct of the study can be instituted without written approval from the Sponsor.

113.8 Confidentiality Regarding Study Subjects

All the data furnished to the PI and his/her staff and all data obtained through this protocol will be regarded as confidential and proprietary in nature and will not be disclosed to any third party without written consent from the Sponsor.

113.9 Reporting and Publication of Results

ACOM Labs, Inc., as the Sponsor, has a proprietary interest in this study. Authorship and manuscript composition will reflect joint between the PI and ACOM Labs, Inc. personnel.

All information, including but not limited to information regarding the study device or the Sponsor's operations supplied by the Sponsor to the PI and not previously published, along with any data generated as a result of this study are considered confidential and remain the sole property of the Sponsor. The PI agrees to maintain this information in confidence and will use the information only to perform the study.

The Sponsor or its designee is responsible for publicly registering this study on http://www.clinicaltrials.gov/ prior to initiating enrolment.

113.10 Financing and Insurance

A separate financial agreement (Clinical Study Agreement) will be made between the Sponsor and the PI at each site. ACOM Labs, Inc. will procure and maintain for the duration of the study a policy of insurance covering its liabilities in the conduct thereof. The certificate of insurance will be provided upon request.

114 APPENDICES

Appendix A: Protocol Version History
Appendix B: Instructions for Use of Photography App
Appendix C: Instructions for Self-Injection

APPENDIX A: PROTOCOL VERSION HISTORY

Version and Date	Description
v.1.0; 31-Jan-2023	*Final Protocol*

APPENDIX B: INSTRUCTIONS FOR USE OF PHOTOGRAPHY APP

Participation in this study requires use of a smartphone app named "Appiell". Participants will be provided instructions and trained on the following:

1. Download Appiell app from App store or Google Play
2. Create account using the email address you provided to the clinical study team
3. Complete introductory questionnaire
4. Complete Baseline visit within app by taking photos
   a. Click "take more photos" button within app
   b. Follow instruction guide within app to prepare for photographs, including setting up study-provided ring light and placing numbered stickers adjacent to each lesion.
   c. Take 3 full face photographs by fitting face in frame included in app
   d. Take 1-3 close-up "lesion specific" photographs by fitting acne spot selected for injection within circle frame on app.
5. Following injection and for each follow-up timepoint, complete the in-app visit by following the instructions in app for photograph collection.

ADDITIONAL INFORMATION

Authentication:

- Each time a participant logs in to the Appiell app, he/she requires a One Time Password (OTP) that is sent to the participant's email address.

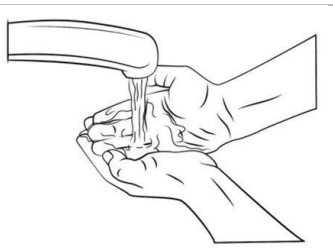
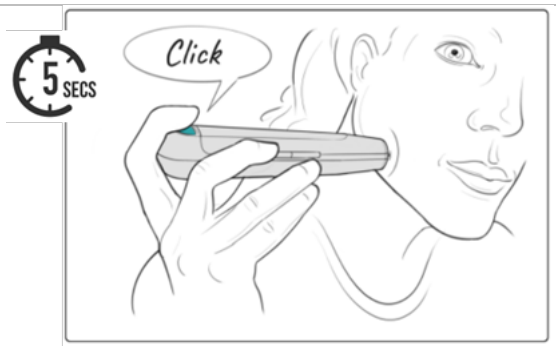
Data Security:

- Source passwords are not contained in the database
- The platform used an advanced PostgreSQL database that allows full data encryption.
- The database server only accepts requests from known servers and a known port number (i.e., the platform's mid-tier servers); a standard practice for high security setups and extremely difficult to hack.

APPENDIX C: INSTRUCTIONS FOR SELF-INJECTION

Important Information to Know Before Use:

1. **Do not** share any components of the intradermal injection system with others. The entire injection system is for single patient use only.
2. **Do not** reuse any needle assembly for more than one injection
3. **Do not** use any system components that have been dropped or appear damaged.
4. The Injection Assistance Device will need to be manually "reset" after or prior to each injection. Clinical staff will reset the device for you prior to each injection.

1. Clean hands	
2. Clean injection site identified by the clinical team ***Do not*** *inject into the eyes, lips, nostrils, ears, or any other body orifices.*	
3. Administer the Injection **Step 1:** Place the device needle end against the injection site so the Button is furthest from the site, as shown. **Step 2:** Press the Activation Button to initiate the dosing sequence, you will hear a click. **Step 3:** Hold and Wait 5 seconds. **THEN** ● Remove device from injection site. ● **Do not** point the intradermal injection system towards your eyes at any time.	
4. Prepare for additional injections ● Return study device to clinical team for device reset and preparation for subsequent injection ● Repeat above process beginning at step 2 for up to 3 injections total.	